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correlation between maternal and fetal plasma levels of glucose and free fatty acids .

correlation coefficients have been determined between the levels of glucose and ffa in maternal and fetal plasma collected at delivery .

significant correlations were obtained between the maternal and fetal glucose levels and the maternal and fetal ffa levels . from the size of the correlation coefficients and the slopes of regression lines it appears that the fetal plasma glucose level at delivery is very strongly dependent upon the maternal level whereas the fetal ffa level at delivery is only slightly dependent upon the maternal level .

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changes of the nucleic acid and phospholipid levels of the livers in the course of fetal and postnatal development .

we have followed the evolution of dna, rna and pl in the livers of rat foeti removed between the fifteenth and the twenty-first day of gestation and of young rats newly-born or at weaning . we can observe the following

facts.. 1. dna concentration is 1100 ug p on the 15th day, it decreases from the 19th day until it reaches a value of 280 ug 5 days after weaning .

2. rna concentration is 1400 ug p on the 15th day and decreases to 820 during the same period .

3. pl concentration is low on the 15th day and during foetal life (700 ug) and increases abruptly at birth .

4. the ratios rna cyto/dna and pl cyto/dna increase regularly from the

18th day of foetal life .

5. nuclear rna and pl contents are very high throughout the development .

6. these results enable us to characterize three stages in the development of the rat liver.. - from the 15th day to the 18th day of foetal life.. stage of growth through hyperplasia without hypertrophy,
- from the 19th day of foetal life to the 3rd day of post-natal life,, stage of cellular reorganisation,
- after the 3rd day of post-natal life.. stage of growth through hyperplasia and hypertrophy .

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surfactant in fetal lamb tracheal fluid .

lambs delivered by cesarean section with intact fetal circulation have a fluid filling the trachea . analysis revealed that this fluid contained material high in surface activity in lambs delivered near term, but less surface activity in premature lambs .

administration of 10 per cent oxygen to the ewe for 1 hour prior to delivery did not alter the surfactant properties of the fetal tracheal fluid .

two analyses of the fetal tracheal fluid revealed it to contain 146 and 198 mg. of lipid per 100 ml., 30 to 40 per cent of which was phospholipid, part of the active component of surfactant .

the investigations reported here offer a model for further research into possible intrauterine factors in the pathogenesis of hyaline membrane disease .

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placental and cord blood lipids.. comparison in a set of double ovum twins, a stillborn and a live-born .

1. determinations of phospholipid, total and free cholesterol, triglyceride and nefa have been made on placental tissue and cord blood in a set of double ovum twins, one stillborn and one live-born .

2. similarities occurred in all fractions studied except the cord blood triglyceride and nefa levels .

3. the serum of the stillborn infant contained one-third as much triglyceride and $2\frac{1}{2}$ times as much nefa as did the live-born infant .

4. the phospholipid content and the total lipid content of the stillbirth placenta were the highest studied in this laboratory which includes determinations on 26 live births .

5. the suggestion is made that increased lipoprotein lipase activity in the cord blood may accompany intrauterine fetal death .

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free fatty acid concentration in maternal plasma and fetal body fat content .

subcutaneous injection of 200 u.s.p. units of heparin into female sprague-dawley rats produced large and sustained elevations of plasma free fatty acids but no significant change in blood glucose . a group of pregnant rats received such injections of heparin 3 times daily throughout pregnancy . the fetuses from mothers of this group, at $19\frac{1}{2}$ and $21\frac{1}{2}$ days of gestation, had significantly more body fat than the fetuses from uninjected mothers . the hypothesis is presented that the maternal free fatty acid concentration in part determines fetal fat

accumulation . it is proposed that the body composition changes noted in babies of mothers with diabetes might thus be ascribed to abnormally high maternal plasma free fatty acid concentrations .

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the concentration of non-esterified fatty acids in maternal and fetal plasma in intact, alloxan-diabetic and x-ray-irradiated rats .

determinations of the non-esterified fatty acids in the plasma of pregnant rats showed that there do not exist any increases in the concentrations depending on pregnancy during the period from the 20th - 22nd day of pregnancy . in the fetal plasma the concentrations of non-esterified fatty acids only amounted to 40 - 50 per cent of the maternal values .

with alloxan diabetes produced 2 days prior to the test the concentration in the maternal plasma increased three- to fivefold, while at the same time a significant rise was absent in fetal plasma with slightly increased average values .

whole-body x-ray exposures (dose.. 400r, dose output.. 40r/min) of non-pregnant female and of pregnant rats beginning on the 17th day of pregnancy did not result in any changes of the concentration of non-esterified fatty acids immediately after irradiation .

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lipid metabolism in toxemia and normal pregnancy .

the amount and fatty acid composition of total lipid extract from serum were examined in normal pregnant women in the first, second, and third trimesters, and early postpartum period, and in patients with mild

and severe preeclampsia and with essential hypertension . placentas at term were also examined for total lipid and its fatty acid composition . in the normal women, total serum lipid increased during pregnancy . the rise was less pronounced in those with preeclampsia or hypertension . serum palmitate was mildly but significantly elevated in preeclampsia . total lipid and arachidonic acid were elevated in the placentas of preeclamptic women . the findings are compared with those obtained from animals developing eclampsia on an experimental basis .

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essential fatty acids and acids with trans-configuration in the subcutaneous and visceral fat of the newborn .

we made an investigation of the subcutaneous and visceral fat in the newborn . we estimated the contents of linolic and linolenic acid and of acids with trans-configuration spectrophotometrically .

we were able to show the penetration of these acids through the placental barrier . the essential fatty acid contents of fat in the newborn is low . in immature ones about 7-14 g, there is a rising trend.

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acetoacetate formation by livers from human fetuses aged 8-17 weeks .

slices and homogenates from livers of human fetuses aged 8-17 weeks have a low rate of acetoacetate formation which can be raised by addition of acetate or octanoate to the incubation medium . it was not possible to demonstrate acetoacetate formation by isolated liver mitochondria from 17-week-old fetuses, probably because mitochondria are injured during isolation .

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changes in blood glucose and non-esterified fatty acids in the foetal and newborn lamb after injection of adrenaline .

changes in blood glucose and non-esterified fatty acids after intravenous adrenaline were measured in foetal, newborn and adult sheep in the foetus and immediately after birth there was very little increase in either blood glucose or non-esterified fatty acids after adrenaline . the response of blood glucose to adrenaline had reached adult levels at twenty-four hours of age . the response of non-esterified fatty acids to adrenaline increased gradually over the first week .

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electron-microscopic observations on transference of fat through the human placenta .

from the results of our previous and present studies on the transportation of fat through the human placenta by means of electron microscopy, we obtained the following conclusions .

1) neutral fat can permeate through the human placenta without dissociation .

2) almost all processes of fat permeation seem to be due to the biological activity . pinocytosis is most representative, but the authors newly found several facts such as dissolution-like change in the basement membrane and transport via the stroma cell . the authors believe that these results will bring a clue to explain the mechanism of biological transportation of materials through the placenta .

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the content of phosphatides, triglycerides and cholesterol in placentas, maternal, fetal and new-born liver of the white rat .

thin-layer-chromatographic examinations in the maternal rat liver showed different rise of the triglycerides and a significant increase of the esterified cholesterol, however, no striking changes in the content of free cholesterol and lipid phosphorus with the fractions examined (lecithin, colamine cephalin, sphingomyelin and lysolecithin) .

as compared to the liver of adult rats, the fetal liver contains a little less than 50 per cent lipid phosphorus . the difference is conditioned by the concentrations of lecithin, and colamine cephalin . on the 19th day the content of triglycerides is lower than in the mother rat . referred to the dry weight, there results a decrease of all phosphatide fractions, as well as of the free cholesterol and a slight rise of the triglycerides from the 19th to the 22nd day .

the rise of the phosphatide concentrations to the values of adult rats occurs immediately after birth under the influence of milk food, which, moreover, leads to a considerable increase of the triglyceride values . phospholipid- and triglyceride concentrations of the placenta correspond to those of the fetal liver . solely the content of free cholesterol is higher at the end of pregnancy . the content of triglyceride drops towards the 22nd day .

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analysis of mammalian lens proteins by electrophoresis .

lens proteins of different mammalian species were analyzed by two-dimensional starch gel electrophoresis . the number of fractions

detected by this means varied from 11-20 . α -crystallin was resolved into two to three components, β -crystallin into 5-11, and γ -crystallin into three to five components . this technique provides a sensitive method for the fractionation of lens proteins and for analyzing species differences .

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an autoradiographic study on cell migration in the eye lens epithelium from normal and alloxan diabetic rats .

lenses from normal and alloxan diabetic rats with and without cataract were investigated by autoradiography 4 hours, 4 days and 8 days after an intraperitoneal injection of ^3H -thymidine (0.4 $\mu\text{C/g}$ body weight) . the rats were made diabetic 8 days prior to the injection of thymidine at an age of 4 weeks . the position of labelled nuclei of the lens epithelium was noted and their grain numbers counted . the diabetic rats had a lower frequency of labelled nuclei than the controls but after 4 hours their grain counts were equal . frequency diagrams of labelled nuclei are given for each of the three experimental periods . a predominant peak appears after 4 hours at a distance of 30-60 cells in front of the beginning of the nuclear arc . a successive shift towards this area was observed for the longer experimental periods . the shift of the peaks was more restricted in the diabetic animals . this result may best be interpreted as an effect of an increased time of cell generation .

as an appendix a histotechnique for the eye lens is given in collaboration with mrs. gertraude moewis .

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lens development.. the differentiation of embryonic chick lens

epithelial cells in vitro and in vivo .

the behavior of lens epithelial cells from six-day chick embryos was studied in three different experimental situations.. (a) explantation into several different fluid culture media, (b) explantation followed by reimplantation into lensectomized embryonic eyes, and (c) explantation followed by reimplantation into the embryonic coelomic cavity .

specimens were examined histologically, and the total volume of the lens material of each specimen was determined from the planimetry of serial sections . the results were interpreted as

follows.. 1. with a small amount of protein supplement in the culture medium, embryonic lens epithelial cells are capable of a limited amount of independent cytodifferentiation . without protein supplement they fail to undergo any fiber formation .

2. when returned to the eye environment, cultured epithelial explants will respond with a resumption of growth, with further cellular differentiation, and with at least some of the morphogenetic changes necessary to form a lens . the embryonic coelom will not support these responses .

3. the initiation of the formation of lens fibers is not sufficient for their complete autonomous maturation .

4. the internal architecture of the developing lens is not the only determinant of its overall shape .

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treatment of active chronic hepatitis and lupoid hepatitis with 6-mercaptopurine and azothioprine .

6-mercaptopurine or azathioprine ('imuran') was used successfully in 3 patients with active chronic hepatitis and 2 with lupoid hepatitis, for periods up to 1 year . these drugs allowed modification and even abolition of discomforting corticosteroid regimes . their action in chronic hepatitis may be analogous to their anti-immune action in suppressing homograft rejection .

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treatment of collagen diseases with cytostatics .

22 patients with collagen diseases and 3 patients with other immunological diseases were treated with the cytostatic antimetabolites ('purinethol') 6-mercaptopurine and ('imuran') azathioprine for an average period of four months (range one to eleven months) . improvement was obtained in 17 patients,. and, in 20 out of 22 patients who had been on long-term glucocorticoid medication, the steroid therapy could be permanently discontinued . serious complications occurred, in the form of two deaths from pancytopenia and sepsis . the treatment requires careful supervision of the patients, and should only be instituted, on strict indications, when the alternative is long-term glucocorticoid medication .

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bilateral popliteal cysts in a patient with rheumatoid arthritis .

a case of bilateral popliteal cysts and multiple joint subluxations in a patient with rheumatoid arthritis on corticosteroid medication for many years is reported . the effect of long-term corticosteroid therapy on all periarticular connective tissue structure and the relationship of

articular disease and popliteal knee cysts to this therapy have been discussed .

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systemic lupus erythematosus and renal transplantation.. report of two cases .

two cases of systemic lupus erythematosus along with terminal uremia secondary to lupus nephritis are presented . both patients were treated with renal hemodialysis and transplantation . certain mechanical, infectious, and immunologic problems were responsible for their death . there was no evidence of resurgence of lupus erythematosus in either patient, and the transplanted kidneys did not show evidence of lupus nephritis . renal transplantation should be considered as a last resort in treatment of patients with terminal lupus nephritis .

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arteritis and localised periosteal new bone formation .

1. three patients with localised periosteal new bone formation associated with periosteal arteritis and other evidence of systemic lupus erythematosus are described .

2. systemic steroid therapy was valuable in the management of this condition .

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fine structure of subtilis phage sp-50 .

some structural details and anomalous forms of subtilis phage sp-50 are described .

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genetic transcription during morphogenesis .

messenger rna's from bacillus subtilis undergoing sporulation, germination, or step-down transition have been characterized and compared . hybrid competition experiments indicate that these messengers are derived from distinct genetic loci . the results are consistent with the hypothesis that differential transcription of the genome occurs during morphogenesis . the data also complement previously observed changes in morphology and enzymatic activity in sporulating bacteria .

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renal amyloidosis a clinicopathological study .

the clinical and histopathological data from 40 cases of renal amyloidosis diagnosed by percutaneous renal biopsy are presented .

twenty-two cases were labelled as 'secondary' amyloidosis, as definite aetiological factors responsible for renal amyloidosis could be discovered . the predisposing disease states leading to amyloid deposits in the kidney in the order of frequency were fibrocaseous pulmonary tuberculosis, bronchiectasis, lung abscess, and ileocaecal tuberculosis five cases were labelled as suspected 'primary' amyloidosis as a definite evidence of the predisposing disease could not be obtained although the skiagram of chest revealed minimal healed foci . no cause could be determined in thirteen cases, which were, therefore, labelled as 'primary' amyloidosis .

albuminuria was a constant feature in all the cases and 32 cases presented as nephrotic syndrome . the rest of the cases presented with

hypertension or renal failure in addition to albuminuria .

the ancillary procedure, viz., congo-red test, gingival and liver biopsies proved to be of limited value in the diagnosis of renal amyloidosis .

the importance of percutaneous renal biopsy as a diagnostic tool has been emphasised .

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idiopathic autoimmune hemolytic anemia and idiopathic thrombocytopenic purpura associated with diffuse hypergammaglobulinemia, amyloidosis, hypoalbuminemia and plasmacytosis .

a case is reported of a sixty-nine year old woman with severe, idiopathic, autoimmune hemolytic anemia which was initially controlled by splenectomy . a relapse associated with the development of severe, autoimmune, thrombocytopenic purpura failed to respond to large doses of prednisone, but was controlled to a variable degree with imuran .

associated features included diffuse hypergammaglobulinemia, excessive gamma-u proteins in the urine, idiopathic hypoalbuminemia with a greatly reduced total exchangeable albumin pool, amyloidosis in the spleen and other organs, and diffuse plasmacytosis of the bone marrow, lymph nodes, and thoracic and peritoneal fat . these features and their interrelationships are discussed . there was no deficiency in the synthesis of specific neutralizing antibodies against viruses, indicating that a qualitative immune deficiency did not exist .

the frequency of occurrence of thrombocytopenic purpura in such a case is discussed, as is the prognosis . the mechanism of action of antimetabolites in inducing a remission in autoimmune hemolytic anemia,

as well as the etiology of the disease, is reviewed .

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corticosteroid therapy of amyloid nephrotic syndrome .

the results of treatment with prolonged adrenal corticosteroids in 26 adults with amyloid nephrotic syndrome are presented . eight subjects were observed in this series, and 18 additional cases were summarized from the literature . twenty-two of the patients were male and four were female . the diagnosis was established by renal biopsy in 19 instances and by autopsy in the others, with 18 patients considered to have primary amyloidosis and 8, secondary amyloidosis .

the majority of the subjects died in renal failure with an average survival after onset of the disease of 17.6 months . the renal disease was indistinguishable from that seen in other forms of the nephrotic syndrome, with the possible exceptions of (a) a high incidence of purpuric skin lesions, (b) a low or negligible incidence of hypertension (at times actual hypotension was prominent), and (c) a rapid and inexorable progression of azotemia despite persistence of the clinical and biochemical characteristics of the nephrotic syndrome . amyloidosis was found by percutaneous renal biopsy in 12 per cent of 83 adults with the nephrotic syndrome .

corticosteroids did not appear to affect the progress of the disease and were neither beneficial nor detrimental . in view of the high incidence of deleterious side effects of prolonged corticosteroid therapy and the availability of potent diuretic agents which may be helpful in relieving edema in this disorder, it is felt that corticosteroids are contraindicated in the treatment of amyloid

nephrotic syndrome .

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renal amyloidosis.. a biopsy study .

the relationship of the amount of amyloid deposition in the kidney to the clinical picture is reviewed in 14 cases of renal amyloidosis diagnosed by renal biopsy . the large percentage of patients who had the nephrotic syndrome (11 patients) probably reflects the criteria for renal biopsy at this institution . the etiology of the amyloid deposition did not seem to be clearly correlated with either the amount of amyloid deposition in the kidney or the severity of the clinical renal disease . all patients had deposits in the glomerulus, and the heavier the deposition the severer the renal disease . of 7 patients who had biopsy of the bone marrow, all had abnormal types or numbers of plasma cells . the age range in primary amyloidosis appeared to be about the same as that in amyloidosis secondary to myeloma . amyloidosis should be suspected in patients with proteinuria, the nephrotic syndrome, or renal failure .

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amyloid goitre a case report .

a case of amyloid goitre in an indian female, aged 27 years, occurring as a sequelae to pulmonary tuberculosis, is reported .

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amyloid.. starch gel electrophoretic analysis of some proteins extracted from amyloid .

proteins extracted by strong urea from washed tissue of patients with amyloidosis secondary to several diseases or associated with familial mediterranean fever have common major electrophoretic components . in hearts of primary amyloidosis one component in common with the secondary amyloid may be present . however, primary amyloid is much more difficult to dissolve and does not regularly give the components observed when the secondary amyloid is extracted . the big question remains as to what constituent or constituents comprise the fibrils now known to be a part of amyloid .

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selectivity of protein excretion in patients with the nephrotic syndrome.

with a gel diffusion precipitin technique and commercially prepared antisera, urine/plasma ratios of specific proteins were determined . individual protein clearances, expressed as a percentage of transferrin clearance, were plotted as ordinates against respective molecular weights on a log-log graph . a straight line was evident graphically, its constants were estimated by the method of least squares, and the slope, expressed as α , was determined . the slope of the line may be said to express the degree of glomerular selectivity to protein excretion . sixty-five determinations were performed in 48 patients . 45 satisfying the usual criteria of the nephrotic syndrome .

1) those patients with primary renal disease and the nephrotic syndrome who displayed high selectivity types of proteinuria (greater than the average for the group + 1 sd) usually respond initially to steroid therapy, regardless of the acute or subacute glomerular changes observed on renal biopsy .

2) those patients with chronic renal disease and the nephrotic syndrome display an average and frequently a low selectivity type of proteinuria .

3) there appears to be no characteristic type of selectivity for a given pathologic group of patients with the nephrotic syndrome .

4) the degree of selective protein excretion is not related to the total daily amount of protein being excreted at any one time and remains fairly constant despite fluctuation in the amount of protein being excreted .

5) there is a slight correlation of borderline significance between the degree of selective protein excretion and the duration of the disease, and the initial para-aminohippuric acid clearance .

6) a statistically significant correlation exists between the initial blood urea nitrogen or inulin clearance and the selectivity type of protein excretion . those patients who were not azotemic and had initially near-normal inulin clearances had an average selectivity type or better .

7) it is suggested that if the adult patient is initially azotemic and has a grossly abnormal inulin clearance, response to therapy is unlikely, whereas if the blood urea nitrogen is normal and the inulin clearance is near normal, response to therapy cannot be predicted with any degree of accuracy . further studies of adult patients with the nephrotic syndrome are required to substantiate this premise .

.I 30

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some aspects of haemostasis after open-heart surgery .

synopsis in two groups of patients undergoing extracorporeal

circulation with hypothermia, changes were found in the coagulation mechanism which were probably due to the dosage of polybrene administered .

the role of heparin and polybrene and the concept of activation of the coagulation mechanism in the production of bleeding after perfusion are discussed .

.I 31

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a case of interventricular septal defect with dextrocardia and situs inversus treated by surgery .

a case of interventricular septal defect associated with situs inversus and dextrocardia in twenty year old male patient was presented along with discussion on three types of dextrocardial complexes and with emphasis on the rarity of occurrence of the intracardiac anomalies in true /mirror-image/ dextrocardia with total situs inversus . a comment was also made on kartagener's syndrome which was excluded by appropriate radiographic procedures in this case .

the closure of the interventricular septal defect with extracorporeal circulation was successfully performed under moderate hypothermia .

.I 32

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excretion patterns of urinary metabolites of estradiol-4-c¹⁴ in postmenopausal women with benign and malignant disease of the breast .

a study of the excretion patterns of the urinary metabolites of estradiol-4-c¹⁴ administered to a group of 43 postmenopausal women, 38 with advanced mammary carcinoma prior to endocrine therapy and 5 with benign mammary dysplasia, is reported . a chromatographic method was

employed for the determination of estradiol, estrone, and estriol and other estrogen metabolites . the urinary excretion pattern is defined by (a) the extent of excretion of isotope in each of 3 successive 24-hr. collection periods, (b) the percentage of the urinary radiometabolites enzymatically hydrolyzed, (c) the relative concentration of the several metabolites in the hydrolyzed fraction . wide subject-to-subject variations were found . the metabolites other than estradiol, estrone, and estriol comprised a large portion of the total estrogens excreted . a significantly lower amount of estradiol was noted in the group of women with mammary carcinoma as compared to the amount found in the group of women with benign mammary dysplasia, suggesting that the former group metabolizes more rapidly the administered estradiol . although the excretion patterns of patients who failed to respond to estrogen treatment (nonresponders) differed the greatest from the patterns associated with benign disease, distinctive patterns of the urinary excretion of isotopic estrogens which allowed a statistically significant or clinically useful separation between responders and nonresponders to subsequent estrogen therapy were not discovered .

.I 33

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the localizing significance of limited simultaneous visual form perception .

a patient presenting with an isolated /spelling dyslexia/ and impairment in picture interpretation (simultanagnosia) was shown by tachistoscopic studies to have a pathological limitation of simultaneous form perception . at autopsy a localized lesion was found within the inferior part of the left occipital lobe .

these findings are discussed in relation to the problem of the disorder of function underlying /agnosic alexia/ .

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visual anosognosia in cortical blindness anton's symptom .

denial of blindness in a case of bilateral hemianopia is presented to acquaint ophthalmologists with this symptom which is well-known to neurologists but is rarely seen by ophthalmologists .

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the development of social attachments in infancy .

this report is devoted to the formation and development of social attachments in infancy . it is suggested that the core of the attachment function is represented by the tendency of the young to seek the proximity of certain other members of the species and that the most suitable operational definition may be found in the behavior of the individual when deprived of such proximity .

the study takes the form of a longitudinal follow-up, in which 60 infants were investigated at four-weekly intervals from the early weeks on up to the end of the first year and again at 18 months of age . with the use of an attachment scale, based on seven everyday separation situations, the following three main parameters were explored.. the age at onset of specific attachments, the intensity of such attachments, and the number of objects to whom attachments are formed . a measure of fear-of-strangers was also included .

results indicate that the age at onset of specific attachments is generally to be found in the third quarter of the first year, but that

this is preceded by a phase of indiscriminate attachment behavior,. that the intensity of specific attachment increases most in the first month following onset and that thereafter fluctuations occur in individual cases which make long-term prediction difficult,. and that multiplicity of objects can be found in some instances at the very beginning of the specific attachment phase, becoming the rule in most of the remaining cases very soon thereafter . correlations between the attachment variables, as well as with the fear-of-strangers measure, are presented, and an examination is also made of the conditions eliciting protest at proximity loss, of the manner in which protest is expressed, and of the conditions necessary to terminate protest .

individual differences with regard to the three main parameters were explored in a subgroup of 36 infants . a number of variables were examined in relation to these individual differences, and suggestions made regarding the conditions which affect the manifestation of the attachment function .

the data are discussed in relation to four themes which emerged from the findings.. the nature of the attachment function, its developmental origins, its developmental trends, and the influence of the social setting .

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separation anxiety as a cause of early emotional problems in children .

in summary, three cases of disturbed behavior in children have been discussed, with particular emphasis on disturbances in feeding, sleeping, and motility . some of the hypotheses have been presented of why such behavior should develop,. the significance of attachment

behavior and separation anxiety in infants has been particularly stressed . difficulties in mothering care are threatening to the child's sense of security and lead to greater experience of separation anxiety, which may then be reflected in various disturbances or alterations in his behavior . this experience of separation anxiety is the result of early life experience, may reach pathologic proportions, and may account for many later problems in children and adults .

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the production of malignant tumours by nickel in the rat .

powdered metallic nickel when injected intramuscularly into rats produced tumours of striated muscle origin, most of which were very well differentiated .

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studies of nickel carcinogenesis fractionations of nickel in ultracentrifugal supernatants of lung and liver by means of dextran gel chromatography .

chromatographic fractionations have been performed on the ultracentrifugal supernatants of homogenates of rat lung and liver by the use of columns of dextran gel (sephadex g-100) . a major proportion of nickel in these tissue supernatants has been demonstrated to be firmly bound to macromolecular constituents . following acute and chronic inhalation of carcinogenic levels of nickel carbonyl, the predominant increases in the concentrations of nickel have been observed in the macromolecular fractions . these findings are consistent with the previous demonstration of nickel in purified preparations of ribonucleic

acids (rna) from several rat tissues, and with the observation of increased concentrations of nickel in high-molecular weight rna from lung and liver following the inhalation of nickel carbonyl .

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a study of the inhibitory effect of ethylenediaminetetra-acetic acid on the thrombin-fibrinogen reaction .

1. ethylenediaminetetra-acetic acid reversibly inhibits the thrombin-fibrinogen reaction by means of a time-dependent diminution in fibrinogen reactivity .

2. this alteration of fibrinogen is due to some property of the edta molecule in an unchelated form, and is not due to the removal of trace metal ions .

3. possible explanations for this phenomenon are discussed .

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intradermal test using cobalt chloride .

selected groups of patients with cobalt allergy and nickel allergy as well as normal controls were tested intradermally with cobalt chloride in the dilutions 10 to 10 . reactions of the wheal and flare type appear during the first hours and make the 24-hour reading misleading . the papular response to cobalt chloride 10, when read 48 to 96 hours after the injection, appears to be a reliable test for cobalt allergy .

patients with combined nickel-cobalt allergy were excluded from the study, and the question of group reactions is not discussed . nickel allergics give a somewhat stronger reaction than controls to the slightly impure cobalt chloride . it would be preferable if the degree

of purity of the cobalt chloride were ten times greater .

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measurements of nickel in biological materials by atomic absorption spectrometry .

an atomic absorption procedure has been developed which facilitates quantitative measurements of nickel in biological materials, including urine, ribonucleic acids (rna), and serum proteins .

the sensitivity of detection of nickel by the atomic absorption spectrometer (0.10 p.p.m.) was insufficient to permit direct measurements of nickel in normal urine . therefore, it was necessary to employ a dimethylglyoxime extraction procedure to concentrate the nickel, prior to atomic absorption spectrometry .

the coefficients of variation of measurements of nickel in urine and human b- globulins were 6.3 and 5.9 per cent, respectively . the recovery of nickel added to urine averaged 96 per cent, with a range from 94 to 97, and the recovery of nickel added to human b-globulin averaged 101 per cent, with a range from 96 to 104 .

the mean concentration of nickel in 24-hr. collections of urine from 17 normal subjects was 1.8 ug. per 100 ml. (s.d. = 0.8), with a range from 0.4 to 3.1 . the mean urinary excretion of nickel was 19.8 ug. per 24 hr. (s.d. = 10.0), with a range from 7.2 to 37.6 .

the mean concentration of nickel in 5 preparations of ribonucleic acids from ultracentrifugal supernatants of homogenates of rat lung was 48 ug. of ni per gm. of rna, with a range from 34 to 64 . the mean concentration of nickel in 5 preparations of rna from ultracentrifugal supernatants of homogenates of rat liver was 29 ug. of ni per gm. of

rna, with a range from 21 to 39 .

measurements of nickel were performed upon fractions of human serum proteins, prepared by continuous-flow electrophoresis, and by cold-ethanol precipitation . the highest concentrations of nickel were found in preparations of serum b-globulins .

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properties of activity of 5'-nucleotidase in human serum, and applications in diagnosis .

the influence of mg , ni , and l-histidine on purified preparations of bone and intestinal alkaline phosphatases and 5'-nucleotidase, and on various mixtures of these enzymes has been studied . the extent to which these findings can be utilized in the quantitative assay of 5'-nucleotidase in serum has been evaluated . results are presented on the possible utilization of l-histidine in the simultaneous evaluation of serum alkaline phosphatase and 5'-nucleotidase activity .

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some 2-iminoselenazolidin-4-ones and related compounds .

a series of 2-iminoselenazolidin-4-ones, selenazolidine-2,4-diones and some 2-alkylidenehydrazones have been synthesised . wide-range screening for biological activity failed to reveal any compounds of promise .

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the influence of methemoglobinemia on the lethality of some toxic anions, 1. azide .

the time course and extent of the methemoglobinemia induced by

intraperitoneal sodium nitrite and p-aminopropiophenone (papp) have been characterized in female mice . the peak methemoglobin formation (34) is achieved in about 40 minutes . comparable levels from papp (15 mg/kg) are achieved more quickly (between 5 and 10 minutes) but decline more rapidly to normal . both nitrite- and papp-induced methemoglobinemia afford a significant degree of protection against poisoning by sodium azide when administered in an appropriate time sequence . it was not possible under the same circumstances to protect mice against death from fluoride, cyanate, thiocyanate, selenate, or borate, although some prolongation of survival time was seen after fluoride . the formation of the azide-methemoglobin complex has been demonstrated within intact mouse red blood cells, and small amounts of the complex were identified in vivo in an antidotal situation . we think it important that the protective action of methemoglobinemia has been demonstrated to date only against established inhibitors of cytochrome oxidase .

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selenium as a trace element .

an account is given of the discovery of selenium by berzelius and gahn the toxic behaviour of large selenium quantities in soils upon vegetation, animals, and man is surveyed . a review is also given of the role of trace amounts of selenium in the prevention of myopathies in animals . finally, some recent theories on the importance of retinal selenium to vision are mentioned .

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toxicity of inorganic selenium salts to chick embryos .

the effects of selenite and selenate treatment by air cell injection on mortality and growth of 14-day chick embryos during a 64-68 hour period were studied . the LD_{50} for selenite-se was about 0.5 ppm, based on weight of the egg contents, and that for selenate-se about 1.8-2.0 ppm . growth depression was evident from these treatments, but other gross effects were not prominent . the treatment of embryos with selenite and sulfate together caused a greater mortality than treatment with selenite alone .

.I 47

.W

lesions of the islets of langerhans during injections of sodium selenite administered intravenously .

sodium selenite was administered intravenously in rabbits and in dogs repeated injections can lead to the development of a diabetic syndrome in the rabbit .

the histological examination of the pancreas in the poisoned animals (dogs and rabbits) has shown the existence of lesions of the islets of langerhans, mostly of the b cells which lose their granules partly or completely .

these changes seem analogous to the ones produced by alloxan,. these two poisons act at first by inactivating the sh groups, which leads to a deficiency to which the b cells are very sensitive .

.I 48

.W

toxicity of sulfur-35, selenium, and tellurium to avian embryos .

continuous internal irradiation of chick embryos with sulfur-35 administered on the 4th or 8th day of incubation produced abnormalities

similar to those observed in selenium toxicosis of avian embryos . the highest level of sulfur-35 (1600 uc) injected into eggs containing 4-day embryos produced morphological abnormalities more severe than those produced by the same level of radiosulfur administered to 8-day embryos, or by any level of stable selenium tolerated . selenium at levels greater than 30 ug killed all the embryos within 24 hours after injection . nearly 20 times more tellurium than selenium was required to kill all the embryos within 24 hours.. no abnormalities were observed in the tellurium-injected embryos .

.I 49

.W

the effect of selenium on the upper respiratory passages .

results are reported of examination of workers exposed to selenium, with special reference to chronic changes in the respiratory passages . the findings are the same as reported in the literature . we emphasize the occurrence of teleangiectasias on the uvula and on the posterior palatal arcs and on the epiglottis . we describe the occurrence of the first poisoning with selenium xyde in this country . the poisoning healed within a few days under symptomatic treatment . the patient had however to be transferred into another shop owing to frequent symptoms due to toxic effect of selenium . we report also on secondary findings in examination of chronic changes and we emphasize particularly the finding of profesional selenium external otitis .

.I 50

.W

the influence of small selenite doses upon the toxic fatty degeneration of the liver .

sodium selenite (10 ug/kg) manifests a lipotropic effect after toxication of the rat by tetrachlorocarbon . this effect is absent when the selenite dose is increased to 50 ug/kg . the level of the total lipides of the liver after ethionine toxication is not significantly influenced by 10 ug selenite/kg . it is increased by 50 ug selenite/kg.

.I 51

.W

selenium-caused tumours .

in 10 out of 23 heterozygous rats administered 10 mg na seo per 1 kg food (containing 12 protein) and surviving for 18 months, cancer of the liver (with metastases in the lungs) along with sarcoma and adenoma was recorded . in another series of the yet incompleated experiment the animals were fed higher quantities of protein and selenium . toward 14-19 months in three of them sarcoma was noted.. in two sarcoma of the lymphatic nodes, and in one- of the mediastinum .

it is suggested that the changes caused by selenium compounds are to some extent due to their antagonistic relationship with methionine .

.I 52

.W

blood and bone marrow damage caused by drugs .

drug side effects on blood and bone marrow are briefly reviewed . they embrace a wide variety of symptoms and pathogenetic mechanisms, and in recent years study of these effects has made important contributions to our knowledge of the immunology, biochemistry and metabolism of the blood cells .

.I 53

.W

hypothermia.. physiologic effects and clinical application .

a survey of the background, physiologic effects, indications, technique and complications of hypothermia is presented . the application of this technique is straightforward and safe when used at the proper levels with the proper indications .

.I 54

.W

ehrlich ascites tumor cells agglutination.. the interference exerted by epsilonaminocaproic acid (eac) and its acetyl derivative (eaca) .

the activity of epsilon-aminocaproic acid (eac) and of its acetyl derivative (eaca) was studied on antigen-antibody reactions, membrane antigens and immune globulins .

in vitro eac and eaca do not affect immune globulins, but they do alter the membrane antigens of ehrlich ascites tumor cells and inhibit the agglutination reaction induced by a specific antiserum . inhibition is only partially due to the antigenic alteration observed, and it represents more prominently a direct interference at the level of the antigen-antibody reaction .

the membrane antigen alternations induced by the drugs and by nitrogen mustard were compared, taking into account their toxicity.. eac and eaca were found to be much more active and more specific than nitrogen mustard .

.I 55

.W

study on the behavior of tumor tissue in diffusion chambers against penetrating host cells in tumor-resistant rats .

tumour cells in diffusion chambers, which were implanted in

tumour-resistant rats, were only destroyed by penetrating immunized host cells when membrane filters of large pore size were used, whereas with filters of small pore size the tumour cells survived and remained virulent .

.I 56

.W

current status of hypothermia .

moderate hypothermia has been recommended for many and varied conditions . today its value is being questioned in the light of controlled groups of patients . at the moment its use is justified in certain cardiac and other operations where circulation may be interrupted for short periods.. in general surgical procedures where massive, sudden blood loss may be anticipated.. in neurosurgical operations where a /relaxed/ brain is required.. following acute hypoxia such as seen in cardiac arrest.. and perhaps in the therapy of acute septicemic shock .

profound hypothermia in association with extracorporeal circulation rests on shakier premises, but can be of value in major cardiac operations where asystole is required and in certain neurosurgical procedures where complete interruption of circulation is indicated .

there is a great hazard in the development of inadvertent or unrecognized hypothermia in the anesthetized patient . monitoring of body temperature is an important feature of the care of the patient in the operating theater and in the recovery room .

.I 57

.W

hyperglycemic coronary perfusion.. effect of hypothermia on myocardial

function during cardiopulmonary bypass .

in a series of 84 animal experiments hyperglycemic perfusion of the heart gave significant protection to the anoxic heart . this protection was evaluated by ventricular function and contractile force studies and was observed after aortic occlusion at 37, 28 and 10 degrees c .

metabolic data revealed a considerable myocardial glucose uptake, higher coronary ph, higher po and lower pco in the glucose-perfused groups as compared to controls .

a hypothesis for the protective effect may be an alteration in metabolic pathway and support of the myocardial enzyme systems associated with high glucose concentration and utilization .

.I 58

.W

specific carcinoembryonic antigens of the human digestive system .

a wide variety of human adult and fetal tissues were studied by immunodiffusion techniques in agar gel to determine whether they contained the tumor-specific antigen(s) previously found in colonic cancers . in the adult tissues it was demonstrated that identical antigens were present in all tested specimens of malignant tumors of the entodermally derived epithelium of the gastro-intestinal tract and pancreas, but were absent from all other tested adult tissues . the common antigenic constituents, therefore, represent system-specific cancer antigens of the human digestive system . system-specific cancer antigens have not previously been demonstrated in humans .

experiments with fetal tissues demonstrated that identical antigens were also present in fetal gut, liver, and pancreas between 2 and 6 months of gestation . these components were named /carcinoembryonic/

antigens of the human digestive system . on the basis of the present findings and the recent work regarding control of the expression of genetic potentialities in various genetic potentialities in various types of cells, it was concluded that the carcinoembryonic antigens represent cellular constituents which are repressed during the course of differentiation of the normal digestive system epithelium and reappear in the corresponding malignant cells by a process of derepressive-dedifferentiation .

.I 59

.W

the course of influenza virus infection in mice.. organ tissues of infected mice tested by electron microscope .

using the electron microscope the presence of inclusions could be shown in the lungs and liver of mice infected with the pr 8 strain . the inclusions contained particles of size and shape closely resembling the most frequently seen forms of influenza virus . the presence of inclusions in liver tissue might perhaps speak for the possibility of virus multiplication in this organ .

.I 60

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comparative bone marrow study using two aspiration needles and two biopsy sites .

bone marrow aspiration is now widely used in the diagnosis of hematologic diseases and many conditions not primarily affecting the blood system . a number of techniques have been devised by which a suitable specimen of marrow can be obtained with relatively little discomfort to the patient . the two needle sets described in this paper

have been found to be equally reliable in obtaining bone marrow for microscopic study and diagnosis . comparative studies of bone marrow aspirated simultaneously from the iliac crest and the sternum in 26 patients show no significant difference . however, there were four instances of dry tap at the iliac site . this fact, in addition to the observation that less discomfort was experienced by the patient when the sternum was used, might indicate that the sternal area is a more reliable and efficient site for obtaining bone marrow .

it was also observed during this study that patients experienced less discomfort when the university of illinois needle was used . the major objection to the use of this needle is the inability to obtain a bone core for biopsy .

.I 61

.W

cell populations in the bone marrow of the normal guinea-pig .

quantitative data have been obtained for cell-populations in the bone marrow of the normal 400g guinea-pig based on a study of 25 animals . there was good agreement between two independent groups of observations and an average of 1880000 nucleated cells per c. mm. was found . of this total, 27 were lymphocytes, 31 granulocyte precursors and 26 nucleated erythrocyte precursors . whole body populations have been computed and the implications of the findings discussed .

.I 62

.W

pneumocystis carinii pneumonia.. case studies with electron microscopy .

this paper deals with the clinicopathologic findings in 2 patients with pneumocystis carinii pneumonia . the first example was in a

51/2-month-old white female infant without an underlying disease . the second occurred, in association with cytomegalic inclusion disease of the lungs, in a 46-year-old white woman who had received steroid therapy, cytotoxic agents, and irradiation to the thorax for hodgkin's disease . an electron microscope was used for the study of the morphology of the organisms in tissue removed at autopsy .

.I 63

.W

the effect of dehydroepiandrosterone on the dehydroxycorticosteroids in the plasms in various stages of breast cancer and mastopathy .

the depressing effect of dehydroepiandrosterone on plasma corticosteroids is, on an average, shortened in advanced breast cancer (stage iv) . the lowest corticosteroid values have been found with the three groups of patients 6 hours after infusion of dehydroepiandrosterone phosphate . the effect of dehydroepiandrosterone being, still provable after 12 hours with the group suffering from mastopathy, the breast cancer group of stage iv had at this time already reached the level of the initial values . the breast cancer group of stage iv had at this time already reached the level of the initial values . the breast cancer group of stage i/ii behaved intermediately . the less lasting effect of dehydroepiandrosterone is attributed to its accelerated transformation in advanced breast cancer .

.I 64

.W

the meaning of ph at low temperatures during extra-corporeal circulation
a review of the temperature gradients occurring during profound hypothermia is made in regard to acid base changes in general, and to ph

readings in particular . it is concluded that terms such as 'body', 'mean', 'average' and 'core' temperature should be discarded and that when a temperature is quoted it should be referred to the site at which it was measured .

the main circumstances in which blood ph is measured at a temperature different from that at which the blood is equilibrated with respiratory gases are reviewed by describing the changes which occur during tonometry experiments . in this way fundamental changes can be understood before considering the more complicated sequences of events taking place in the living body .

the alterations that occur in the concentrations of protein and bicarbonate ion when whole blood is cooled are reviewed, together with their influence on 'correction factors' . the reasons why these factors should not be applied to blood when the living body is undergoing hypothermia involving the use of an extra-corporeal circulation are discussed .

examples of the numerical values for blood ph during the two main methods for producing profound hypothermia, one using autogenous lung perfusion and the other a pump-oxygenator are given, with reference to the influence of p_{CO_2} upon these values .

the existing methods of acid-base measurement appear to be sufficiently accurate to reflect the metabolic component during profound hypothermia .

.I 65

.W

induced tumour resistance in rats .

the human sarcoma hs has been grown in weanling rats treated with

cortisone . this growth was modified by prior injection of various tissue antigens . active /immunity/ was produced by using human placenta or embryonic tissue as antigen, and similar results were obtained using suspensions of rapidly growing human tumours .

the response to other human tissues varied.. foetal muscle and spleen were active, whereas adult plasma was inactive except from some patients with extensive malignant disease .

passive protection was produced by using certain human sera at the time of challenging with hs . sera from five women who aborted showed this characteristic . where the pregnancy continued to term, antistances were not found,. and they were present in the puerperium in only two out of fifty cases .

further groups of rats were given rat embryonic tissues as antigen, and the tumour challenge was then made with walker tumour,. the results were variable .

with a benzpyrene-induced tumour in a pure line of /wag/ rat the effect was not obtained except in isolated cases .

in experiments in mice, using as challenge an iron-dextran induced mouse sarcoma, prior injection with embryonic mouse liver or placenta increased the resistance to the growth of the tumour, but the tumour has not as yet been produced in a pure-line mouse . on the other hand mouse experiments, using as challenge the crocker tumour, proved negative .

it is suggested that immune reactions may play a part in causing some abortions .

.I 66

.W

urinary steroid estimations in the prediction of response to

adrenalectomy or hypophysectomy .

a clinical trial has been carried out to test the use of the discriminant in assessing the suitability of patients with advanced breast cancer for hypophysectomy or adrenalectomy .

patients with positive discriminants submitted to hypophysectomy have a much better prognosis than patients with negative discriminants submitted to adrenalectomy .

patients selected for adrenalectomy because of negative discriminants have a significantly worse response to the operation than patients selected by random sample .

patients selected for hypophysectomy because of positive discriminants tend to have a better response to the operation than do patients selected by random sample, but the difference is not significant .

adrenalectomy is not recommended for patients with negative discriminants .

.I 67

.W

primary epidermoid cancer of the lung.. ultrastructural study .

the early epidermoidic epithelioma of the human lung are initiated by the proliferation of body cells whose structure is analogical to that of the medium cells and/or the modified basal cells of the normal bronchial wall .

the presence of desmosomes and tonofibrils in the cells of the stratum germinativum of the bronchial epithelium and in the cells derived from it, allows us a better understanding of the malpighian metaplasia of this wall and gives account of the epidermoidic evolution of the bronchial epithelioma .

certain nuclear and cytoplasmic modifications suggest the possibility of a causal virus .

.I 68

.W

biosynthesis of glycoproteins i. incorporation of glucosamine- c into liver and plasma proteins of the rat .

it has been shown that glucosamine-1- c administered intravenously to fed rats is rapidly removed from the blood stream and appears first as trichloroacetic acid-soluble derivatives in the tissues . this is followed by a conversion to macromolecules . at least 80 of the administered compound can be recovered in tissues . the liver is by far the most active organ in accumulating glucosamine . this is rapidly converted to protein-bound components of the liver particulate fraction (microsomes and mitochondria) and is then released to the plasma without appreciable accumulation in the soluble proteins of the liver . it is concluded that the glucosamine is transferred to the peptide chains of glycoproteins at some stage before these proteins are released from the liver particulate fraction .

.I 69

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acute experimental pneumococcal (type i) pneumonia in the mouse.. the migration of leucocytes from the pulmonary capillaries into the alveolar spaces as revealed by the electron microscope .

in this preliminary study of experimental pneumococcal pulmonary pneumonia in the mouse the leucocytes were observed to pass from the capillaries into the interstitial tissue and eventually into the alveolar spaces through the intercellular junctions of the endothelial

and epithelial cell membranes .

.I 70

.W

a light and electron microscope study of developing respiratory tissue in the rat .

1. light microscopic observations on the development of the rat lung have shown the presence of glandular, canalicular and alveolar stages .

2. these same three stages can be identified by electron microscopy and all may be present in different parts of the lung at one time, e.g. at 40 and 45 mm. c.r. length .

3. in the glandular stage, the lung tissue itself has an immature appearance by light microscopy and by electron microscopy individual cells also are immature in respect of organelles . glycogen is present in immature cells .

4. during the canalicular stage, lung tissue becomes more vascular .

5. throughout all stages of development, the 'duct' or 'air' spaces are always lined by a continuous and complete epithelium, and blood vessels by a complete endothelium .

6. lamellated inclusion bodies are present in epithelial (endodermal) cells at an early stage of development .

7. micropinocytotic vesicles are present in large numbers in both epithelial and endothelial cytoplasm and it is suggested that in the foetus they may indicate absorption of amniotic fluid from alveolar spaces .

8. the mechanism of alveolar distension is discussed and its nature remains uncertain .

9. respiratory tissue of the rat is not fully differentiated at birth

and the importance of this fact in human infants is discussed .

10. the adult blood-air barrier, consisting of epithelium, zona diffusa and endothelium, varies in thickness .

this project was performed whilst both of us were in receipt of grants from the medical research council of canada, for which gratitude is expressed . our gratitude is also expressed to miss sylvia smith for typing the manuscript .

.I 71

.W

the pathogenesis of viral influenzal pneumonia in mice .

the pathogenesis of influenzal pneumonia in mice was studied by electron microscopy . mice were inoculated with 1.5 ld of pr8 influenza virus and killed at varying intervals after inoculation . observations by light microscopy were correlated with those by electron microscopy in order to evaluate the lesions produced .

at the periphery, the earliest lesions were focal areas of edema of alveolar lining cells, the capillary endothelium and the interposed basement membrane . this caused an appreciable thickening of the blood-air pathway . hypertrophy, degeneration and desquamation of the alveolar lining and proliferation of alveolar macrophages resulted in complete consolidation, which was progressive up to 1 week after infection .

the central areas of the lung were affected somewhat differently . at 3 days after infection, the nonciliated bronchiolar cells showed considerable hyperplasia of endoplasmic reticulum and apical cytoplasmic edema . viral particles matured at the lumen surface of these cells and were then released into the bronchiolar lumen . the bronchiolar cells,

both ciliated and nonciliated, underwent degeneration and sloughed into the bronchiolar lumen . the regenerating epithelium was stratified, and the surface cells were elongated and flattened . the peribronchiolar interstitial tissue gradually became totally infiltrated by cells, mostly of the mononuclear type .

.I 72

.W

studies on aging with horse crystalline lens gel as a contribution to biomorphosis of the mammalian crystalline lens .

the effects of biomorphosis -dash the continuous material change in the chemical composition of the organs and tissues -dash are studied on the horse crystalline lens in respect of its amino acid content subject to substantial variations in the course of life . it is shown by electrophoretic and paperchromatographic methods that the qualitative composition of horse crystalline lenses remains quite the same, but that within the individual age stages there occur quantitative variations between the individual amino acids .

.I 73

.W

the role of alveolar inclusion bodies in the developing lung .

the developing alveolar epithelium of man and rat contains characteristic inclusion bodies which are heterogeneous structures but basically consist of a system of membranous profiles and a limiting membrane of the unit type .

inclusion bodies appear to result from focal cytoplasmic degradation which occurs in the rapidly changing cuboidal alveolar epithelium . some inclusion bodies in the developing rat lung are similar to the so-called

/lamellar transformed mitochondria./ however, evidence is presented suggesting that alteration of all cytoplasmic membranes may be involved in the process of inclusion body formation . certain images associated with the golgi complex are interpreted as early forms of inclusion bodies . there is also evidence that inclusion bodies enlarge by accretion of membranes which finally are extruded into the alveolar space . inclusion bodies are formed and /secreted/ in greater number late in fetal life and in early infancy, i.e., at the time when the cuboidal alveolar epithelium is differentiating to the mature flattened type . the latter contains no inclusion bodies .

on the basis of the morphologic characteristics of the inclusion bodies and the distribution of the acid phosphatase reaction, it is concluded that inclusion bodies are lysosomal structures active during remodeling of the developing alveolar epithelium .

the possible interrelationship of inclusion bodies and pulmonary surfactant is discussed .

.I 74

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retinal detachment, cataract, keratoconus as ocular symptom complex in endogenous eczema .

with reference to personal observations the authors describe the ocular changes encountered in endogenous eczema . besides the cataract which has been known to occur already for a long time, retinal detachment, keratoconus and keratoconjunctivitis do still belong to the symptom complex .

.I 75

.W

postural changes in blood distribution and its relation to the change in cardiac output .

(1) cardiac output and the blood content indices of the several parts of the body were measured in 18 subjects including patients with various diseases using external radioisotope counting techniques . changes in these 2 parameters induced by standing were compared with each other .

(2) average changes in blood distribution produced by standing were as follows . decrease in blood content in the /lung/ (-25) and in the /heart/ (-26) and increase in the /thigh/ (+56) were statistically significant . no significant change was revealed in the /head/, /palm/, /liver/ and /abdomen/ .

(3) cardiac output and stroke volume decreased by standing in most of the cases . recent data were added to those reported previously and were treated statistically . average decrease in cardiac output was -13 in 6 control cases, -35 in 16 cases with neurocirculatory asthenia and -35 in 10 cases with hyperthyroidism . the difference was significant between control and neurocirculatory asthenia . standing induced a substantial increase in cardiac output in a case of idiopathic nodal rhythm, although there remains a doubt whether it is the ordinary response in this disease .

(4) significant linear correlation was revealed between per cent change of blood content in the /thigh/ or in the /lung/ and that of cardiac output or stroke volume induced by standing . minimal blood shift was observed when the latter was extreme, and vice versa . this implies as follows.. reactivity of the heart might be influenced by posture, and transmural pressure of veins and or capillaries is probably adjusted, as in arterioles, to compensate for changes in cardiac output

.I 76

.W

comparative studies of the glycogen content of heart, liver and brain before and after iodine treatment and under conditions of asphyxia .

blood sugar level and glycogen concentration in the heart, brain and liver of rabbits after treatment with inorganic iodine, depot insulin, iodine and insulin combined, hostacortine and hostacortine and iodine combined are being examined . a control group remains untreated . in a second test series the glycogen determination under asphyxia (the trachea is being pinched off for three minutes) is repeated .

contrary to the brain the glycogen content of the heart muscle is not dependent upon the blood sugar level . after iodine treatment a lowering of the blood sugar becomes noticeable, but also an increase in heart glycogen . the liver glycogen shows greater variations . the levels achieved in these test series therefore show no significant differences during asphyxia there is a significant lowering of glycogen in all three organs . preliminary treatment with iodine succeeds in stopping the lowering of glycogen in the heart muscle and the brain . the possible causes for this phenomenon are being discussed .

.I 77

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altered immunologic activity in sarcoidosis .

studies in 16 patients with sarcoidosis revealed evidence of immunologic alterations other than impaired delayed hypersensitivity . transient impairment of the response of lymphocytes cultured from patients with sarcoidosis to phytohemagglutinin stimulation was found to parallel the clinical severity of the disease . the hemolytic activity

of serum complement was increased . a disproportionate increase in serum
iga was found characteristic of the hyperglobulinemia of sarcoidosis .
these observations indicate that an altered immune response may be
important in the pathogenesis of sarcoidosis . a simple hypothesis as to
the specific kind of interaction of infectious agent and immunity which
might result in the immunologic alterations observed is formulated and
presented .

.I 78

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electron microscopy of cytoplasmic inclusions within /macrophages/ of
human tissue .

the fine structure of inclusions found within the cytoplasm of
macrophages of human lung, spleen, skin, lymph node, and rectum has been
described .

the inclusions appear as concentric or whorled lamellae arranged
around a core . each lamella is constructed of discrete, parallel
filaments . the inclusions do not resemble currently described viruses
or virus-like particles, nor do they resemble asbestos bodies or other
known atmospheric pollutants or ingestants .

there is some resemblance to lipid phase systems as well as mast cell
granules,. possibly the inclusions represent partial intracellular
digestion of phagocytized tissue membranes or ingested mast cell
granules, respectively . differences and similarities exist between the
inclusion bodies of macrophages and the granules of mast cells . such
variations could be due to alterations in mast cell granule morphology
before or after macrophage ingestion .

cytologic distinctions between macrophages laden with mast cell

granules and mast cells proper, remains obscure and requires additional experimental evidence for clear electron microscopic differentiation of these two cell types .

the exact nature of these highly structured bodies remains speculative

.I 79

.W

histological research on the lens in condition of hypoxia, changes in the mitotic activity of the epithelium .

the effect of hypoxia on the mitotic activity of the cells of the lens epithelium was studied in 24 rats of the same strain and weight . the hypoxia was obtained in the decompression chamber .

the results show that the mitotic activity of the lens epithelium is depressed at any of the examined altitudes (6.500, 8.000, 9.500 m),. in particular, a marked reduction in the number of the prophases and an accumulation in metaphase was observed .

the results were examined from the statistical standpoint and discussed .

.I 80

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rate of change of carbon dioxide tension in arterial blood, jugular venous blood and cisternal cerebrospinal fluid on carbon dioxide administration .

1. the rate of change of p in arterial blood and cisternal c.s.f., was measured following 5 percent co administration in eight anaesthetized patients undergoing routine air encephalography . ventilation was maintained constant throughout the procedure by a respirator . in three of the experiments the rate of change of p in the jugular venous blood

was also measured .

2. the rise in p varied between 25.7 and 14.8 mm hg . the final samples of blood and c.s.f. were taken 20-25 min after the start of co administration in five experiments . at this time the mean rise in p was 65.9 (maximum range 68.1-61.6 percent) of the rise in p . in the remaining three experiments the final samples were taken at 15 min when the rises in p were 53.2, 39.4 and 38.1 percent of the arterial change .

3. the increases in p were 57.5, 76.2 and 76.1 percent of those in the arterial blood . the changes in p in the c.s.f. were smaller than in the jugular venous blood in all three experiments . in two of the experiments the final samples were taken 15 min after the start of co administration when the increases of p in the c.s.f. were 68.5 percent and 50 percent of those in jugular venous blood . in one experiment where the final samples were taken at 20 min the increase in p was 89 percent of the rise in p .

4. there was a delay, following the start of co administration, in the rise of p in jugular venous blood and in the c.s.f . this delay was about 1 min in the jugular venous blood but in the c.s.f. it varied from 1.6 to 4.2 min (mean 2.3) .

5. the rise of p in blood and c.s.f. was exponential . the rise in p in all experiments consisted of a fast component with time constants which varied between 0.2 and 0.9 min (mean 0.5) and a slow component with time constants varying between 6.7 and 14.7 (mean 11.6) .

the rise in p and p consisted of only one component . the time constants for the changes in jugular venous blood were 2.1, 3.8 and 4.3 min, whilst in the c.s.f. they varied between 6.7 and 14.7 (mean 11.6) .

6. it is probable that about 40 percent of the increase in ventilation

following co administration is due to stimulation of an area in the antero-lateral surface of the medulla sensitive to changes in pH or p (Mitchell et al. 1963) . this area is superficial and ventilation is affected by changes in the p of the overlying c.s.f . it can be predicted from our experiments that the rise in p on co administration will take some 30 min to be complete . this may explain the slow rise in ventilation on co breathing when compared with the rate of rise of arterial and jugular venous p .

.I 81

.W

studies on the compound lipids from x-ray irradiated animal, ii. biological and biochemical properties of the compound lipids in the x-ray irradiated rabbit organs .

for the purpose to clarify the causes of x-ray disturbances a series of experiments have been conducted on biological and biochemical properties of compound lipids extracted from normal and x-ray irradiated rabbit organs with a special reference to the p -labeled compound lipids uptake, inhibitory action to l cell proliferation and uncoupling of oxidative phosphorylation, and the following results have been obtained the compound lipids (lysophosphatide rich fraction) isolated from the x-ray irradiated rabbit organ have been found to possess a strong hemolytic action and also an action to inhibit the cell proliferation as well as to accelerate the respiration of the mitochondria in the rabbit liver and spleen . it has also been proven that they act as to induce a marked swelling of mitochondria, to impede the formation of high energy phosphate as well as to act as an uncoupler of oxidative phosphorylation in vivo . in the test to see the uptake of p -labeled compound lipids by

various organs, a marked uptake has been observed in spleen, bone marrow, and liver of both irradiated and non-irradiated groups . further, the uptake of p -labeled compound lipids in the rabbits given intravenous injections of compound lipid fraction for 30 consecutive days previously has been found to be greatest in pancreas followed by bone marrow, spleen, liver in the order mentioned in male group, whereas it is greatest in spleen, followed by liver and bone marrow in the female group .

with these results the discussion was conducted concerning the relation between the lipid metabolism and x-ray disturbances .

.I 82

.W

cesium-131 uptake and distribution in the human heart.. an analysis of cardiac scans in 104 patients .

when properly used, cesium-131 is a satisfactory agent for the study of cardiac morphology by photoscanning, which we believe is a useful adjunctive diagnostic procedure in patients for whom the results of other methods of evaluation are at variance with the clinical symptoms of cardiac disease . the studies reported here suggest that perhaps infarction of a subclinical type, size, or location may occur earlier than has been previously thought and that the damage it leaves may not be detectable by any means other than autopsy or a technique such as scanning . we have not yet been able to measure the actual concentration of cesium-131 in the heart at autopsy so that the cold and cool areas could be examined by histologic sections .

.I 83

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oxygen consumption of paralysed men exposed to cold .

1. oxygen consumption and carbon dioxide output were measured when human subjects were cooled for 80-210 min . two subjects were normal, one had been almost completely paralysed below the neck by poliomyelitis, and two were unconscious as a result of intracranial damage and were observed with and without paralysing doses of muscle relaxants (d-tubocurarine and gallamine) .

2. when normal subjects and unconscious subjects receiving no drugs were cooled, oxygen consumption and carbon dioxide output rose .

3. when subjects paralysed by disease or drugs were cooled, oxygen consumption and carbon dioxide output were not increased .

4. these observations are consistent with the view that in man the increase in metabolism on cooling for periods up to 3 1/2 hr occurs solely in skeletal muscle .

.I 84

.W

heparin levels during and after hypothermic perfusion .

1. perfusion-temperature influences the rate of heparin-loss during extracorporeal circulation, and therefore, the requirement of re-heparinization .

2. heparin half-lives of approximately 13/4 hours and 21/2 hours were calculated during perfusions conducted at average temperatures of 31.5 and 22.6 c. respectively .

3. the rate of heparin-loss during extracorporeal circulation is inconstant in an individual, and variable between individuals, so that exact neutralization requires an accurate estimation of the heparin concentration present at the end of perfusion .

4. the protamine titration test provides a crude but simple and satisfactory means of monitoring free-heparin levels .

5. complete neutralization of heparin is an important factor in minimizing postoperative blood losses .

6. protamine is a less efficient neutralizing agent than polybrene at the same dosage level . it may be most effective in divided dosage .

7. /rebound/ was detected in 5 of 45 cases studied, although in only one instance was it of a degree likely to be significant .

8. significant prolongation of the clotting-time resulting from excess neutralizing agent, was not evident in this study .

.I 85

.W

platelet sequestration in man . i. methods .

current methods of labeling platelets with chromium using ethylenediamine tetraacetate (edta) as an anticoagulant were found to cause rapid hepatic sequestration of nearly all the transfused platelets about 50 returned to the circulation but then were partially destroyed in the spleen . less than one-third survived . evidence is presented which indicates that edta is injurious to platelets .

when an acid-citrate medium that buffered plasma at ph 6.5 was used as an anticoagulant, 36 to 85 of the labeled platelets survived (average, 62), and marked temporary sequestration did not occur . studies in thrombocytopenic persons showed that circulating platelet cr activity measures the true survival of such transfused platelets .

the survival and sequestration of platelets were studied in normal subjects . the survival data support the concept that platelets die chiefly by a process of senescence . external scintillation scanning of

the various organs suggests that normally the majority of platelets is destroyed in the liver .

.I 86

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acute leukemia associated with phenylbutazone treatment.. a review of the literature and report of a further case .

the possible toxic reactions to phenylbutazone have been listed, and a review of the literature of haematological complications has shown that 16 deaths attributable to agranulocytosis, aplastic anaemia and thrombocytopenia have been recorded . the association between leukaemia and phenylbutazone first suggested by bean (1960) has been amplified by further reports, which have been reviewed .

a further case history has been presented . of the 15 patients with acute leukaemia in which the association has been recorded, there were other possible leukaemogenic factors in three, and in a further three the drug had been given for only a short time before the leukaemia was diagnosed . however, in the remaining nine, the histories are such that the phenylbutazone ingestion may have been associated with the development of the leukaemia . further studies, which should include matched controls, are indicated, and will be required before a definite opinion can be given as to any causal relationship between the drug and the disease .

.I 87

.W

absorbed radiation dose and excretion of cesium-131 in humans .

data relating to the effective half-life, absorbed dose of radiation, and excretion rates of cesium-131 have been presented . cesium-131 is an

excellent material for cardiac scanning, since a very low amount of radiation is absorbed -dash a dose of the order of one twentieth that received in diagnostic x-ray studies of the gastrointestinal tract .

absorption of radiation can be reduced further by the administration of a thiazide type of diuretic and, probably, by catharsis after the scan .

.I 88

.W

radiocardiography.. principles and methods .

the aa show the importance of radiocardiography, as a method to evaluate the cardiac output, the ventricular volumes and the pulmonary blood volume .

in this first paper, they are particularly concerned with some technical aspects, which are very important to collect data .

the position of the collimator on the precordium, the injection of isotopes through a catheter, just behind the ventricle near the tricuspid valve, the selection of ratemeter constants the velocity of paper on the recorder and the way to read the area of the curve, were specially discussed .

finally, they present the formula used to calculate cardiac output, ventricular volumes and pulmonary blood volumes .

.I 89

.W

reaction of the adrenal cortex during controlled experimental hypothermia .

the stress reaction caused by hypothermia was studied in rabbits subjected to controlled hypothermia by immersion in an icebath . some of the animals were re-warmed . to anesthetize the animals, pentobarbitone

sodium (nembutal) was given intraperitoneally, and, in some cases, followed by ether anesthesia . further, the stress reaction produced by pentobarbitone alone was studied in five animals, and that of ether anesthesia alone in three . no anesthesia was given to the three rabbits placed in the refrigerator . the variation in distribution and amount of adrenocortical lipids served as an indicator for evaluation of the stress reaction .

in all the hypothermia tests there occurred changes in the distribution and amount of cortical lipids, denoting a stress reaction brought about by hypothermia . in rabbits, the barbiturate did not seem to inhibit the stress reaction . this may be attributed partly to the test animal, as such and partly to the fact that shivering of some extent always occurred during the hypothermia experiments .

.I 90

.W

use of a cross-circulation technique in studying respiratory responses to co .

the effect of hypercapnia and hypocapnia on ventilation was investigated in cross-circulated dogs in which the recipient dog's head and neck regions were perfused by blood from a donor dog . hypercapnia of the donor dog was produced by administering co -o -n gas mixtures in the inspired air . hypocapnia was produced by hyperventilating the donor dog with the aid of a respiratory pump . when the donor dog was hyperventilated, the ventilation of the recipient was maintained at or just below its resting level and it was independent of the arterial pco of the donor . the donor dog was apneic when the artificial hyperventilation was suspended and this response was not abolished by

vagotomy . bilateral vagotomy caused an increase in ventilation in the recipient when its head was perfused by hypocapnic blood . bilateral removal of the carotid receptors did not influence the response to co qualitatively although there was some reduction in the ventilation of the recipient to cephalic hypercapnia . the ventilation of the recipient dog was best correlated to the ph and pco of its cerebrospinal fluid in both hypercapnic and hypocapnic states .

.I 91

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action of phytohaemagglutinin in vitro on the lymphocytes of chronic lymphoid leukaemia .

the in vitro action of phytohaemagglutinin has been the subjects of a comparative investigation of the lymphocytes of 13 normal subjects and of 15 cases of chronic lymphatic leukaemia .

in both groups there is cellular change shown by the appearance of large basophil nucleolated cells showing mitotic activity .

in all the cases of lymphatic leukaemia the percentage of cells undergoing such change is lower than in normal subjects, and the transformation occurs more slowly .

the two phenomena are more striking the higher the initial leucocytosis .

these results suggest, in chronic lymphatic leukaemia, the cells affected by the transformation are residual normal lymphoid elements . leukaemic lymphoid cells appear to be incapable of this transformation .

.I 92

.W

demonstration of ventricular aneurysms by radioisotope scanning .

radioisotope scanning of the cardiac blood pool after the intravenous injection of ¹²⁵I-labeled iodipamide was carried out in 14 patients with ventricular aneurysm . in 4, the aneurysm could be demonstrated on neither the anteroposterior chest roentgenogram nor the scan . in 5, the aneurysm was apparent on the radiograph, but the blood pool did not enter the area, suggesting a thrombus within the aneurysm . in 5, the aneurysm was detectable on the film and was also seen to be filled with radioactivity on the scan . presumably these findings showed that a thrombus had not yet formed . blood pool radioisotope scanning appears to be another tool in the diagnosis of ventricular aneurysm, useful also in demonstrating in some patients the presence or absence of an intraluminal clot within the aneurysm .

.I 93

.W

propagation of lactic dehydrogenase-elevating virus in cell culture .

primary cultures of adult mouse lung, spleen, and liver and of mouse embryo support the multiplication of the lactic dehydrogenase-elevating virus . such cultures produced virus continuously until they had been subcultured 2-3 times . this corresponded to 20 weeks in the case of lung and spleen and to 2-3 weeks with cultures of embryo . viral multiplication was not accompanied by cytologic alterations in the cells or by changes in their rate of synthesis of nucleic acids or protein . infection did not cause detectable changes in either the production of ldh or in its release from cells .

.I 94

.W

transformation of bovine cells in vitro after inoculation of simian

virus 40 or its nucleic acid .

cells of bovine embryonic lung tissue in culture were inoculated with simian virus 40 (sv 40) or a phenol extract of a high titer suspension of sv 40 . both the virus and the nucleic acid preparation induced proliferative morphological changes characteristic for sv 40 transformation . non-infected control cultures and cultures which were inoculated with a preparation of nucleic acid exposed to dnase and maintained under the same conditions as infected cultures showed a regular fibroblastic growth .

cell lines of rapidly growing transformed cells have been obtained . most attempts to isolate virus from the transformed cells were negative, but minute amounts of virus were recovered from occasional passages .

.I 95

.W

rapid transformation of human fibroblast cultures by simian virus 40 .

the risk of systemic embolism is assessed in a group of 754 patients with chronic rheumatic heart disease followed over a period of 5,833 patient-years .

the incidence of embolism was 1.5 per patient-year for the whole group it was seven times higher in atrial fibrillation than in sinus rhythm when the duration of atrial fibrillation was known, it was found that one-third of the emboli occurred within one month and two-thirds within 12 months after the onset of atrial fibrillation . the incidence of embolic recurrences was 8 per patient-year, irrespective of the nature of the cardiac rhythm, but 66 of the recurrences took place within 12 months of the initial embolic episode .

mitral valvotomy did not eliminate the danger of embolism . it is

questionable whether it reduced its incidence .

anticoagulant treatment reduced the incidence of embolic recurrences .

.I 96

.W

the tissue reaction to hyperbaric oxygen .

hyperbaric oxygen damages tissues exposed in vitro, but their sensitivity varies . if exposure is limited some tissues may recover . the effect appears to depend on oxygen tension rather than raised pressure per se . the tissue reaction may be involved in the clinical application of hyperbaric oxygen .

.I 97

.W

attitudinal factors in congenital heart disease .

this study considers the behavioral implications of congenital heart disease for the pediatric patient, his siblings, and his parents . the effects of a disease on the child, on his siblings, and on his parents and the interplay among these individuals are explored . the impact of the physician's diagnosis is illustrated by the induced significant changes in family attitudes, which are not necessarily related to disease severity or child incapacity .

poorer adjustment and anxiety in the cardiac child related more highly to maternal anxiety and pampering than to his degree of incapacity . maternal protectiveness and pampering were significantly greater in the cardiac than in the normal group and were highest in the cyanotic group the best predictor of maternal protectiveness was maternal anxiety, and it was found that the addition of other variables such as incapacity and child dependence failed to improve prediction substantially .

maternal anxiety seemed related to the presence rather than to the severity of the heart condition .

.I 98

.W

maternal anxiety during pregnancy and adequacy of mother and child adjustment eight months following childbirth .

fifty pregnant women were administered a battery of psychological tests . on the basis of scores obtained from the manifest anxiety scale, these pregnant women were dichotomized into a /high anxiety/ group and a /low anxiety/ group . eight months following childbirth, the mothers and children were seen for a psychological assessment . it was found that the women in the /high anxious/ group evidenced significantly more negative childrearing attitudes . that is, the /high anxious/ mothers obtained significantly higher scores on the hostility and control factors measured by the pari . on the basis of the examiner's ratings of the mother's personality traits, it was found that the women who were highly anxious during pregnancy received much less favorable personality ratings at the time of the 8-month assessment . moreover, there was a significant difference in the proportions of mothers in the two groups who received a favorable rating from the examiner on the basis of his observation of the mother-child interaction during the session . in studying the children of these mothers, it was found that the children of the /low anxious/ mothers received a significantly higher developmental quotient on the infant mental scale . in keeping with this finding, they also obtained a higher developmental quotient on the motor scale, although on this aspect of the intellectual assessment the difference was not statistically significant . also, the children from

the /low anxious/ mothers tended to receive a score indicative of a more favorable general emotional tone than did the offspring of the /high anxious/ mothers . this difference between the two groups of children was not statistically significant . in general, the findings were consistent with the predictions that the children who were being reared by women who had been highly anxious during pregnancy would fare less well on tests of intellectual development and indices of emotional adjustment . the findings also were in keeping with the prediction that the highly anxious women during pregnancy would evidence less desirable parental attitudes during their child's early development and that they would present a less favorable personality picture at a time approximately 8 months following pregnancy .

.I 99

.W

maternal separation in the rhesus monkey .

the present study involved separation of eight monkey mother-infant pairs for a period of two weeks and measurement of the behavior of the infants before, during and after reunion with their mothers, and of the mothers before and after reunion . all infants showed emotional disturbance in response to separation and drastic decreases in play and other complex social behaviors while separated .

it is clear that infant-mother separation produces emotional disturbance in both human and macaque infants and that the patterns of responses following separation are similar in both species . the results obtained in studies of monkey infant-mother separation indicate that sheer physical separation is the crucial aspect of maternal separation for monkeys . undoubtedly other factors associated with separation from

the mother are vitally important for human children, and may account in part for the absence or rarity of the detachment stage (as seen in human response pattern) in separated monkey infants . the overall results show considerable similarity in the responses of human children and infant monkeys to separation from the mother .

.I 100

.W

the ophthalmologist's role in the management of dyslexia .

dyslexia is a clinical entity characterized by subnormal reading ability in a person of average or above average intelligence .

it is a disease which has different causes in different children . the causes include brain damage in the /language area,/ hereditary predisposition and such ophthalmic factors as hyperopia, muscle imbalance, aniseikonia or visual immaturity . emotional disturbances, educational immaturity and cerebral dominance may also play some role in the etiology of this condition .

the universal symptom is poor reading ability . however, these cases frequently have other associated symptoms such as poor writing, difficulty in reading and writing numbers, inability to read or write musical notes and disorientation for left and right . many of these patients develop personality maladjustments . visual fields often reveal a hemianopia .

in any group of poor readers, a large percentage will have ocular, neurologic, psychiatric or psychologic abnormalities and/or a strong hereditary tendency . the degree to which reading can be learned depends upon the ability of the individual to adjust to the psycho-physiologic needs that are present at the time he reaches /reading age/ in school .

if compensating abilities are present, and if the child's reaction is a favorable one, he may read well in spite of unfavorable factors,. if not, he may become a /poor reader/ . these children should be recognized in their first year of school .

a complete medical work-up should be managed by an ophthalmologist . a complete ophthalmic examination should first be performed and all possible visual anomalies should be corrected . the ophthalmologist may want a psychometric evaluation, a neurologic opinion to determine the role of organic brain damage, psychiatric consultation for evaluation of emotional disturbances, pediatric consultation for evaluation of the status of the general health and/or consultation by an otolaryngologist to determine the patient's hearing ability . with all the necessary information at hand, the ophthalmologist will be able to recommend corrective medical therapy and to advise the parents and teachers about available remedial reading aids .

the prognosis is good for most patients since they are of average or above average intelligence,. nearly all cases can be helped .

.I 101

.W

unusual course of internal carotid artery accompanied by bitemporal hemianopia .

a case is reported with bitemporal relative hemianopia, craniotomy showing internal carotid arteries to have an unusual course, corresponding to the carotid siphon, with resultant change in shape of the optic nerves .

abnormalities of the carotid siphons could not be detected on reviewing the carotid angiograms . evaluation of the optic nerve's

relationship, as can be measured on the pneumograms, indicated that the optic nerves in this case were exposed to compression from the abnormal arteries .

.I 102

.W

frontal lobes and vision .

the influence of the frontal lobe on vision is discussed based on the presentation of a rather unusual case . after the operation of a right frontal brain abscess, which never had led to papilledema, there was a pronounced diminution of the visual capacities of the patient,. gradually these disturbances regressed to the point of return of full visual acuity,. but there remained a hemianopic field defect . this and psychological defects in the sense of a partial visual agnosia (which latter are also regressing very well) prompted a discussion of those neuroanatomical and neurophysiological observations pertinent to the findings in this patient . the many data on the fronto-occipital connections in subhuman primates point to the role of the frontal lobe (area 8) in the development of visual disturbances in the sense of a temporary hemianopia with partial visual agnosia and some intellectual deficits . contrary to a single observation in an anthropoid ape, our case would seem to indicate that the aforementioned combination of symptoms may originate in the frontal lobe,. and we hope it will prompt other long-term follow-up studies of similar patients . the continued observation of this patient and perhaps of others will give a possibility to gain insight into the role of the frontal lobe in vision, as has been assumed for animals .

.I 103

.W

physiologic bitemporal hemianopsia in pregnancy .

a severe case of bitemporal hemianopsia occurring late in pregnancy is presented . the patient illustrated a typical rapidly progressive course and rapid recovery with complete return of visual fields and visual acuity after delivery was accomplished . the presumed pathologic physiology of this entity is briefly reviewed .

.I 104

.W

evoked response in visual disorders .

1. erg and ver have been recorded from eyelid and lateral occipital electrodes in response to diffuse stroboscopic stimulation . in 45 normal subjects ver was found to be composed of an early triphasic potential arising from the occipital region . wave i was present in 67 percent of subjects, wave ii in 97 percent, and wave iii in 100 percent later waves were inconstant and contained components from the vertex reference . no overall asymmetry in ver from right to left was found in normal subjects, although average asymmetry with smaller side compared to larger was 19 percent 12.5 . on monocular stimulation the contralateral ver was regularly larger than the ipsilateral reflecting predominant retinal representation of the temporal field .

2. a statistically determined criterion of 50 percent depression in wave ii successfully identifies most patients with hemianopic defects involving the central 10 percent of visual field on tangent screen campimetry .

latency asymmetry of six msec. or more and grossly asymmetrical aberrant wave forms are seen in some patients with diffuse cerebral

disease and hemianopic defects .

3. severe or diffuse retinal disease is associated with alteration or loss of erg and ver on stimulation of the involved eye .

4. optic nerve disease is indicated by bilateral loss or suppression of ver on stimulation of the involved eye . erg is normal .

5. bilateral prechiasmal involvement is associated with complete suppression of ver . if only waves i and ii are lost, disease is probably, but not conclusively, demonstrated .

6. involvement of nasal retinal fibres is indicated by reversal of the normal contralateral preponderance of ver on monocular stimulation . these changes are observed in chiasmal disease .

7. retrogeniculate blindness is associated with loss of early ver and preservation of late response . nonspecific projections are felt to contribute to the late cortical response to photic stimulation .

.I 105

.W

optokinetic nystagmus and occipital lesions .

six cases are presented to invalidate the rule that horizontally symmetric optokinetic responses indicate a vascular etiology in patients with occipital lobe type hemianopias . the converse of this rule is, in our experience, still a valuable observation . that is, asymmetry of horizontal optokinetic responses accompanying an occipital type field defect is a strong indication of a mass lesion . optokinetic nystagmus may be helpful, therefore, as corroborative evidence in diagnosing occipital lobe tumor but not in ruling it out .

.I 106

.W

anaphylactoid shock induced by oral penicillin and resulting in gerstmann's syndrome .

an anaphylactoid reaction to oral penicillin in a 46-year-old woman is described.. after hours of unconsciousness and weeks of confusion she was left with a residual gerstmann's syndrome . these reactions are less rare than is generally supposed . symptomatology, treatment, diagnosis, and mechanism are discussed, and some of the relevant literature is briefly reviewed .

.I 107

.W

disturbances of the verbal body image.. a particular syndrome of sensory aphasia .

1. the pto syndrome of the dominant hemisphere varies according to the extent and depth of the lesion in the angular and supramarginal areas . the mildest clinical syndrome consists of a vague contralateral sensory impairment associated with dyscalculia, dysgraphia, dyslexia and difficulty in naming . a more extensive lesion is needed to cause the wide variety of classical signs described in parietal lobe disease, among them being gerstmann's syndrome, which is usually found in association with other manifestations of parietal loss (case 1) . an even more extensive corticosubcortical lesion in the area leads to complete disintegration of naming and understanding of speech (cases 3, 4 and 5) .

2. attention is drawn to the difficulties arising from lack of differentiation between the concrete gnostic body image and the abstract verbal body image in investigation of these patients . the aphasic syndrome should be differentiated from disturbances of gnosis by

application of separate, non-verbal methods of testing to elicit the impairment of the gnostic body image . the latter may be well compensated for and it is apparently unimpaired in the presence of an aphasic syndrome limited to the verbal body image .

3. disturbances of speech in pto lesions if investigated along quantitative scales of impairment of repetition, understanding and naming, show a regular interrelation . nomination is the most affected, understanding is less affected . repetition is the best preserved function (cases 1-4) . the same interrelation of these functions is found with regard to the verbal body image . however, understanding and naming of parts of the body show far greater disintegration than understanding and naming of any other categories of words (all cases presented here) . if the aphasic syndrome is subsiding, finger aphasia with some other minor disturbances of verbal body image associated with acalculia may persist (case 1) . thus gerstmann's /finger agnosia/ may represent a partial impairment of the verbal body image and be limited to finger aphasia .

4. it is assumed that the verbal body image differs from other categories of verbal symbols owing to the mainly proprioceptive, vestibular and tactile experience forming its specific physiologic background . telereceptive experience is of minor importance in the initial development of the understanding of words defining the body image .

in the patients described here, the selectively worse aphasic impairment of the verbal body image, as compared with other categories of words, seem to confirm this assumption .

.W

chromosomal patterns in cancer patients during treatment .

radiation damages the chromosomes of human cells, and through short-term cultures of white blood cells some of this damage can be assessed . patients with cancer were selected for this study because of the large portions of the blood-forming tissues irradiated in the course of treatment . chromosomal damage may be quantitative with variations from the normal number of 46, or qualitative, thereby showing structural aberrations . counting the chromosomes in cells from cultures grown prior to therapy and at intervals during treatment enables us to determine the variation .

stained preparations examined microscopically allow us to recognize these abnormalities which are apparent before, during, and after radiotherapy . the damage appears to be largely random in the chromosomes affected in the different cancers, and the specific aberrations differ from cell to cell . however, there does seem to be some correlation between the appearance of persistent aberrant chromosomes and their frequency . while the peak incidence or /plateau/ may remain unchanged, the frequency may change .

.I 109

.W

a few interesting neurologic manifestations of migraine .

migraine is a complex vascular phenomenon presumably of genetic origin which, through changes induced by either vasoconstriction or vasodilatation, can produce interference with the neurologic system and result in many bizarre and alarming clinical pictures . a few examples of the more interesting neurologic manifestations have been shown .

.I 110

.W

visual neglect .

clinical trainees in nursing and in psychology from boston college and simmons college, boston, mass., collected data and observed patients under the direction of the authors in a pilot program designed to measure visual spatial neglect and to develop rehabilitative material . these measurements and exercises might also be used by nurses in their care of those patients who have had cerebral vascular accidents .

the diversity of daily activities in which the patient becomes involved during his hospitalization should provide some indication of the extent to which the compensatory visual neglect therapeutics have been effective . more formal estimates can be obtained by re-administering the battery of visual neglect tests at periodic intervals . nursing personnel adopting a program of therapeutics such as this must bear in mind that patients suffering cerebral insult are usually less adaptive than their nonbrain-injured peers . they develop new habit patterns slowly and regression often will follow apparent fixation at a more adaptive level of response habituation(11) . however, experimental inquiry has shown that the dimension of behavioral difference between the brain-injured adults and normal adults is one of degree rather than kind -dash a difference that skilled nursing can often reduce(12) .

.I 111

.W

respiratory changes after open-heart surgery .

patients who undergo cardiac surgery with extracorporeal circulation

develop significant alveolar-arterial oxygen tension differences and venous admixture in the early post-operative period . up to 50 of this abnormality is due to anatomical right to left shunting through the lungs.. the remainder is most likely to be due to ventilation-perfusion inequality . the changes appear to be completely reversible . the cardiopulmonary bypass procedure may be responsible for initiating the underlying pathology, since changes of this magnitude were not found in cardiothoracic surgery patients in whom this technique was not required .I 112

.W

cardiac malformations associated with ventricular septal defect .

in this study, 46 necropsy-proved cases of ventricular septal defect associated with another anomaly but not part of a recognized complex were selected .

the associated anomalies were classified as (1) obstructive or positional anomalies of the great vessels, (2) anomalies responsible for additional shunts, (3) anomalies causing intraventricular obstruction and (4) aortic valvular insufficiency .

clinical findings were often those of the ventricular septal defect, and the findings related to the associated lesion were frequently obscure . even with special studies, including cardiac catheterization and angiocardiography, there was often failure to arrive at a complete diagnosis . the findings which led to an erroneous or incomplete diagnosis have been presented . when a complete diagnosis was made preoperatively, the procedures leading to it have been outlined . while the diagnostic approach varies with the malformations which may coexist with ventricular septal defect, it was observed that aortography and

selective left ventricular angiocardiology were most commonly helpful in identifying occult malformations associated with ventricular septal defect . it is therefore recommended that complete studies, including left-sided cardiac catheterization with left ventricular angiocardiology and aortography, should be considered in all cases in which the clinical, electrocardiographic, and right-sided cardiac catheterization studies are not entirely typical for isolated ventricular septal defect .

.I 113

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anatomic types of single or common ventricle in man morphologic and geometric aspects of 60 necropsied cases .

in 60 necropsied cases of single or common ventricle in man, four major unrelated ventricular malformations were found.. (1) absence of the right ventricular sinus, in 47 cases (78 percent), designated type a,. (2) absence of the left ventricular sinus, in 3 cases (5 percent), type b,. (3) absence or rudimentary development of the ventricular septum, in 4 cases (7 percent), type c,. and (4) absence of both ventricular sinuses and of the ventricular septum, in 6 cases (10 percent), type d .

three types of relationship between the great arteries were present.. a normal (solitus) interrelationship, in 9 cases (15 percent), designated type 1,. d-transposition, the transposed aortic valve lying to the right (dextro, or d), relative to the transposed pulmonary valve, in 25 cases (42 percent), type ii,. and l-transposition, the transposed aortic valve lying to the left (levo or l), relative to the transposed pulmonary valve, in 26 cases (43 percent), type iii . in none was the

inversus interrelationship, type iv, displayed .

three types of visceral and atrial situs were found.. solitus, or normal, in 50 cases (83 percent),. inversus, an exact apparent mirror image of normal, in 2 cases (3 percent),. and heterotaxy, the uncertain visceral and atrial situs associated with asplenia, in 8 cases (13 percent) .

the 60 cases were classified segmentally, according to the anatomy of the three cardiac segments.. the great arteries, the ventricular sinuses, and the atria .

the classic single ventricle with a rudimentary outlet chamber was found morphologically to be a large left ventricle with a right ventricular infundibulum, the sinus of the right ventricle being absent (type a) .

the myocardium of the right ventricular infundibulum, of the right ventricular sinus, and of the left ventricular sinus was identified by the distinctive gross morphologic characteristics of each .

the planes of the atrial and ventricular septa, and the relationships between the great arteries at the semilunar valves, were measured as projections upon the horizontal plane, relative to the anteroposterior line .

an approach to cardiac anatomy is presented which is segmental, morphologic and geometric . this approach has angiocardiographic, electrocardiographic and embryologic applications .

.I 114

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congenital heart disease in the adult .

events in the natural course of 310 adult patients with proved

significant congenital cardiac anomalies have been reviewed to determine incidence, longevity, complications and cause of death .

atrial septal defect and patent ductus arteriosus were the most frequently encountered lesions and comprised over one third of the entire series . ventricular septal defect and pulmonic stenosis made up almost a quarter of the group . twenty-two instances of the eisenmenger syndrome secondary to a variety of shunting lesions are included .

bacterial endocarditis, sudden death and cardiac decompensation were the greatest threats to these patients . symptoms were minimal until the appearance of heart failure, which was the most common cause of death, especially with older patients . sudden death occurred most often in patients with ventricular septal defect .

although the clinical features are usually characteristic of a congenital malformation, young adults with acyanotic congenital heart disease are often misdiagnosed as rheumatic,. and in older patients, presenting manifestations are frequently attributed to arteriosclerotic heart disease . at times an associated acquired cardiovascular disorder may alter the basic syndrome .

three quarters of the patients survive and continue under observation the ability of many to live active, productive lives and to withstand stress, surgery, both cardiac and non-cardiac, and pregnancy was impressive . further observation of the patient with congenital heart disease but without surgical intervention is essential for accurate evaluation of the long term efficacy of cardiac surgery .

.I 115

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a study of ventricular septal defect associated with aortic

insufficiency .

clinical, electrocardiographic, radiographic, and hemodynamic findings in 12 children with the combination of a ventricular septal defect and aortic insufficiency are presented . the left-to-right shunt was determined to be small or moderate in all, and significant aortic insufficiency was documented by aortography in 11 patients . clinical indication of aortic insufficiency as manifested by an aortic diastolic murmur first appeared at an average age of 6 years in 7 patients, with concomitant widening of the pulse pressure in 4 . progressive left ventricular hypertrophy was noted electrocardiographically, with progressive cardiac hypertrophy and aortic dilatation on x-ray examination in 2 patients . progression of the hemodynamic disability does not appear to be common in childhood, however .

.I 116

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ventricular septal defect and aortic regurgitation clinical, hemodynamic and surgical considerations .

the clinical, hemodynamic, angiographic and anatomic findings in fifteen patients with ventricular septal defect complicated by aortic regurgitation are presented . in this combination of malformations the aortic regurgitation is acquired and results from prolapse of an aortic valve leaflet into the septal defect . the strategic location of the septal defect in relation to the aortic leaflets appears to be more important to the development of this complication than the size of the defect or the magnitude of the shunt through it . the onset of aortic regurgitation occurs during early childhood and, once present, tends to become more severe . careful observation of patients with these defects

is indicated following the appearance of aortic regurgitation since rapid progression to severe left ventricular failure is not uncommon . ventricular septal defect and aortic regurgitation must be distinguished from other cardiovascular abnormalities producing a wide pulse pressure with a continuous or to-and-fro murmur . cardiac catheterization and thoracic aortography are the diagnostic procedures most helpful in this differentiation . the operative treatment of ventricular septal defect and aortic regurgitation is reviewed and, on the basis of the present and previously reported results, suggested plans for surgical management are presented .

.I 117

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current techniques in the surgical approach to aortic and mitral valvular disease .

1. the aortic and mitral valves can be operated upon successfully and totally replaced with a prosthetic device of the ball-valve type with good long-term results . seventy-four cases are reported .

2. in aortic valvular disease the outcome in the immediate postoperative period is influenced primarily by the presence of calcific aortic stenosis as well as the presence or absence of disease in the coronary arteries .

3. we have significantly decreased the appearance of a low-output syndrome postoperatively in patients who are suffering from severe mitral disease by leaving the papillary muscle-chordae tendineae-mural leaflet relationship intact . we feel this adds strength to each contraction .

4. there have been no late deaths in the follow-up period to date

(thirty months) in any patient with replacement of aortic or mitral valves with the ball-valve prosthesis .

.I 118

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effects of aortic regurgitation on left ventricular performance direct determinations of aortic blood flow before and after valve replacement . the volume of regurgitant blood flow and its effects on the performance of the left ventricle were assessed at operation in 14 patients with varying degrees of aortic regurgitation . instantaneous forward and regurgitant flows in the ascending aorta were measured with a sine-wave electromagnetic flowmeter simultaneously with left ventricular and aortic pressures . in eight patients who had aortic regurgitation without associated stenosis, 63 to 75 percent of the total forward stroke volume regurgitated during the succeeding diastole . the calculated regurgitant orifice areas ranged from 0.13 to 0.44 cm ²/m . after replacement of the aortic valve with a starr-edwards prosthesis, the absence of regurgitant flow was proved in every patient, and the records of aortic blood flow closely resembled those seen in patients with normal aortic valves . net forward blood flow increased by an average of 60 percent, total left ventricular stroke volume fell 42 percent, and the mean aortic pressure rose 29 percent . the pressure work of the left ventricle was elevated preoperatively in five of the eight patients (average 89 g-m stroke/m) and fell significantly to an average of 34 g-m stroke m after valve replacement . kinetic ventricular work was high in seven of the eight patients and comprised 10 percent of total work before replacement but only 4.8 percent afterward .

similar observations were made in five patients with aortic stenosis

and associated aortic regurgitation, ranging in severity from 24 to 72 percent of total forward stroke volume . in four patients in whom the valve was replaced, no residual regurgitation was present afterward, and net forward flow rose an average of 49 percent . kinetic left ventricular work was extremely high in every patient and averaged 26 percent of total work preoperatively and 13 percent after valve replacement . in this group, pressure work was variable both before and after operation .

the studies described provide definitive information concerning the effects of aortic valve disease on left ventricular performance in man and document the favorable changes in flow, pressure, and left ventricular work which immediately follow aortic valve replacement .

.I 119

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the absorption and hepatic uptake of orally ingested radioactive vitamin b in hepato-splenic bilharziasis .

the absorbed plasma radioactivity and hepatic uptake of orally ingested vitamin b tagged with co were measured in 52 subjects, 26 normals and 26 suffering from bilharziasis .

the results of the present work indicate that the absorption and hepatic uptake of this vitamin are within normal limits in hepatosplenic bilharziasis irrespective of the stage of the disease, the size of the organs affected and the presence or absence of associated peripheral neuritis .

.I 120

.W

early effects of digitalis on central hemodynamics in normal subjects .

the intravenous administration of lanatoside c in 7 normal subjects had the following

effects.. 1. an early significant reduction of heart rate .

2. a significant transient reduction of cardiac output .

3. a significant increase of the stroke volume initially accompanied by a significant rise of the end-diastolic volume with unchanged systolic rate of emptying . the increase of end-diastolic volume seems to be related to the lengthening of the diastolic filling period . later on, the systolic emptying rate increases, and the ventricular volumes decrease, suggesting an inotropic effect of the drug .

4. a significant increase of pulmonary blood volume, parallel to the increase of the stroke volume, suggestive of a passive relation between the two variables .

.I 121

.W

measurement of pericardial fluid correlated with the i -cholografin and ihsa heart scan .

in 23 patients undergoing open-heart surgery in whom the pericardial contents were accurately measured, and in 11 additional patients examined at autopsy or by pericardiocentesis, isotopic photoscans of the heart were made and the results were correlated .

the most accurate means of diagnosis of pericardial effusion was found to be the ratio of the maximum transverse cardiac diameters on scan and roentgenogram . in patients with less than 100 cc of pericardial fluid this ratio was greater than 0.80, and it was less than this in cases of effusion of 200 cc or more .

measurement of the difference of these diameters, and visible

separation of the cardiac blood pool from the pulmonary vasculature and liver aided in the diagnosis .

pericardial effusions of 200-300 cc or greater can be detected by isotopic photoscanning . although cardiac dilatation and/or hypertrophy decrease the sensitivity of the technique somewhat, a definite diagnosis of pericardial effusion can be made even when cardiomegaly exists .

.I 122

.W

aneurysm of the membranous septum .

1. aneurysms of the membranous septum are relatively rare lesions presumably developing on a congenital basis . these aneurysms originate in the left ventricle immediately beneath the aortic valve and bulge into the right ventricle, the septal leaflet of the tricuspid valve or into the right atrium .

2. many of these aneurysms do not produce symptoms . others may cause right ventricular outflow tract obstruction or may rupture and result in a septal defect . the resulting shunt will be from the left ventricle into the right atrium or ventricle .

3. an aneurysm of the membranous septum may be an isolated abnormality or be associated with other congenital cardiac defects, particularly aortic valvular insufficiency . membranous septal aneurysms may be the site of bacterial endocarditis or thrombus formation .

4. aneurysms resembling those arising from the membranous septum may occur as part of the complex of deformities produced by an endocardial cushion defect . however, the angiographic features diagnostic of a cushion defect can still be recognized .

5. the presence of a septal aneurysm can be established only by

angiocardiology . the diagnostic features as seen on the left ventricular angiogram are presented .

.I 123

.W

distribution of transfused tritiated cytidine-labeled leukocytes and red cells in the bone marrow of normal and irradiated rat .

in normal rats and after total body irradiation with 550 r of x-rays, the fate in the bone marrow of labeled nucleated and red cells of transfused peripheral blood was observed autoradiographically .

labeled nucleated cells, most of which were lymphocyte-like cells, readily migrated into the marrow parenchyma in normal animals (2 cells/1,000 parenchymal cells/hr.) . following irradiation to at least 27-51 hr., this migration appeared to be relatively increased . beyond this time, parenchymal areas were more difficult to be defined as such .

labeled red cells were rarely observed to enter parenchyma despite the presence of nonlabeled erythrocytes within the parenchymal structure after irradiation .

the vascular bed following irradiation increased greatly as the parenchyma diminished to a minimum of less than 10 percent control at 75 hr . despite these changes in the architecture of the marrow, the average density of labeled cells per area of marrow corresponded to values expected on the assumption of a free-flowing circulation . the technique used at present did not allow us to distinguish, at all times, between a free-flowing circulation through intact sinusoids or through areas in which the sinusoidal wall, as such, was destroyed .

.I 124

.W

factors limiting survival after circulatory occlusion under hypothermia and hyperbaric oxygenation .

thirty minutes of circulatory occlusion with mild hypothermia and hyperbaric oxygen ventilation resulted in a mortality of 83.3 percent in animals . when coronary perfusion from a reservoir was added, the mortality rate was 22 percent . ventricular fibrillation was much more easily reversed after coronary perfusion . there was no evidence of brain damage in survivors which leads to the conclusion that the brain tolerates circulatory arrest better than the heart under these conditions .

.I 125

.W

the effect of hypothermia on circulatory reflexes in the human .

total circulatory occlusion and release result in hemodynamic phenomena which provide an index of integrity of some cardiovascular reflexes . these include carotid sinus and aortic baroreceptors, arteriolar vasomotor tone, and venomotor reactivity .

baroreceptor depression appears at a more moderate level of cooling than does the sympathetic, vasomotor, depression . below 28 degrees c. both are significantly depressed, although probably not totally abolished .

the level of 28 degrees c. is a critical physiological level and may represent an important limit in the clinical use of hypothermia .

.I 126

.W

studies in perfusion hypothermia with special reference to /deep hypothermia/ and circulatory arrest .

1. perfusion hypothermia produces large temperature gradients within

the body since organs are cooled roughly in proportion to their basal blood flows . the difference between the coldest and the warmest portion of the body after 30 minutes of perfusion exceeds 25 c .

2. the average body temperature, which provides a proper measure of total body cooling, may be calculated from the arteriovenous temperature difference and the extracorporeal flow rate .

3. true /deep/ hypothermia is not obtainable by reasonable periods of perfusion alone .

4. an important rise of core temperatures occurs during circulatory arrest in hypothermia because of relatively high average body temperature .

5. high average body temperatures lead to continuing production of lactic acid in muscle tissue, whereas low core temperatures impair lactic acid metabolism . thus metabolic acidosis is progressive in prolonged perfusion hypothermia, and is accentuated by total circulatory arrest . progressive acidosis may be minimized by uniform profound cooling by combining external with perfusion hypothermia .

6 diluents appear to have little effect on total body heat exchange during perfusion cooling .

7. perfusion warming has a differentially greater effect on core organs . though these are readily brought to a normal range, much of the animal may remain cold .

.I 127

.W

application of the emission spectrograph to the analytical needs of the industrial hygiene laboratory .

examples of unique applications of the principles of emission

spectroscopy to industrial hygiene problems are provided . a discussion of qualitative, semiquantitative and quantitative methods of spectrographic analysis is presented . these methods include representative applications which are made for the analysis of the metallic constituents of body tissues and fluids from human and animal subjects, industrial process materials, ores, and environmental dusts and fumes . brief descriptions of sample preparation techniques required for successful analyses are also presented .

.I 128

.W

nickel carbonyl.. its detection and potential for formation .

recent recommendations for control of nickel carbonyl exposures have been considered in the design of a simple, sensitive field method for sampling nickel carbonyl in air and process gases . the method involves collection in dilute aqueous hcl, ph adjustment, nickel complex development with alpha-furildioxime, and extraction with chloroform . color intensity is compared visually (or for greater accuracy, spectrophotometrically) with liquid standards . sensitivities on the order of 0.001 ppm are obtainable . a detailed development of the thermodynamics associated with the formation of nickel carbonyl is also presented to show the maximum concentrations of nickel carbonyl that may be formed over a wide range of co concentrations, temperatures and pressures .

.I 129

.W

polarographic determination of heavy metals in air samples .

the polarograph possesses the required sensitivity and specificity to

make it the method of choice for analysis for a variety of heavy metals in air . two commercial polarographs are compared and both found adequate on the basis of analysis for lead . determinations may be made for antimony, copper, lead, cadmium, chromium, nickel, cobalt, manganese, and others .

.I 130

.W

the inorganic constituents of human teeth and bone examined by x-ray emission spectrography .

x-ray emission spectrography has been applied to study of the elemental composition of human teeth, enamel, dentine and bone . the material consisted of eight crushed teeth, enamel and dentine powder separated from eighteen teeth, and four pieces of buccal cortical mandibular bone . the teeth did not have fillings . the whole material contained nineteen elements, of which the main ones were calcium and phosphorus . in all the samples of tooth material, there were found ca, p, cl, fe, zn, sr and k, and the bone also contained ni . the time needed for a semi-quantitative analysis compares very favourably with that needed for other methods .

.I 131

.W

a kinetic study of nickel(ii), complexes of sulfur-containing amino acid

the rate expression for the ethylenediaminetetraacetic acid (edta) ligand exchange reaction with nickel(cysteine) is.. $\text{rate} = k(\text{complex}) + k_{\text{edta}}(\text{complex})(\text{edta})$. this two-term rate expression is characteristic of square planar complexes and agrees with the square planar configuration of ni(cysteine) reported on the basis of spectral studies

the edta-independent term of the rate expression is an acid-catalyzed term and can be written $k(h)$ (complex). the value of k_n is 2.5×10^6 m sec while the value of k_{edta} is only on the order of 10^{-10} m sec. the edta reaction with $ni(\text{cysteine})$ methyl ester) is very similar to the reaction with $ni(\text{cysteine})$. when the sulfur-containing amino acid ligand contains a thiol ether, the kinetic differences are striking.

ligand exchange reactions of edta, triethylenetetramine, and diethylenetriamine with nickel-methionine complexes are several orders of magnitude faster and give products that are mixed-ligand complexes. the results of this kinetic study of amino acid complexes containing sulfhydryl and thiol ether sulfur groups support other studies at equilibrium which suggest sulfur coordination and square planar complexes for the sulfhydryl groups and octahedral complexes with no sulfur coordination for thiol ethers.

.I 132

.W

the action of metal ions on tobacco mosaic virus ribonucleic acid.

added transition metal ions stabilize the secondary structure of tobacco mosaic virus ribonucleic acid (tmv-rna) as evidenced by a reduction in the absorbancy change of heated nucleic acid solutions. in spite of this stabilization of secondary structure, heating in the presence of metal ions results in the loss of biological activity due to the hydrolysis of phosphodiester bonds. thus, all heavy metal ions of the iib and first-transition elements studied caused a rapid loss of biological activity of tmv-rna at ph 6.5 and 65. calcium and magnesium ions, while not affecting secondary structure at 65 and ph 8.5, caused a rapid loss of biological activity. at ph 5.8 and room temperature lead

ions catalyzed the hydrolysis of rna to i'(3')- mononucleotides,. on long standing, nucleosides were formed .

.I 133

.W

chromium, lead, cadmium, nickel and titanium in mice.. effect on mortality, tumors and tissue levels .

about 700 mice were given throughout their lives 5 ppm cadmium, lead, chromium, nickel or titanium in drinking water while fed a diet deficient in cadmium and low in other metals . tissue concentrations comparable to those of man were observed . sex differences appeared . mortality of females was unaffected . mortality of males on cadmium, lead and nickel was increased compared with that of the chromium group, and of those on cadmium and lead compared with the controls . longevity of the oldest 10 of both sexes was less in lead and titanium groups, and of males in cadmium group, compared with controls . no metal was carcinogenic,. incidence of tumors in males on cadmium and lead, and in females given nickel was decreased . body weights at death were greater in titanium, chromium and lead groups . large increments of titanium, moderate increments of cadmium and nickel, and lesser increments of chromium and lead were observed in 5 organs, compared with controls . higher concentrations of cadmium and titanium occurred in younger mice and the other metals did not increase markedly in tissues with age . all metals except chromium exhibited one or more signs of innate toxicity .

.I 134

.W

synergistic effects between antioxidants and selenium or vitamin e .

several antioxidants when fed to chicks at relatively high levels in

an experimental diet were ineffective in preventing the exudates and mortality from a combined deficiency of selenium and vitamin e . some of the compounds were toxic, as evidenced by sudden death or subcutaneous hemorrhages . when amounts of either selenite or a-tocopheryl acetate, which individually had little or no effect on symptoms, were given with the antioxidants signs of deficiency and mortality were prevented, and toxicity also was eliminated .

.I 135

.W

the expression of urine analysis results -dash observations on the use of a specific gravity correction .

urine analyses are very useful for measuring the extent of exposure to certain toxic substances . the types of specimen obtainable from persons employed in industry, and the effect of concentration variations are discussed . in expressing the results of analysis it is shown that a concentration correction is essential . the correction based on specific gravity is the easiest to apply . the mean specific gravity for persons resident in the u.k. has been found to be around 1.016, a figure considerably lower than the mean of 1.024 used by many workers (particularly in the u.s.a.) . the implications of this on the results of urine analysis are indicated .

.I 136

.W

activation and inactivation of p-hydroxyphenylpyruvate hydroxylase .

1. p-hydroxyphenylpyruvate hydroxylase (ec 1.99.1.14) is reversibly inactivated by dialysis, storage, purification involving ammonium sulfate fractionation, and treatment with oxidizing agents . the

inactive enzyme is reactivated by various reducing agents .

2. metal-chelating agents inhibited enzyme activity . 1,10-phenanthroline and 4,7-diphenyl-1,10-phenanthroline (fe sensitive) strongly inhibited, but 2,9-dimethyl-1,10-phenanthroline (cu specific) did not . 1,10-phenanthroline-treated p-hydroxyphenylpyruvate hydroxylase was reactivated specifically by fe in the presence of a reducing agent, indicating a role for fe in enzyme activity .

3. nonoxidative sulfhydryl reagents did not materially inhibit the enzyme activity under various conditions .

.I 137

.W

responses of *b. subtilis* (atcc 558) to streptomycin .

to observe in detail the influence of streptomycin on the growth of sm dependent type, the author chose *b. subtilis* (atcc 558) and made experiments on its responses to streptomycin, with special reference to the relation of the sm concentration with spore formation of its sm dependent type together with germination and outgrowth of the spores formed . the results are as follows .

1. among 18×10^6 cells of wild type of *b. subtilis* (atcc 558) about 3,200 cells of sm resistant and one cell of sm dependent are found as its mutant .

2. *b. subtilis* (atcc 558) shows normal growth at sm concentration below 10 r/ml, but the growth declines rapidly between sm 10 r/ml-20 r/ml, and the growth stops entirely at sm concentration 20 r/ml .

3. sm resistant type grows well between sm 0.1 r/ml-sm 2,000 r/ml, the growth declines rapidly at about sm 10,000 r/ml .

4. sm dependent type shows normal growth between sm 10,000 r/ml-20 r/ml

l, the growth get worth below sm 10 r/ml, and the cell shape elongates several times, at sm below 1 r/ml each cell becomes filamentous form and has several ten times length of normal cell, as if the cells have stopped to divide at low sm concentration .

6. the germination and outgrowth of spores of the sm dependent type slow down with decline of sm concentration, but the germinated spores grow in normal forms until sm concentration reaches 7.8 r/ml, then the germination becomes much slower, and the cells grow in filamentous forms or irregular forms . at extremely low sm concentration both germination and outgrowth nearly stop .

.I 138

.W

phospholipids of the bovine, rabbit, and human lens .

the phospholipids of bovine, rabbit, and human lenses contain cephalin lecithin, and sphingomyelin but their distribution differs with each species . there is suggestive evidence that there may also be plasmalogen in the lens, but, if so, it represents a minor phospholipid component . the fatty acid composition of each phospholipid differs in each species, with most of the differences centering around 16..0, 18..1, and 24..1 .

.I 139

.W

surgical aspects of heart disease in pregnancy .

the ideal management of the pregnant woman with heart disease is medical, if feasible . the operative experience with mitral valvulotomy in pregnancy has expanded . this procedure is now indicated when progressive cardiac disability develops during the first or second

trimester and when the proven dominant lesion is mitral stenosis . when other lesions are present, especially those requiring pump oxygenator perfusion, the risk must be carefully measured . damage to the fetus may result from reduced placental blood flow .

.I 140

.W

traumatic lesions of the optic chiasma.. a report of four cases .

case histories of four patients who suffered severe head trauma resulting in complete bitemporal hemianopia are presented . the optic chiasm was visualized in only one patient . it was markedly swollen and disintegrated . this appearance was consistent with multiple minute tears of the crossed fibres in the median sagittal plane . other theories to explain the bitemporal field defect are discussed .

.I 141

.W

lung cancer.. an evolutionary approach .

lung cancer is presented as an example of somatic mutation . in contrast to previous theories the following are defined.. (a) the major growth controlling mechanism,. (b) the mutation found in cancer,. and (c) the environmental changes in the lungs of patients who smoke cigarettes which can select this mutant .

.I 142

.W

the effects of electrophoretically separated lens proteins on lens regeneration in *diemyctylus viridescens* .

in the present study, lenses were removed from the eyes of adult anesthetized newts, macerated in 0.03 m borate buffer at ph 8.6, and

separated by starch gel electrophoresis . upon staining with amido black 10-b, seven distinct staining areas appeared in the blocks . three bands moved toward the anode, and three toward the cathode . in addition, a seventh moiety represented by a smear of material moved toward the anode one millimeter times five tenths millimeter plugs were removed from each of these areas and were placed into freshly lentectomized eyes . plugs from most strongly positive and most weakly negative proteins inhibited lens regeneration . in addition, plugs from the area containing the weakly negative protein induced either lenses with aberrant polarity or double centered lenses with centers of opposed polarity . all other protein bands had no significant effect on regeneration .

in addition to the above experiments, homogenates and proteinase digested homogenates of lenses were injected into eyes following lentectomy . three 5- μ l samples were injected in each case over a six day period . injection of the plain homogenate stimulated lens regeneration markedly, while the proteinase destroyed the stimulatory activity .

theoretical considerations of the above data are discussed .

.I 143

.W

enzymic synthesis of deoxyribonucleic acid xviii. the repair of partially single-stranded dna templates by dna polymerase .

a partially single-stranded dna, prepared by limited digestion of each strand with exonuclease iii, can be restored to its native, fully double-stranded structure by escherichia coli dna polymerase . the rate of synthesis observed in the repair of such a partially degraded primer

in the polymerase system is faster than that seen with a native dna . the newly synthesized dna is covalently attached to the primer . the fully repaired dna resembles the original native dna as judged by its appearance in electron micrographs, cscl density-gradient analysis, denaturability and genetic activity . dna synthesis which follows the repair phase produces a structure that is not covalently linked to the primer and resembles, in its nondenaturability, branched appearance, and lack of genetic activity, the product obtained with a native dna primer (schildkraut, richardson + kornberg, 1964) .

.I 144

.W

on the mechanism of genetic recombination in transforming bacillus subtilis .

the molecular fate of transforming dna in competent bacillus subtilis has been studied . the physical differentiation of transforming dna and the genetic material of recipient bacteria was effected by employing the isotopes n and p . competent bacteria labeled with n and p were allowed to incorporate n p-labeled transforming dna intracellularly . dna was isolated from these recipient cells and centrifuged in cesium chloride . analysis of drop fractions collected at equilibrium showed the presence of radioactivity in a region of density corresponding to recipient dna . material contribution from donor dna to the resident dna did not occur when genetically inert bacillus cereus dna was substituted for homologous dna . it was concluded that radioactivity appearing in the unlabeled resident dna was not the result of degradation of input (p)dna and subsequent incorporation by normal metabolic processes . since single-stranded dna of donor origin was not detected, nor was there

evidence for the non-specific aggregation of donor and recipient dna, it was concluded that the observed physical association of transforming and recipient dna occurs as a result of genetic recombination in transformed *b. subtilis* .

.I 145

.W

physical and biological studies on transforming dna .

bacillus subtilis transforming dna prepared by the method described, has an average molecular weight of 11.6 million . the dna is heterogeneous, as judged by chemical composition, thermo-spectral and pyrenographic properties . these properties have been used to fractionate some of the biologically active molecules which show higher specific activities in transforming respective auxotrophs .

.I 146

.W

comparison of mutation and inactivation rates induced in bacteriophage and transforming dna by various mutagens .

inactivation and mutation rates were measured for t4 phages and *bacillus subtilis* transforming dna treated by low ph, nitrous acid, or hydroxylamine at different temperatures . the frequency of mutants increased linearly with time for all three agents, whereas the logarithm of survival gave a linear plot only for nitrous acid and low ph . an arrhenius plot showed the same slopes for both inactivation and mutation rates after treatment with low ph or nitrous acid,. for the latter agent the slope remained unaltered even when the dna was treated in the denaturated state . in contrast, mutation rates obtained after the exposure to hydroxylamine differed greatly for native or denatured dna,

phage t4 being intermediate .

treatment by low ph or nitrous acid interrupted the genetic linkage between tryptophan and histidine, the interrupting hits being about 1/3 as frequent as lethal hits, independent of the temperature .

.I 147

.W

autolysis of bacillus subtilis by glucose depletion .

in cultures in minimal medium, rapid lysis of cells of bacillus subtilis was observed as soon as the carbon source, e.g. glucose, had been completely consumed . the cells died and ultraviolet-absorbing material was excreted in the medium . the results suggest that the cells lyse because of the presence of autolytic enzymes . in the presence of glucose the damage to the cell wall caused by these enzymes is repaired immediately .

.I 148

.W

plasma 17-hydroxycorticosteroids and 17-oxosteroids in patients with breast cancer and in normal women .

(1) 17-hydroxycorticosteroids (17-ohcs) and 17-oxosteroids were measured in the plasma of normal women, patients with early breast cancer and in patients with advanced metastatic disease .

(2) the mean plasma 17-ohcs level was found to be normal in the early stages of the disease but was raised in the advanced disease . in both groups of patients the variance was significantly greater than in normal women .

(3) the mean plasma 17-oxosteroid level in both early and advanced breast cancer was not significantly different from the normal level but

the variance was increased .

(4) there is a significant correlation between the plasma 17-ohcs and 17-oxosteroids in normal women which was not found in the cancer patients .

(5) in patients with advanced breast cancer, the levels of plasma 17-oxosteroids were significantly correlated with the amounts of 11-deoxy-17-oxosteroids found in the urine . there was no correlation between plasma and urinary 17-ohcs .

(6) the physiological significance of these findings is discussed .

.I 149

.W

hormone therapy in metastatic breast cancer.. clinical response and urinary gonadotrophins .

the total urinary gonadotrophin output of a group of post menopausal women with metastatic breast carcinoma undergoing hormone therapy, which in every case initially consisted of treatment with diethylstilboestrol, des (ca. 20 mg/d), has been studied for periods varying from seven months to 31/2 years .

no correlation between gonadotrophin output and clinical response was found, except that in all cases showing objective regression urinary gonadotrophin remained low throughout the remission period . a low level of gonadotrophin output was not, however, necessarily indicative of a good clinical remission . following withdrawal of des, and independent of the period of therapy, recovery to pre-treatment levels was the rule rather than the exception .

a small group of patients maintained on a lower dose of des (3-5 mg/d) showed the same degree of suppression of urinary output as those

receiving 20 mg/d, and several of these exhibited objective remissions .

the study has emphasised the importance of site specificity in the response to hormone therapy, and underlines the difficulties of relating the clinical response of the patient as a whole to changes in hormonal environment .

.I 150

.W

plasma androgens in women i. normal and non-hirsute females, oophorectomized and adrenalectomized patients .

1. in a group of 20 normal non-hirsute females age 17 to 38, 18 non-hirsute patients with varied genito-urinary disorders, 8 oophorectomized and or adrenalectomized patients plasma testosterone was measured by the method of finkelstein et al. (1961) . conjugated androsterone and conjugated dheA were determined by a modified method of migeon + plager (1955) .

2. mean baseline values in normal females were .11 .06 ug/100 ml testosterone, 11.8 5.5 ug/100 ml conjugated androsterone, and 29.5 15.5 ug/100 ml conjugated dheA . no significant response to hcg could be seen dexamethasone affected the conjugated dheA significantly, but did not seem to affect conjugated androsterone or testosterone .

3. the non-hirsute patients showed essentially the same pattern . an effect of dexamethasone on the levels of conjugated androsterone was demonstrated .

4. oophorectomized women had baseline values for the conjugates in the range of normals . testosterone, however, was low with an average of .016 ug/100 ml . in the adrenalectomized patients no androgens were detectable .

.I 151

.W

oophorectomy and cortisone treatment as a method of eliminating oestrogen production in patients with breast cancer .

the urinary excretion of oestrone, oestradiol-17b, oestriol, and 17-hydroxycorticosteroids has been estimated in 55 premenopausal and 91 postmenopausal women with breast cancer at various stages of the disease before therapy . the depletion of oestrogen excretion caused by oophorectomy combined with cortisone treatment was studied in the patients with metastasising breast tumours (32 premenopausal and 56 postmenopausal subjects) .

patients with disseminating breast cancer excreted significantly larger quantities of oestriol than healthy women of the same age, whether pre- or postmenopausal . the excretion of oestrone and oestradiol-17b was similar in cancer patients and healthy women of corresponding age .

oophorectomy reduced the oestrogen excretion not only in premenopausal subjects but also in quite a number of postmenopausal patients, particularly in those who were still excreting significant amounts of oestrogens . this decrease in the oestrogen output was transient and was followed by a compensatory increase, possibly of adrenal origin .

cortisone administered within a month after the oophorectomy at a dosage of 50 mg per day rapidly depressed the secondary rise in the oestrogen output to a level of about 4 to 5 ug/24 h irrespective of the age of the patient . this excretion level was unchanged as long as cortisone was given in an adequate dose, but increased rapidly when the cortisone treatment was discontinued .

oophorectomy combined with adequate cortisone treatment seems to offer an alternative to the extensive surgical procedures undertaken to eliminate oestrogen production in breast cancer patients .

.I 152

.W

some reactions of cytotoxic antibodies against previously unknown mouse isoantigens .

the antiserum produced in c3h/he against c3h/st lymphosarcoma 6c3hed contains a mixture of at least two antibodies of different properties and specificities . anti h-5a is a hemagglutinating antibody removed by absorption with red cells and many tissues . anti v is a cytotoxin reacting with c3h/st tissue and 6c3hed but not with red cells.

the reciprocal antiserum c3h/st anti c3h/he sarcoma mc1m is more complex . it contains the hemagglutinin anti h-6a and a variety of cytotoxins . one appears to be specific for c3h/he tissues and the tumor mc1m . another reacts with antigens on the c3h/go carcinoma bp8. two additional cytotoxins may also be present .

immunization between sublines of the same inbred strain can result in the production of a variety of antibodies directed against unrelated antigens present on even long transplanted cells . the significance of

.I 153

.W

on the value of thymectomy in adult mice as a means of potentiating the immunosuppressive action of melphalan (l-phenylalanine mustard) .

thymectomy has been found to be ineffective as a means of potentiating the immunosuppressive action of melphalan in adult cba-p mice challenged with a-strain mammary carcinoma transplants . this was true when the

thymectomy was performed 2 days, 4 weeks or 7 weeks prior to injection of a single dose (15 mg/kg body weight) of melphalan, administered 24 hours prior to tumour transplantation, and also when thymectomy was combined with multiple doses of melphalan given before and after tumour transplantation . these findings are discussed .

.I 154

.W

studies on the kinetics of transplantation immunity .

using the parameter of the number of tumor cells necessary to produce s.c. tumors in allogeneic animals at varying intervals after antigenic stimulation, immunity was found to be in force as early as 2 days after primary antigenic stimulation . it reached a peak at 8-10 days and had largely subsided by the end of a month . this method was also applied to the quantitative study of the onset, degree, and duration of immunity elicited by skin grafts . the results obtained with inocula of large numbers of tumor cells (10 percent) were comparable to those obtained with massive skin grafts .

the differences in the degree of antigenic stimulation resulting from different routes of inoculation were studied . it was found that the intradermal (i.d.) route of inoculation resulted in a more intense antigenic stimulation than the s.c. route . when both routes of inoculation were used simultaneously the pattern of growth of the s.c. tumor was influenced by the i.d. inoculation.. an i.d. inoculum given 24 or 48 hr earlier caused marked suppression of growth of the s.c. tumor, while when an i.d. inoculation was preceded by an s.c. inoculation, although there was an appreciable effect on the growth size, the growth curves of the 2 tumors were always parallel .

there was no correlation between cytotoxic activity and the degree of immunity in force at a given time .

.I 155

.W

evidence for an immunological reaction of the host directed against its own actively growing primary tumor .

cells isolated from primary benzo(a)pyrene-induced fibrosarcomas in rats of a pure line were tested for their ability to grow as autografts when injected back into the autochthonous host . the autograft did not take if the primary tumor had been removed but grew occasionally in animals in which the major part of the tumor was left . in every instance the sarcoma cells grew when injected into syngeneic recipients in these recipients the growth of the sarcoma cells was prevented or retarded when they were mixed in vitro, prior to injection, with spleen cells from animals that had been immunized against the tumor .

autochthonous spleen cells taken from the animal with the tumor behaved in this test like those from immunized animals as long as the spleen was taken 3 weeks after removal of the tumor . when the spleen and tumor were removed at the same time, however, autochthonous spleen cells did not behave like spleen cells from immunized animals and did not interfere with the growth of the tumor . the results of both the autograft and spleen cell experiments suggest that rats react actively against their own growing primary tumors, but that the tumor exhausts the supply of lymphocytes responsible for this reaction . after the tumor is removed, the concentration of antitumor lymphocytes in the spleen builds up and the animals can reject an autograft .-j nat cancer inst 36.. 29-35, 1966 .

.I 156

.W

a comparison of the cytologic effects of leurosine methiodide and vinblastine in tissue culture .

comparison of the degree and duration of arrest of metaphases in tissue culture cells by leurosine methiodide and vinblastine was made,. colchicine and demecolcine were included for reference purposes . all four drugs produced a similar cytologic effect, but vinblastine was most active and remained active for the longest period of time .

.I 157

.W

comparison of central aortic and peripheral artery pressure curves .

brachial artery and central aortic pressures were compared in 50 consecutive patients subjected to retrograde left heart catheterization in order to re-emphasize the fact that the two pressures are not necessarily identical . in 43 cases the systemic systolic pressure peaks exceeded those in the central aorta while in seven these pressures were equal . the average pressure difference was 22.6 mm. hg . the greatest differences occurred in cases of aortic regurgitation and could be extreme, the brachial artery systolic pressure exceeding that in the aorta by more than 100 mm. hg in some instances . the least differences occurred in cases of aortic stenosis but significant differences occasionally existed, leading to erroneous estimation of valve orifice size if the systemic rather than the aortic systolic pressure was used .

.I 158

.W

changes in sphingosine and fatty acid components of the gangliosides in

developing rat and human brain .

rat brain increases in weight after birth in three stages.. (i) rapidly for the first 2 weeks, (ii) at a lower rate from 2 to 5 weeks, and (iii) at a still lower rate from 5 weeks to 5 months . during the succeeding period, designated iv, it maintains constant weight up to 1 year of age . brain ganglioside content increased linearly during i and ii, more slowly during iii, and diminished during iv . the appearance of measurable amounts of brain sphingomyelin and cerebroside succeeded that of ganglioside .

ceramide with c -sphingosine and c fatty acid was found in a large proportion of all three sphingolipids upon their first appearance in measurable quantity . c fatty acid in cerebroside rapidly declined to a negligible level, while in gangliosides and sphingomyelin it declined slowly but remained the major fatty acid component .

cerebroside and sphingomyelin contained c -sphingosine almost exclusively at all stages of rat brain growth . gangliosides contained c -sphingosine almost exclusively at birth, but subsequently accumulated c -sphingosine until they had nearly equal quantities of each base type .

changes in human brain gangliosides resemble those in rat . in tay-sachs disease, gangliosides have c -sphingosine predominantly, and a high content of c fatty acid .

.I 159

.W

studies of the generalized shwartzman reaction induced by diet vi.
effects of pregnancy on lipid composition of serum and tissues .

pregnancy induced profound alterations in the lipid composition of serum and tissues . (1) there is an elevation of total serum lipid,

phospholipid, triglyceride, free fatty acid and cholesterol,. (2) while the total lipid of the liver and kidney are increased, that of the depot fat is decreased,. (3) palmitate and oleate are increased in serum and liver,. (4) arachidonate and stearate are decreased in serum and liver,. and (5) placentas contain more stearate than the other organs of the pregnant rat and also have a higher water content . the decrease in depot total fat,. elevation of serum, liver and kidney total fat,. and elevation of serum free fatty acids suggest that pregnancy induced mobilization of depot fat . the increase in proportion of liver and serum palmitate suggests that pregnancy induces increased lipogenesis from the acetate pool . the appearance of an increased amount of long-chain fatty acids in the liver may be due to the increased intake of dietary fat . the decrease in arachidonate and stearate in serum and liver suggests a relative decrease in mitochondrial fatty acid synthesis .I 160

.W

electron microscopy of the bovine lung.. the normal blood-air barrier .

lungs of 20 healthy, mature cattle were fixed in osmium tetroxide , embedded in a polyester resin, and studied via electron microscopy . the blood-air barrier was widely variable in thickness and consistency . there was a continuous epithelial alveolar lining . the cytoplasm of some of the epithelial cells contained membrane-bound aggregates of granules which may be secretory structures . the epithelium rested on a basement membrane, which in turn was continuous with or rested on an adjacent capillary endothelial basement membrane, or continued into merging connective tissue . the capillary endothelium was not fenestrated,. it was a continuous cellular membrane . both the epithelium and endothelium

contained numerous caveolae and pinocytotic vesicles . cells of the alveolar wall included fibroblasts, lymphocytes, macrophages, and an occasional mast cell . very little elastin was observed .

.I 161

.W

a sensitive and specific fluorescence assay for tissue serotonin .

a sensitive and specific method for the estimation of serotonin in biological materials is described . in this method, serotonin is reacted with ninhydrin to form a product whose fluorescence is eight times more intense than the native fluorescence of serotonin in strong acid solution . with this method it is possible to measure serotonin in organs in which endogenous serotonin had not been previously detected and to study the subcellular distribution of this amine in the rat pineal and adrenal glands .

.I 162

.W

effects of ruminal insufflation on cerebral circulation and metabolism in the goat .

the effects of nitrogen insufflation of the cannulated rumen were studied in 10 goats . parameters which were measured included cerebral blood flow, mean carotid arterial pressure, pressure in the confluence of sinuses, cerebrospinal fluid pressure, blood oxygen and carbon dioxide contents, packed cell volume (pcv), and hemoglobin concentration values for cerebrovascular resistance and cerebral o utilization were calculated .

increased ruminal pressure had little effect on cerebral blood flow and cerebrovascular resistance . cerebral o utilization was decreased

when the intraruminal pressure was increased . this decrease was caused by a reduction in arterial o content and a consequent decrease in cerebral arteriovenous o difference . mean arterial, venous sinus, and cerebrospinal fluid pressures were increased as the intraruminal pressure was increased . increases in pcv and hemoglobin concentration were not related to the elevated intraruminal pressure .

central nervous system signs in goats with acute ruminal tympany may be caused by cerebral hypoxia . the nature of the hypertensive changes associated with increased ruminal pressure were demonstrated, but due to the influence of multiple factors on fluid compartments, no conclusions could be made about the mechanism of these pressure responses . mechanical factors, however, may be involved .

.I 163

.W

a comparison between inhaled dust and the dust recovered from human lungs .

experiments on the loss of dust particles during breathing indicate total deposition in the respiratory tract,. subjection of the results to qualitative arguments may give information about alveolar deposition . measurements of insoluble dust recovered post mortem from human lungs give the absolute retention of dust which was deposited in the alveoli and subsequently shifted, probably to a large extent, to the lymphatic vessels of the lungs .

experimental results for total deposition and absolute retention are discussed in connection with the health risk due to inhaling insoluble particles, such as plutonium dioxide .

.I 164

.W

dual cation activation of bovine lens autolysis .

the autolytic activity of bovine lens extracts at 55 c. and ph 7.4 has been shown to be markedly influenced by the simultaneous presence of mono- and divalent cations . of the cations tested, na at 2.5 to 5 mm . and mg at 5 to 10 mm. produce the best activation . the stimulation is synergistic . on the basis of results obtained here and in other laboratories, the suggestion is made that this combination of cations may be required for activation of the neutral proteinase of the lens . in the presence of mg and average physiologic lenticular levels of both na and k , autolysis is suppressed to the basal level obtainable in the presence of mg alone .

.I 165

.W

nucleic acid metabolism in the lens iii. effect of x-radiation .

a previous communication reported an increased in vivo incorporation of p-32 into the albuminoid rna fraction of the rat lens 6 hours after the animal had been exposed to x-radiation (1,500 r) .

in the present study, the in vitro uptake of p-32 and c-14-adenine by albuminoid, ribosomal, and soluble rna fractions of normal and x-irradiated rat lenses was measured . the rna fractions were extracted by sodium dodecyl sulfate in 0.9 per cent nacl . the specific rna fractions were also hydrolyzed, chromatographed (on paper), and the activity of the individual nucleotides (as well as the specific rna fractions) was determined . an experiment was also performed in which the capsules were removed (after the 3 hour incubation period) and the activities determined in the nucleic acids extracted from the capsules and in the

three rna fractions of the remaining lens matter .

the results of these experiments indicate that the incorporation of p-32 and c-14-adenine into albuminoid rna was markedly stimulated 1 hour after 1,500 r whole body radiation . there was no significant effect on ribosomal or soluble fractions .

the effect of formaldehyde and heating on x-irradiated albuminoid rna was much less than on the albuminoid rna derived from control animals .

.I 166

.W

changes in dna, rna, and protein synthesis in the developing lens .

lens cell dna, rna, and protein synthesis in the developing mouse eye were studied with the use of tritium-labeled thymidine, uridine, and l-leucine and autoradiographic techniques . in the mouse embryonic lens, epithelial cells undergoing dna synthesis were found over the entire anterior lens surface . from birth and until the eyes opened the percentage of epithelial cells undergoing dna synthesis rapidly decreased . later the percentage of epithelial cells undergoing dna synthesis was nearly constant as the germinative zone became localized in the lens equator region . rna synthesis occurred in all nucleated cells of the developing lens from the embryonic stage until the eyelids opened . with lens maturity the h uridine was incorporated into the rna of only the more superficial cells . a similar pattern of tritium incorporation was seen with h l-leucine .

.I 167

.W

amino acid transport in the lens in relation to sugar cataracts .

the steady state distribution of free amino acids between the lens and

aqueous humor is significantly reduced in diabetic rabbits and also in rats fed rations containing high concentrations of xylose or galactose .

the reduction in the level of amino acids in the lens is apparently a direct effect of the high concentration of sugars, but it is doubtful whether it is related to cataract formation .

.I 168

.W

visco-elastic properties of the lens .

the dynamic visco-elastic properties of human, monkey and rabbit lenses have been measured with a dynamic rheometer . the value for the apparent elastic modulus (young modulus) of the lens was found to be 10^{10} dyne/cm in humans and 10^{10} dyne/cm in monkeys and rabbits . the value for the loss tangent was 0.3-0.4 in the human lens and 0.3-0.6 in rabbit and monkey lenses .

elastic moduli and loss tangents of the lenses showed poor dependence on temperature at 15 -55 c and on frequency of oscillation at 0.01-25 c/s . the lenses showed linear visco-elasticity when the amplitude of oscillation was below 0.02 mm, and they showed nonlinear visco-elasticity when the amplitude exceeded 0.03 mm .

.I 169

.W

carbonic anhydrase distribution in rabbit lens .

the distribution of carbonic anhydrase activity in the mature rabbit lens was determined . the activities in nucleus, cortex, epithelium with anterior capsule, anterior capsule, and posterior capsule were, respectively, 2484 (256), 1571 (87), 545 (93), 159 (39) and 65 (49) moles co /kg wet tissue wt per hr at 0 c . it was concluded, on the

basis of the available evidence, that carbonic anhydrase cannot play a primary role in the cation transport system of the lens .

.I 170

.W

changes in weight and adenosine triphosphate content in the lens of the xylose-fed rat .

xylitol and sorbitol accumulated in the lens of the xylose-fed rat two days before loss of adenosine triphosphate, and cataractous changes, were apparent . the maximum degree of cataract occurred when the level of the polyols was at its highest . regression of cataract was accompanied by decrease in polyol concentration and restoration of the level of atp . the lens of the xylose-fed rat did not usually increase in weight .

.I 171

.W

identification of species-specific and organ-specific antigens in lens proteins .

the species-specific and organ-specific antigens of lens were investigated by gel diffusion and immunoelectrophoresis techniques . it was found that rabbit antiserum to bovine lens showed cross reaction with other bovine tissues . these cross-reacting antigens were the b- - and γ -crystallins . there were two major and a minor organ-specific antigen in lens . both the major antigens had a mobility and were identified as the α -crystallin of lens .

.I 172

.W

an electron microscopic study of wolffian lens regeneration in the adult

newt .

changes in the morphology of cells during the regenerative tissue transformation of the pigmented epithelium of the iris into lens in the adult newt *triturus viridescens* were studied in ultrathin sections using the electron microscope . in addition, quantitative analyses with electron micrographs were performed . the cells of the normal iris are characterized by an abundance of melanin granules, an extensive smooth-surfaced endoplasmic reticulum, and irregular indentations of the nuclear membrane . after lens removal, the first visible changes are detected in nuclei of the mediodorsal iris cells and involve an increase in the number of primary nucleoli . later, the nuclei enlarge and become spherical, and prominent nucleoli appear . these nucleoli can be distinguished from the normal nucleoli by the presence of the granular cortex surrounding the fibrous core . the pigment granules seem to be completely extruded into the intercellular spaces and subsequently taken up by leucocytes . the endoplasmic reticulum disintegrates gradually and finally almost disappears . there is a significant increase of ribosomes in the cytoplasm . later, the cytoplasmic matrix also acquires fibrous elements (about 50 Å wide) of low density, probably corresponding in nature to the main components of a normal lens cell . these and other changes in the transforming cells are discussed .

.I 173

.W

growth of several human cell lines in newborn rats .

when injected intravenously into newborn rats, eight human tissue-cultured cancer cell lines -dash h.ep. 2, detroit 6, j-111, rp 41, rp 212, adeno cx 1, ovary 2, and mac 21 -dash grew progressively in

lung and other organs of more than 50 per cent of the animals and commonly caused death after 5-8 weeks . two other human cell lines -dash the carcinoma h.ep. 1 and the presumably normal amnion b -dash grew less frequently and rarely caused death or illness .

.I 174

.W

the human tumor-egg host system iii. tumor-inhibitory properties of tenuazonic acid .

the fermented broth of a culture of *alternaria tenuis* auct. inhibited the growth of the human adenocarcinoma (h.ad. 1) in the embryonated egg with the aid of studies in the egg-tumor system the active agent was isolated and identified as tenuazonic acid . tenuazonic acid was produced by a number of *alternaria* isolates and by an *aspergillus tamarii* and a *phoma* sp . compared with tenuazonic acid, on a molar basis, about 20 times as much hadacidin or 6-mercaptopurine, 2 times as much azaserine, but only 1/20 as much triethylenemelamine (tem) were required to achieve the same inhibition of h.ad. 1 tumor growth in the egg . tenuazonic acid was more effective against h.ad. 1 than against another transplantable human tumor, a-42 . tenuazonic acid, compared with puromycin, more specifically inhibited tumor growth in the egg-tumor system .

.I 175

.W

the occurrence of biologic crystals in tumor and nontumor cultures of c3h/hej mice .

crystalline structures of various types have been found in primary tissue cultures of neoplastic and non-neoplastic tissues from c3h/hej

mice . all of the cultures of mammary carcinoma tissue contained the crystals . the crystals were found in varying incidence in the cultures of several other tissues with the exception of those from the kidney . a 'dialysis compartment' was not essential for the formation of the crystals . the development of the crystals was accelerated by a modification of the culture medium .

.I 176

.W

a comparison of the fine structure of cultured mac-21 and hela cell .

the fine structure of a cultured mucoid adenocarcinoma cell of human lung (mac-21) is described and compared with the fine structure of the hela cell . the differences in fine structure between the two strains are primarily quantitative . the mac-21 cell differed, however, in the following respects.. a spindle-shaped cell with larger nucleus and increased nuclear membrane invaginations, and considerably larger amounts of perinuclear golgi apparatus . the cytoplasm contained areas of low density, undefined by a limiting membrane, which are thought to be accumulations of mucin .

the two cell strains contained numerous multivesicular bodies, some with lamellae in various stages of development, suggesting that these organelles may be involved in the formation of the lipide-rich, myelinated structures observed in both hela and mac-21 cells . the number of myelinated bodies was found to be inversely proportional to the ph of the medium .

.I 177

.W

effect of parathyroid and other human tumors and tissues on bone

resorption in tissue culture .

mouse calvaria were grown in tissue culture in combination with single or multiple fragments of a variety of human tumors and glandular tissues to determine their capacity to enhance bone resorption . single fragments of parathyroid adenoma tissue consistently enhanced resorption in both the frontal and the parietal bones . except for one squamous-cell carcinoma of the lung which had some activity all other tissues tested as single fragments had no enhancing effect . on the other hand, all human tissues enhanced resorption when multiple fragments were placed in a halo around the calvarium, suggesting the presence of lesser amounts of resorption-enhancing factors in other human tissues .

.I 178

.W

limited growth period of human lung cell lines transformed by simian virus 40 .

summary--infection of human cell strains with simian virus 40 induced virus replication and cell transformation with the changes in morphology and cytology described by previous investigators . although transformation greatly enhanced growth potentials of the strains, only 2 of 23 transformed cultures appear to have attained autonomous growth.--j nat cancer inst 33.. 227-236, 1964 .

.I 179

.W

bacteriophages that lyse mycobacteria and corynebacteria, and show cytopathogenic effect on tissue cultures of renal cells of cercopithecus aethiops.. a preliminary communication .

bacteriophages isolated from sputum and resection specimens of pa-

tients suffering from carcinoma of the lung were found to lyse corynebacteria and mycobacteria, and to produce a cytopathogenic effect on certain cells in tissue cultures . from the same and other patients with neoplastic disease, bacteria were isolated and described as coryne-mycobacteria because of bacteriological features they shared with both species . these bacteria, which either were sensitive to mycobacteriophages and corynebacteriophages or were phage-immune lysogenic bacteria, could be induced to produce lytic particles with phagolytic activity on corynebacteria and mycobacteria and a cytopathogenic effect on hela cells and on the renal cells of cercopithecus .

.I 180

.W

gel filtration of the soluble proteins from normal and cataractous human lenses .

the soluble proteins of normal and cataractous lenses were separated according to their molecular size on the polysaccharide gel sephadex g-100 . in cataractous as well as in normal lenses 4 different components were obtained . during the evolution of cataract there is a preferential decrease of the low molecular weight proteins of the lens . these disappeared completely in mature and hypermature cataract . on the other hand, the proteins of high molecular weight (e.g., -crystallin) are very resistant to the pathological process . the electrophoretic pattern of the low molecular weight proteins in the normal lens revealed several fractions distributed over a large mobility area . after immunoelectrophoresis, 3 different precipitin lines were obtained .

.I 181

.W

the insoluble proteins of bovine crystalline lens .

the insoluble lens proteins, the albuminoids, of the adult bovine lens

cortex can be rendered soluble by raising the ph of their washed

suspension in 0.9 nacl to 10.5 and then reducing it again to ph 7.4 .

the sedimentation constant of the dissolved protein is 10.8 s, . its

molecular weight is estimated to be 360,000 12,000 . the amino acid

composition is approximately the same as that of the soluble -crysta-

llin fraction, a kinship which is also apparent from their immunochemi-

cal properties . it is suggested that the initial insoluble protein is a

molecular aggregate of -crystallin, which is dissociated in alkaline

solutions to molecules exhibiting a sedimentation constant of 10.8 s .

.I 182

.W

glucose 6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase

in lens and blood of different species .

the activities of glucose 6-phosphate and 6-phosphogluconate dehydro-

genase were measured in the lens and erythrocytes of man and several

other species . there is a wide variation between individuals of the

same species, but there seemed no correlation between the activity of

either enzyme in the lens and their activity in the erythrocytes of the

same species . there is a wide range of activity of both glucose 6-phos-

phate dehydrogenase and 6-phosphogluconate dehydrogenase in the lens and

in the blood of different species . several species had glucose 6-phos-

phate dehydrogenase activity in erythrocytes below the level considered

/deficient/ in man . the sorbitol content of the lens was not correla-

ted with glucose 6-phosphate dehydrogenase activity .

.I 183

.W

nucleic acid metabolism in the lens iii. effect of x-radiation .

a previous communication reported an increased in vivo incorporation of p-32 into the albuminoid rna fraction of the rat lens 6 hours after the animal had been exposed to x-radiation (1,500 r) .

in the present study, the in vitro uptake of p-32 and c-14-adenine by albuminoid, ribosomal, and soluble rna fractions of normal and x-irradiated rat lenses was measured . the rna fractions were extracted by sodium dodecyl sulfate in 0.9 per cent nacl . the specific rna fractions were also hydrolyzed, chromatographed (on paper), and the activity of the individual nucleotides (as well as the specific rna fractions) was determined . an experiment was also performed in which the capsules were removed (after the 3 hour incubation period) and the activities determined in the nucleic acids extracted from the capsules and in the three rna fractions of the remaining lens matter .

the results of these experiments indicate that the incorporation of p-32 and c-14-adenine into albuminoid rna was markedly stimulated 1 hour after 1,500 r whole body radiation . there was no significant effect on ribosomal or soluble fractions .

the effect of formaldehyde and heating on x-irradiated albuminoid rna was much less than on the albuminoid rna derived from control animals .

.I 184

.W

an investigation of mitotic control in the rabbit lens epithelium .

a water soluble substance which inhibits mitosis in the rabbit lens epithelium has been found to be present in young and old rabbit lenses . it has a high molecular weight and is relatively stable at room tempera-

ture . the inhibitory factor is associated with the γ -crystallin fraction and exists throughout the young lens, although the activity in the nuclear region (on a wet weight basis) is less than half that of the cortex and epithelium .

.I 185

.W

the identification of lysosomal enzymes in bovine lens epithelium .

biochemical studies are described for the isolation of lysosomes (identified as such by the activities of their enzymes) in the cells of the bovine lens epithelium . the various fractions assayed for lysosomal enzymes showed contamination of mitochondrial and soluble cytoplasmic material in the two isolation procedures employed .

.I 186

.W

protein synthesis and polyribosomes in the calf lens .

a cell-free system capable of incorporating amino acid into protein has been isolated from calf lens . polyribosomes have been shown to be present in the ribosomal fraction and to be responsible for most of the protein-synthesizing capacity of this fraction . the polyribosomes have been examined by electron microscopy and appear to be composed of long strands of ribonucleic acid, ranging from 7,000 a to 20,000 a, and containing a large number of ribosomes with an average diameter of about 140 a .

.I 187

.W

measurement of oxygen tensions in cerebral tissues of rats exposed to high pressures of oxygen .

brain and cerebrospinal oxygen tensions have been measured in rats breathing air or in various high pressures of oxygen (ohp) . addition of 5 percent co₂ to the inspired oxygen raised cerebral oxygen tensions when rats were exposed to 2 atm abs or above . inhibition of 75 hemoglobin saturation by para-aminopropiophenone lowered cerebral po in rats breathing air, but not in rats exposed to ohp . the rate of rise of cerebral po to a steady level after rapid compression was found to be faster than the rate of fall to a steady level following decompression . addition of co to the inspired gas mixture increased the rate of rise of cerebral po . the anesthetics urethane and pentobarbital sodium did not affect cerebral po in rats breathing air or oxygen at 4 atm . the results are discussed in relation to factors contributing to oxygen poisoning at high pressures .

.I 188

.W

release of free fatty acids from adipose tissue obtained from newborn infants .

summary the role played by mobilization of free fatty acids (ffa) from adipose tissue in producing the typically high serum ffa levels of human infants has been studied . ffa concentrations in the serum and subcutaneous adipose tissue from the gluteal region were determined during postnatal development . a maximum level was reached within 24 hr after birth, after which there was a gradual fall . in serum the ffa level at the end of 12 months was still higher than that in adults, while the ffa level in adipose tissue was lower at 3 months than in adults .

incubation of small pieces of adipose tissue in krebs-ringer phosphate buffer containing 4 albumin led to release of ffa into the medium . this

release could be suppressed by the addition of glucose (200 mg/100 ml)
for tissue from all age groups except the youngest (0-15 hr after birth)

.I 189

.W

detection of pericardial effusion by radioisotope heart scanning .

a marked difference between the cardiac silhouette on the six-foot chest roentgenogram and the cardiac blood pool, determined by radioisotope scanning, has been shown to be consistent with pericardial effusion and/or thickening . it has also been observed that the cardiac blood pool is separated from the liver margin by the interposition of pericardial fluid and/or thickening . this separation was not demonstrated in the presence of a normal pericardium . to appreciate these features, 400 c. of radioiodinated human serum albumin and 50 c. of colloidal radiogold were used for scanning . the former outlined the blood pool and the latter demonstrated the position of the liver .

.I 190

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on the mechanism of erythropoietin-induced differentiation iv. some characteristics of erythropoietin action on hemoglobin synthesis in marrow cell culture .

some of the characteristics of the erythropoietin stimulation of hemoglobin synthesis by rat marrow cells in culture have been studied . the relationship between cell number and rate of hemoglobin synthesis at various levels of erythropoietin is sigmoid rather than linear suggesting a cooperative action among the sensitive cells . the magnitude of the erythropoietin effect on the cells increases with time of contact with the hormone,. at the time of one-half maximal effect there is no discer-

nible loss of erythropoietin from the culture medium . a previously described lag time in the response to erythropoietin appears to be largely due to the conditions of culture and disappears when the cells are pre--incubated for 9 h . replacement of a large fraction of the medium at 24-h intervals enabled the cells to continue hemoglobin synthesis for an additional 24 h .

.I 191

.W

the occurrence of megakaryocytes in the peripheral blood of dogs .

a study of megakaryocytes in buffy coat smears from 26 dogs revealed that no unusual characteristics were consistently associated with appearance of megakaryocytes in the peripheral blood .

.I 192

.W

moderate hypothermia in man.. haemodynamic and metabolic effects .

studies were performed on four patients undergoing intracranial operation during the induction and reversal of surface hypothermia to 30 c .

oxygen uptake decreased an average of 26 per cent from 34 to 30 c to a

mean value of 48 per cent of predicted basal uptake . at the same time,

cardiac output decreased only 11.5 per cent, resulting in a consistent

rise in calculated mixed venous oxygen saturation from a mean of 76 to

81 per cent at 30 c . as a result of this and the effect of cooling on

oxygen dissociation, the estimated tension of oxygen in mixed venous

blood remained virtually unchanged . when shivering was allowed to occur

in two patients, oxygen uptake increased approximately 50 per cent

without any concomitant increase in cardiac output . observed right

atrial and svc oxygen saturations correlated well with calculated mixed

venous oxygen saturations with regard to direction and magnitude of change with change in temperature .

.I 193

.W

the spectrum of lupus nephritis .

fifty cases of sle have been collected over a ten year period and the incidence and clinical picture of ln reviewed in the light of other published data .

lupus nephritis, like sle, has a variable pattern of its own with a wide spectrum of renal involvement -dash evaluation of therapy and prognosis will have to be conducted against this background .

lupus nephritis may present as a renal syndrome only, without any of the other manifestations of sle .

renal involvement in sle is common, but this does not necessarily indicate a poor short-term prognosis . in the peter bent brigham hospital series a sustained raised blood pressure and the onset of renal insufficiency influenced the prognosis adversely .

.I 194

.W

comparison of ultraviolet sensitivity of bacillus subtilis bacteriophage spo2 and its infectious dna .

deoxyribonucleic acid extracted from a clear plaque mutant of the temperate phage, spo2, was infectious when incubated with competent cultures of bacillus subtilis 168 m . the relationship between numbers of infectious centers and dna concentration was linear .

the sensitivity of the infectious dna to ultraviolet light was much greater than that of the free phage when b. subtilis 168 m was used as

host . acriflavin, which inhibits host cell reactivation, increased the rate of ultraviolet inactivation of the free phage so that it approached the inactivation rate of the phage dna . acriflavin had little effect on the survival curves of the infectious dna .

non-host reactivating mutants (hcr) of b. subtilis 168 m were isolated . the survival curves of spo2 phage were much steeper when the hcr mutant was used as a host than those obtained when the hcr parental strain was used as a host .

ultraviolet sensitivity of the phage dna was still greater than that of the free phage even when b. subtilis hcr was used as host, but the difference in sensitivity was much less than the difference obtained with b. subtilis hcr as a host .

possible explanations for the greater ultraviolet sensitivity of the infectious dna are discussed .

.I 195

.W

the isolation and morphology of some new bacteriophages specific for bacillus and acetobacter species .

the best natural habitat for bacteriophages is probably a semi-solid medium containing actively dividing host bacteria . such conditions are provided for bacillus and acetobacter species in rotting grass and apples, respectively . the bacillus phages found included one with a large head and a contractile tail, and also a so-called killer particle, which had a 350 a head and a long contractile tail . this particle had the property of killing but not multiplying within a sensitive cell . a new morphological type of virulent bacillus phage was also isolated,. its head was oblong and the tail consisted of a short needle and a plate

the one acetobacter phage found resembled coliphage t3 but was of particular interest because of the prominence of the head capsomeres and the three-pronged tail .

.I 196

.W

characterization of bacillus subtilis bacteriophages .

brodetsky, anna m. (university of california, los angeles), and
w. r. romig . characterization of bacillus subtilis bacteriophages .
j. bacteriol. 90..1655-1663. 1965.--a group of six phages, sp5, sp6, sp7, sp8, sp9, and sp13, which use the marburg strain of bacillus subtilis as host was characterized . these phages, referred to as group 1, were examined for the following properties.. host range, plaque morphology, stability, adsorption kinetics, one-step growth characteristics, calcium requirements, serum neutralization, thermal inactivation, and inactivation by ultraviolet irradiation . five unrelated b. subtilis phages, sp3, sp10, pbs1, sp alpha, and sp beta, were included in the studies . when first isolated, none of the group 1 phages was able to replicate efficiently on b. subtilis sb19, a mutant of the /transforming / b. subtilis 168 . host range mutants capable of growth in sb19 were isolated for all of the group 1 phages except sp13, and are designated the /star/ phages (sp5 through sp9) . for characterization, sb19 was used as host for the star phages, and another b. subtilis mutant, 168b, was host for sp13 .

.I 197

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transduction in bacillus subtilis .

(i) comparative examinations have shown that the temperate subtilis

phages can be divided into two groups . b. subtilis strain nrs 231 was an adequate common host sensitive to all the examined temperate phages .

owing to certain technical advantages this strain was found suitable for the titration subtilis phages .

(ii) some cultural differences have been revealed among substrains of b. subtilis 168 ind auxotrophs maintained in various laboratories . cells in one of these cultures were partly capable and partly incapable of using ammonia . ammonia assimilation was transducible to ammonia negative bacteria .

(iii) after mitomycin c or ultraviolet ray induction the examined b. subtilis strains liberated /bacteriocin/-like principles . this finding is probably analogous to that of seaman et al. concerning pbsx defective phages . on the basis of bacteriocin production the examined strains were divided into two groups .

(iv) several temperate phages isolated in our laboratory were presumably identical with phage pbs 1 . phage sp 10 differed from these agents both in antigenic structure and in host range .

(v) transduction by some lysates of pbs 1-type phages was observed at frequencies of the order of 10^{-6} . considerably more and less effective phage materials were yielded by some lysogenic transductants . thus transducing phages active in the order of 10^{-6} were prepared .

(vi) transduction frequency, in addition to the properties of the phage, was influenced by the physiological condition of bacteria .

(vii) transduction of indole and histidine loci was studied by use of his derivatives of strain 168 ind .

.I 198

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the carrier state of bacillus subtilis infected with the transducing bacteriophage sp10 .

bacteriophage sp10 may infect bacillus subtilis to form a carrier system . the infected bacteria give rise to infected organisms after six or more successive single-colony isolations . about 60 of the spores derived from such an infected culture yield clones that produce phage, and such spores retain their ability to produce phage even after treatment with antiserum and heating at 80 . four hours' incubation of carrier spores in nutrient broth yields cultures having more than 10 infective centers per bacterium . cultivation of infected organisms in medium containing sp10 antiserum leads to loss of phage and loss of immunity to phage infection . dna with a density characteristic of viral dna can be detected in infected bacteria . extracts of infected bacteria contain a phage-induced deoxyribonuclease activity which attacks both phage and bacterial dna in vitro . the phage-bacterial complex is therefore best described as a carrier state .

the dna of the phage and of b. subtilis are chemically different . enzymatically prepared complementary virus rna has no homology with bacterial dna . the lack of homology of this transducing phage dna with the dna of its host and the failure to form a truly lysogenic relationship reinforce previous conclusions that transducing bacterial dna is incorporated into the sp10 virus particle without any recombination between viral and bacterial dna .

.l 199

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infectivity of dna isolated from bacillus subtilis bacteriophage, sp82 .

sp82, a newly isolated bacteriophage of bacillus subtilis, is

described . sp82 is closely related to sp8, but differs from sp8 in the density of its denatured dna and in its plating efficiency on b. subtilis strain sb-1 .

dna isolated from this phage can be recovered in molecular weight equivalent to the amount contained in a single phage (approximately 130×10 daltons) . dna of this molecular weight, but not half pieces, is infective in competent b. subtilis . the response of plaque-forming ability to dna concentration suggests that four whole molecules are required to initiate an infective center . recombination studies with mixed dna's of two non-allelic temperature-sensitive mutants confirm the existence of an obligatory co-operative infective process . a second infective procedure that utilizes extracted phage dna is described . in this system, low concentrations of wild-type dna are exposed to the cells . at these concentrations the multiple-event nature of phage dna infection precludes the formation of unaided plaques . however, by subsequently superinfecting the dna-infected cells with a temperature-sensitive mutant and plating under selective conditions, genetic rescue of the infecting dna is accomplished and detected . infective centers elicited by this /marker rescue/ phenomenon are directly proportional to dna concentration . the time of attainment of dnase resistance by phage dna infective centers that have irreversibly adsorbed dna can be measured . phage dna infective centers require at least 13 minutes to become totally dnase resistant . the reasons for the failure of single phage dna molecules to carry out an infection are discussed in terms of a specific breakage-reunion

.I 200

.W

psychology of children's dental treatment .

the communication deals with influences involved in the development of the child's attitude to dental treatment . they are extrinsic (educational etc.) and intrinsic (constitutional and hereditary) . their understanding helps to determine the correct psychological policy for the management of the child in the surgery .

the aim of psychology applied in dentistry is to discover a mode of treatment procedure which would ensure that the child will not be subject to any psychic traumatization (psychophylaxis) . its second aim is the management of the so called difficult child and his treatment .

to understand better the child's frame of mind during dental treatment the situation in the surgery is dealt with step by step as the child experiences it through his senses and his psyche . beside the basic senses -dash hearing and seeing -dash others are also affected.. touch (pressure sensation), smell and taste .

children during dental treatment are nearly always in a state of raised emotional tension and are susceptible to anxiety reactions . according to the degree of fear which they manifest children may be classed into categories of cooperating and difficult patients . the psychological procedure for the treatment of children of both groups is based on the principles summarized in the section 'psychophylaxis in dentistry' . in difficult children it is often necessary to employ yet other psychological measures-psychotherapy, suggestion etc . in extremely exacting cases premedication helps sometimes to find contact with the child .

the experimental part of the work demonstrates the following findings

1. dental treatment consists of a series of interdependent

traumatizing impulses . many of them appear only after a close analysis of the situation . 2. the adverse response similar to that elicited by pain may be due also to sensory impressions with a negative emotional background . 3. psychic traumatization of the child during dental treatment can be prevented by relatively simple psychological measures .

.I 201

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relation of emotional changes during pregnancy to obstetric complications in unmarried primigravidas .

this study was designed to assess the psychological changes experienced by white unmarried primigravidas during pregnancy, the relationship between manifest anxiety and clinical factors such as labor time and mean birth weight, and the personality differences between /normal/ and /abnormal/ obstetric cases . the kent ege intelligence scale, the taylor manifest anxiety scale, and the mmpi were administered to 160 obstetric patients at the beginning of the third trimester of pregnancy, with the mmpi and taylor being readministered post partum . reliable group personality changes observed from pre- to postdelivery supported the contention that pregnancy is a time of emotional upset .

following delivery, each patient was classified as normal or abnormal dependent on the clinical course of parturition, delivery, and condition of the offspring . there were no significant differences between these groups with respect to age or intelligence . reliable differences were found, however, for manifest anxiety and total labor times . in addition, a positive relationship was found between manifest anxiety and birth weights . personality differences found at predelivery between the subgroups were largely attributable to the abnormal group's greater

neuroticism, anxiety, and use of the ruminative ego defenses .

post partum, the personality characteristics of the subgroups were quite similar . both groups showed greater personality stability following delivery, with the most striking changes from predelivery demonstrable in the abnormal group . the magnitude of these changes were interpreted as emotional lability and related to obstetric complications by activation of various physiological regulator systems .

.I 202

.W

stranger and separation anxiety in infancy .

anxiety responses to strangers and to separations from mother were studied longitudinally in 19 infants between the ages of three and 23 months by direct observations and by interviews with the mother .

benjamin's hypotheses concerning the differentiation and immediate dynamics of infantile stranger and separation anxiety were supported by the findings . differences in onset, period of highest intensity, termination, and ratios in individuals were found between the two anxieties . tests of the relationship between the two anxieties were supportive of deductive predictions made by benjamin . sex differences in intensity of the two anxieties were found .

.I 203

.W

mental retardation related to hypercalcaemia .

for more than 20 years a number of retarded children and adolescents have been observed who show points of striking similarity . we recognise in them a well-defined type that is clearly distinguishable from other forms of mental deficiency . they are therefore described in detail .

some of the children have had infantile hypercalcaemia but it is assumed that other aetiological factors are also involved .

there is a characteristic facies and usually congenital heart disease ordination is poor . there is a constant failure to thrive in infancy, with episodes of vomiting, often with constipation . mentally the children also show great similarities . their iq is about 40-50 but they show outstanding loquacity and a great ability to establish interpersonal contacts . this stands against a background of insecurity and anxiety .

.I 204

.W

psychological effects of circumcision .

in order to evaluate the psychological effects of circumcision, a small study was arranged in which twelve children, from average and low socio-economic level, were given goodenough dam test, cat, rorschach and two sets of stories, prior to the operation and following it . the results of the tests showed that circumcision, performed around the phallic stage is perceived by the child as an act of aggression and castration . it has detrimental effects on the child's functioning and adaptation, particularly on his ego strength . by weakening the controlling and defensive mechanisms of the ego, and initiating regression, it loosens the previously hidden fears, anxieties, and instinctual impulses, and renders a feeling of reality to them . what is expressed following the operation is primitive, archaic, and unsocialized in character . as a defensive control and protection against the surge of the instinctual forces coming from within and the threats coming from outside, the ego of the child seeks safety in total

withdrawal, thus isolates and insulates itself from disturbing stimuli .

the results of the study raised some questions concerning certain psychoanalytic formulations, for which further research was suggested . possibilities for future research were also discussed .

.I 205

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changes in children's behavior after hospitalization some dimensions of response and their correlates .

changes in 387 children's behavior following hospitalization were evaluated by means of a questionnaire sent to parents a week after discharge . factor analyses revealed that children's responses to hospitalization and illness were of six types.. (i) general anxiety and regression, (ii) separation anxiety, (iii) anxiety about sleep, (iv) eating disturbance, (v) aggression toward authority, and (vi) apathy-withdrawal . scores for these six factors (types of responses) as well as a total score, were analyzed by univariate and, in most cases, multivariate analyses of variance . four variables -dash sex, prior hospitalization, degree of pain experienced during hospitalization, and birth order -dash were essentially unrelated to any type of response by any analysis . age, duration of hospitalization, and occupational status were each significantly related to one or more types of responses . comparison of the mean factor and total scores for the full sample with the levels indicative of no overall change indicated that the combination of illness and hospitalization is a psychologically upsetting experience for children in general, resulting in increased separation anxiety, increased sleep anxiety, and increased aggression toward authority .

.I 206

.W

isozymes of lactic dehydrogenase.. sequential alterations during development .

applications of isozymes in various biological contexts have been reviewed . diagnosis of several disease states has been facilitated by examination of the serum isozyme pattern which has been shown to correlate in some conditions with the isozyme pattern of pathologically involved tissues . physico-chemical studies of human Ldh isozymes have revealed differences among isozymes in affinity for a given substrate . comparative studies of Ldh isozymes within the erythrocyte from various vertebrate species demonstrated a marked species variation in the number of Ldh isozymes, in the distribution of total Ldh activity among them, and in their electrophoretic mobilities . during development of chick, rabbit, and human tissues characteristic sequential alterations in the Ldh isozyme pattern occurred and consisted for liver and muscle in loss of the most rapidly migrating anodal bands and increased activity in the cathodal bands and slower migrating anodal bands . in heart the reverse changes were observed . if high enough Ldh activities of early fetal tissue extracts were applied to the gel the full complement of Ldh isozymes was observed,. however, in lower concentrations the cathodal bands, which in the starch gel disappear more rapidly on dilution than do the anodal bands, were not observed . a species-specific isozyme pattern is obtained in long term culture of rabbit, chick, and human cells . independently of the tissue of origin, there occurs in cells in culture a sequential series of isozyme alterations characterized by decreased intensity of rapidly migrating anodal bands . the shift toward

prominence of cathodal isozymes during both fetal development and tissue culture can be explained by postulating the increased activity of the gene producing one of the subunits of ldh with a concomitant decrease in the activity of the gene producing the second subunit . practical applications of the study of isozymes in tissue culture were discussed .

.I 207

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establishment of a cell line in vitro from a case of human lung cancer .

1) one cell line has been established from the pneumonectomized specimen of a case with lung cancer, which was diagnosed as undifferentiated cell carcinoma and partially adenocarcinoma by its histological findings and was characterized with intracytoplasmic fat droplets in them .

2) the morphological changes of the cells were repeated but they have been stabilized to their epithelial shapes after the 35th transfer . the cell atyp of the culture was remarkable . phagocytosis of the cell line has not been observed . it was characterized that the intracytoplasmic droplets found in the original cancer cells have been maintained in the cultured cells, even in their mitotic stage, throughout the cultural course .

3) concerning the chromosomal constitution diploid cells were only 15 per cent . the range of chromosome number did not show sharp peak, forming two groups of near diploid and near tetraploid ranges .

4) transplanting the cell to cheekpouches of golden hamsters, the implanted cells grew from the inoculum of 10 cells in conditioned animal but did not show the invasiveness to neighbour tissue and metastasis to other organs .

.I 208

.W

factors influencing development of tumors in frogs .

(1) study of 75 spontaneous tumors of vermont frogs showed three pathological grades of malignancy present.. aggressive renal adenocarcinoma in some 30 per cent, medium adenocarcinoma in 50 per cent, and lower grade mixed with tumors of undetermined origin in the remaining 20 per cent .

(2) correlation with parasite infections (trematodes) was demonstrable in only few cases in the kidney . hyperplasias and neoplasias grading into lung primary carcinoma have been found in the lung in r. pipiens . temperatures below 15 c. protected animals from lung as well as kidney disease . higher temperatures disturbed the host-parasite relationships and led to higher incidence of malignancy . in the bullfrog, precancer was clearly associated with the worm attachment discs .

(3) other histological types of tumors in vermont frogs included lymphosarcomas, liposarcoma, mesothelioma, epithelioma, and adrenal and cartilage tumors of uncertain malignancy .

(4) improved methods of obtaining tumor filtrates allowed greater probability of inducing malignancy with direct renal injection . in 106 frogs 37 per cent developed histologically provable cancers in the ranges of three to seven months . twenty-six per cent showed some pre-cancer response and 43 per cent were negative . within the series receiving filtrate from high malignancy donors one group yielded 100 per cent positive, the others 50 and 38 per cent, respectively .

(5) among animals injected with /low/ malignancy filtrate, fewer tumors resulted . some of these were clearly vesicular carcinomas and

could be classed as lung tumors .

(6) improved tissue culture methods allowed explants to live in liquid media under perforated cellophane up to one year . slower growth, aided by lower temperatures (16 c.) improved the microecology of cell types and allowed detailed daily observations of each cell's intranuclear and intranucleolar physiology for extended time-lapse cine-photography .

(7) mechanisms for malignant transformation are related to increased activity and production of nucleolar dna and rna . the infective dna hypothesis is not classical virus theory, but it does offer detailed support .

.I 209

.W

mitotic lymphocytes in primary tissue cultures of normal and neoplastic human lung .

normal and tumor tissue explants from 33 resected human lungs were studied in vitro . lymphocyte mitoses were observed in tissue cultures derived from 12 of the lungs . the ability of lymphocytes to undergo mitotic division in human lung tissue culture has not been reported previously . in the autologous systems used lymphocyte mitoses were much more common in cellular outgrowths derived from non-neoplastic tissue than they were in the outgrowths derived from cancer-bearing explants . no differences were observed in the total number of nondividing lymphocytes present in the non-neoplastic and neoplastic preparations . the in vitro systems employed are promising tools for further contributions to an already well established clinicopathologic relationship between lymphocytes and cancer cells .

phase contrast and time-lapse cinephotomicrographic records were

obtained of the mitotic process and special attention was paid to the structural details . certain findings were of particular interest, namely the formation of a dense chromatin ring during telophase, the variable occurrence of cytoplasmic bubbling, and the death of lymphocytes during early metaphase (/exploding/ metaphase) . an elaboration and discussion of these findings have been presented .

.I 210

.W

studies on transformation of syrian hamster cells by simian virus 40 (sv40).. acquisition of oncogenicity by virus-exposed cells apparently unassociated with the viral genome .

lines of syrian hamster lung and liver cells originally exposed as primary cultures to large doses of sv40 exhibited increased growth rate, high plating efficiency, morphological transformation, and, in some instances, oncogenic potential after unusually long intervals . in at least two lines acquisition of oncogenic potential occurred independently of morphological transformation . in none of a total of 11 cell lines studied in detail was conclusive evidence for the presence of the sv40 genome obtained .

.I 211

.W

eye and kidney tissue reactions to heterologous anti-uveal antibodies .

the uvea, lens capsule and kidney glomerulus in the albino wistar rat have a common antigenic component(s) . the uvea and lens capsule in the pigmented bovine eye also have a common antigenic component(s) . these results were demonstrated by the immunofluorescence technique . the common antigenic sites in the uvea were assumed to be the basement

membrane surrounding the vascular trees in the tissues . the possibility of the basement membrane participation as an antigenic source for inducing sympathetic ophthalmia is discussed .

.I 212

.W

experiments dealing with the role played by the aqueous humor and retina in lens regeneration of adult newts .

1. these three groups of experiments involve approximately 140 eyes of adult newts, *triturus v. viridescens* . they were devised to examine what, if any, role the aqueous humor plays during lens regeneration from the dorsal iris .

2. many daily injections of aqueous humor from normal eyes were made in lentectomized eyes for as long as 96 days in some cases . as controls some lensless eyes were daily injected with holtfreter's solution . in others aqueous humor was merely withdrawn .

3) procedures for the injection experiments are difficult to control . however, the most successful cases showed varying degrees of inhibition and retardation of lens regeneration .

4. pairs of eyes were united at large adjacent wound openings to provide a common reservoir of aqueous humor bathing both lenses and dorsal irises . in some cases the eyes were placed on the side of the body . in others more successful unions were made by fusing a transplanted eye to the right eye of a host .

5. approximately three months after operation one of two large lens regenerates in a pair of perfectly fused eyes was removed . six weeks later a new large lens regenerate reappeared in most of the lentectomized units in the presence of the intact lens of the other unit

6. there is a strong possibility that the more than normal amount of neural retina present provided a more powerful retinal factor for lens regeneration than the inhibiting influence of the intact lens in the environment .

.I 213

.W

correlation between the mast cells and histamine content of the eye in cattle .

the authors have examined the mast cell content of the eyes of cattle and have established that most of the mast cells are contained in the conjunctiva, the optic nerve and the ocular muscles,. fewer occur in the sclera and iris, and least in the ciliary body and choroid . cornea, lens and retina do not contain mast cells . the histamine content of the ocular tissues and their mast cell contents generally run parallel . however, the cornea is exceptional in that its histamine does not occur in a bound state but in some form which is readily available to a mild process of extraction (tyrode solution at 4 c) .

.I 214

.W

studies in sickle cell anemia xxi. clinico-pathological aspects of neurological manifestations .

neurologic manifestations are frequent in patients who have sickle cell disease . these manifestations may be the earliest presenting signs and symptoms and they are so variable that the patient may be erroneously diagnosed as having conditions such as meningitis, poliomyelitis, subdural hematoma, neoplasm, subarachnoid hemorrhage, lead encephalitis, subacute bacterial endocarditis, and congenital

malformations of the brain . furthermore, development of these manifestations cannot be predicted on the basis of the type of crisis involved .

prognosis following neurological involvement is unpredictable, but recurrent episodes, together with abnormal electroencephalographic readings suggest a poor outcome . such patients die or are the victims of rather severe neurological deficits .

neurological examination of these patients suggests diffuse involvement of the cerebral hemispheres . examination of the pathological material, however, often fails to reveal thromboses . the striking findings are infarcts in the white matter and perivascular hemorrhages .

the thesis that the abnormal neurological findings in these patients are actually due to sickle cell disease is supported by the fact that all such symptoms appear in association with clinical circumstances known to induce sickling . these include surgery and anesthesia, fever and infection .

.I 215

.W

attenuation curves of the human eye under normal and pathological conditions .

a method is described which allows the determination of /attenuation curves/ of the human eye . those curves are obtained by plotting the critical depth of modulation (cmd) as a function of the critical fusion frequency (cff) . routine experiments were carried out for a 2 test field showing a sinusoidal periodical variation of its luminance, surrounded by an extensive area with a luminance equal to the average

luminance of the test field . attenuation curves were obtained for normal observers under different experimental conditions and for a number of patients . it is shown that this method affords us information which cannot be obtained by means of the classical methods for measuring the cff .

.I 216

.W

central nervous system manifestations of periarteritis nodosa .

in the 114 cases of pathologically proved periarteritis nodosa reviewed, 53 patients (46 percent) had symptoms and signs of central nervous system or cranial nerve involvement . thirty-nine patients had both cerebral manifestations and neuropathy, 38 had neuropathy alone, and 14 had only cerebral symptoms and signs .

the most common cerebral manifestation was that of mental derangement, usually an organic psychosis or confusional state . headache, convulsions, blurred vision, vertigo, and sudden unilateral visual loss were the most common symptoms referable to the central nervous system .

the most common abnormalities on examination were retinopathy, hemiparesis, and signs of a brainstem lesion . there was no difference in duration of life, after onset of disease, in those with and those without central nervous system involvement .

.I 217

.W

see-saw nystagmus an unusual sign of lesions near the third ventricle .

a case of see-saw nystagmus in a child with craniopharyngioma and bitemporal hemianopsia is described, and reference is made to previous case reports . the basis for this curious sign is not clear, but the

site of the lesion must be considered to be in the region of the third ventricle, since bitemporal hemianopsia is a necessary part of the syndrome . the sign is not common but when present points to a lesion near the third ventricle .

.I 218

.W

implications of gerstmann's syndrome .

of 465 consecutive patients subjected to a standardized battery of neuropsychological tests, 111 had one or more components of gerstmann's syndrome . each of these 111 patients had some evidence of organic brain dysfunction in addition to gerstmann components . as the number of gerstmann components increased, the responsible brain lesions tended to be larger, more highly destructive of tissue, and to cause greater neurological impairment . every patient with four gerstmann components had associated evidence of severe impairment of brain functions and the lesion or underlying disease was likely to compromise survival of the patient . the syndrome is not to be regarded as an autonomous entity, but merges with numerous other neurological deficits, notably dysphasia in agreement with benton, we find no justification for singling out the four gerstmann components as a separate syndrome, unless one is also prepared to recognize that any other arbitrary groups of concurrent deficits are also separate syndromes .

in at least three of 23 patients with all four gerstmann components, the angular gyrus, as shown by necropsy examination, was not involved by the lesion . however, the probability that the left hemisphere contained a lesion increased with the number of gerstmann components, and the probability of involvement of the left posterior parasyllian area also

increased with the increase in the number of gerstmann components . with two, three, or four gerstmann components, the lesions were never restricted to the angular gyrus but tended to spread widely over the parietal, temporal, and occipital lobes . as to localizing significance, gerstmann's syndrome has approximately the same degree of cogency as dysphasia .

.I 219

.W

alterations of visual evoked response in the presence of homonymous visual defects .

the visual evoked response (ver) was studied by means of computer averaging in 32 normal subjects, nineteen patients without visual disorder but with unilateral cerebral lesions, and 30 patients with homonymous visual field defects . an early negative-positive-negative complex was recorded between laterally placed occipital electrodes and a vertex reference . latencies were prolonged in the hemianopic patients . some amplitude asymmetries were noted in the brain-damaged controls but were more pronounced in patients with visual defects . the recordings in the hemianopic patients were differentiated from those in both control groups by the presence of aberrant wave forms (2 cases),. prolonged latencies (3 cases),. and amplitude depression of greater than 50 per cent of the positive wave on the abnormal side (16 cases) . pathologic verification was obtained in three patients and demonstrated a correspondence between alterations in the ver and the presence of lesions of the geniculocalcarine system .

.I 220

.W

cerebro-vascular lesions and livedo reticularis .

extensive livedo reticularis has been observed in one man and five women who have suffered from a series of cerebrovascular lesions . the neurological disabilities have included aphasia, homonymous hemianopia and hemiplegia but have been remarkable for the degree of recovery which has occurred . it is presumed that the livedo which has been found in only one patient without neurological lesions is related to the cerebrovascular incidents . investigations have failed to show any evidence of polyarteritis nodosa, disseminated lupus erythematosus and thrombocythaemia and an arteritis of unrecognized type is suggested as the etiology .

.I 221

.W

seesaw nystagmus case report elucidating the mechanism .

the eighth recorded case of see-saw nystagmus is reported . features in this case are analyzed and evidence to suggest that this form of nystagmus is ocular rather than central in origin is offered . see-saw, nystagmus, unlike true vertical nystagmus, is not of itself indicative of a brain stem lesion .

.I 222

.W

supratentorial paratransversal meningiomas .

the author describes 6 cases of supratentorial paratransversal meningioma . clinically, the development of these tumours is slow and the chief neurological signs are.. homonymous hemianopia, contralateral hemiparesis and speech disorders when the tumour is on the dominant side radiologically, carotid angiography permits identification of these

tumours easily . surgically, the tumours were removed completely and, although in 2 cases the transverse sinus had to be resected, this caused no damage . one patient, who was operated on twice and whose histological specimen on the second occasion showed that the meningioma was malignant, died seven months after the second operation . the other patients are well and free of neurological deficits from 1 to 12 years after operation .

.I 223

.W

life span and lymphoma-incidence of mice injected at birth with spleen cells across a weak histocompatibility locus .

newborn congenic c h mice receiving injections across a weak (h-i h-i) histocompatibility barrier exhibited life-shortening and a high incidence of lymphomatous disease during mid-adult life . in control experiments (h-i h-i) lymphomatous disease developed much later life . both mouse strains when not given injections as new-borns manifest only a negligible incidence of lymphoma or leukemia . these findings are variably interpretable in terms of oncogenic virology, and of the immunologic theories of aging and cancer by analogy with transplantation disease mechanisms .

.I 224

.W

the heterogeneity of rheumatoid factors and the genetic control of polypeptide chains of globulin .

(1) evidence is presented that most rf proteins are heterogeneous in their antigenic composition although occasional ones are homogeneous and thus resemble the paraproteins .

(2) studies pointing out some of the difficulties encountered with currently available preparations of polypeptide chains in the genetic mapping of globulin are described .

.I 225

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progynon, a depot preparation with oestrogenic action, in the treatment of prostatic carcinoma .

a derivative of a natural oestrogen -dash oestradiol undecylate, progynon-depot -dash was given in depot form by injection to a group of patients with prostatic carcinoma . the study showed progynon-depot to reduce the excretion of androgen metabolites in the urine . the results suggest that the preparation reduced the testicular production of androgens but probably not that of the adrenal glands . the depot effect and clinical action of the preparation are described briefly .

.I 226

.W

/urinary 17-ketosteroid excretion study in radiation induced menopause in carcinoma breast./ .

(1) urinary 17-ketosteroid estimation results are given in 11 patients subjected to radiotherapeutic sterilisation .

(2) a high dosage level was used in all these cases .

(3) results indicate some suppression of ovarian function within 2 weeks of sterilisation .

.I 227

.W

prostatic cancer of a young person with primary hypogonadism .

the prostatic carcinoma of a 34 years old man with primary

hypogonadism was presented . endocrine environment of relative estrogenic excess is suspected to have played the leading part in pathogenesis of this case .

.I 228

.W

urinary excretion of neutral 17-ketosteroids and pregnanediol by patients with prostatic cancer and benign prostatic hypertrophy .

urinary neutral 17-ketosteroid fractions and pregnanediol excreted by 21 patients with prostatic cancer, 17 patients with benign hypertrophy, and 59 clinically well subjects were assayed to determine whether differences exist .

patients with prostatic cancer and those with benign hypertrophy excreted significantly less androsterone than the clinically well subjects . a disproportionately lower level of androsterone than etiocholanolone resulted in a significantly lower androsterone/etiocholanolone ratio in both groups .

the specificity of the findings is discussed . the lower levels of androsterone excreted by patients with benign hypertrophy were associated with an extended period of hospitalization . patients hospitalized less than 5 days excreted androsterone at levels not significantly different from the clinically well subjects .

lower levels of androsterone excreted by patients with prostatic cancer were not explained by the presence of metastasis, the duration of hospitalization, loss of appetite, or other definable differences, when each was considered singly . the possible interrelationships of clinical differences prevent assigning lower excretion levels to the cancer state alone .

.I 229

.W

i. urinary excretion of neutral 17-ketosteroids and pregnanediol by patients with breast cancer and benign breast disease .

urinary levels of neutral 17-ketosteroid fractions and pregnanediol excreted by 114 women, 56 premenopausal and 58 postmenopausal, were determined . subjects studied were included in 4 premenopausal groups (breast cancer 6, benign breast disease 18, sick control 8, well control 24) and 3 postmenopausal groups (breast cancer 21, sick control 17, well control 20) .

levels of androsterone and etiocholanolone excreted by premenopausal patients with breast cancer were significantly less than levels excreted by other premenopausal groups, and they did not differ significantly from levels excreted by postmenopausal patients with breast cancer .

disproportionately lower levels of the 11-desoxy-17-ketosteroids than 11-oxy-17-ketosteroids excreted by premenopausal patients with cancer resulted in significantly lower ratios than those found in other premenopausal groups . ratios associated with premenopausal patients with cancer did not differ significantly from those of postmenopausal patients with cancer .

lower levels of androsterone and etiocholanolone were not explained by debilitation .

.I 230

.W

the morphologic demonstration of an alveolar lining layer and its relationship to pulmonary surfactant .

the presence of an alveolar lining layer was histologically

demonstrated in animal lungs by ultraviolet microscopy . this layer appeared as a thin fluorescent line at the air-tissue interface .

the fluorescent lining layer could be abolished from lung sections by extraction with chloroform..methanol and was diminished by digestion with cl.welchii a-toxin lecithinase, suggesting that the structure was a lecithin-containing lipid . an alveolar lining structure was also identified by the use of phosphatide and polysaccharide stains, suggesting that the lipid was a phosphatide, but that a mucopolysaccharide component might also be present .

bilateral cervical vagotomy resulted in diminution or loss of the fluorescent alveolar lines and abnormal surface tension properties of lung extracts . this suggested that the presence of the fluorescent material was associated with the surface activity of the lung .

alveolar lining structure could not be demonstrated by electron microscopy, even with special staining techniques .

.I 231

.W

experimental emphysema basis, review, and critique .

normal lung structure has been described as a rich capillary bed in a finely partitioned airspace with unique surface-active effects .

morphologic criteria of the lesions of human pulmonary emphysema include evidence of destruction, residual vascular remnants, the absence of significant amounts of fibrosis, and altered conducting airways without anatomic obstruction .

experimental studies relating to the pathogenesis of emphysema have been reviewed and critically evaluated . stress has been placed on the necessity to control the biologic factors influencing the action of any

specific etiologic agent .

.I 232

.W

alveolar lining cells and pulmonary reticuloendothelial system of the rabbit .

complete freund's adjuvant was injected intravenously into rabbits and the cellular response in the lungs was investigated . the population of cells within the alveolar spaces was contributed to by monocytes of the circulation, mesenchymal cells of the alveolar walls and epithelial lining cells of the alveoli . the abnormal epithelial lining during the proliferative phase was the result of an increase in size and number of the cells that line the normal alveoli . as healing progressed, a structurally normal alveolar lining was found .

.I 233

.W

time course of changes in surface tension and morphology of alveolar epithelial cells in co₂-induced hyaline membrane disease .

atelectasis and hyaline membranes produced by exposure of guinea pigs to 15 percent co₂ were found to be associated with disappearance of lamellar bodies in the large alveolar lining cells (granular pneumocytes) and an associated decrease in surfactant as indicated in the rise of minimal surface tension of the lungs . this process is limited to the uncompensated phase of respiratory acidosis and is reversed during the compensatory phase . the parallel time course in changes of surface tension and alterations of lamellar bodies in the granular pneumocytes provides additional evidence for the identification of the latter as the cells responsible for the secretion of surfactant .

.I 234

.W

cortisone and atypical pulmonary /epithelial/ hyperplasia further studies including electron microscopy, tissue culture, animal transplantation and long term observations .

previous work in rabbits showed that there was a proliferation of cells within pulmonary alveoli following intratracheal injection of nitric acid and that the proliferation was greatly enhanced by the administration of cortisone to the animals .

electron microscopic observations indicated that these were morphologically large alveolar lining cells . tissue culture studies of damaged and normal lung with and without cortisone showed no evidence for a direct effect of the drug on the proliferation of these cells .

this observation, together with the knowledge that fibrosis was delayed in the cortisone treated animals, support the thesis that the cortisone effect is an indirect one . transplantation of damaged lung tissue to hamster cheek pouch failed to reveal evidence of growth . within the period of observation (99 to 420 days) there was evidence that the proliferation subsided considerably and no neoplasms developed

.I 235

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some observations on myelin-glial relationships and on the etiology of the cerebrospinal fluid exchange lesion .

the present paper presents cytological observations from developing kitten spinal cord and from spinal cord white matter reacting to injury it also presents some recent experiments on the mechanism of etiology of the csf exchange lesion . drawing on these various sources, the

authors propose specific functions for some of the cell types present in spinal cord white matter .

.I 236

.W

lactate and pyruvate in the brain of rats during hyperventilation .

experiments on anesthetized and curarized rats under artificial ventilation show that during hyperventilation lactate and pyruvate are markedly increased both in blood and in brain . the lactate/pyruvate ratio which remains in blood the same as in control conditions, is systematically decreased in brain . during hypoxia (ventilation with 7 oxygen in nitrogen) lactate rises markedly in blood and in brain . the lactate/pyruvate ratio which is strongly increased in blood shows a small rise in brain . these observations could indicate that a different mechanism is responsible for the rise of lactate in brain during hypoxia and hyperventilation . the important augmentation of lactate in brain during hyperventilation can give an explanation for the delayed rise which is seen in the lactate level in cerebrospinal fluid in these conditions .

.I 237

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cisternal fluid oxygen tension in man .

using a beckman micro-oxygen-electrode we have studied the oxygen tension simultaneously in the cisterna magna, the internal jugular vein and in arterial blood under various conditions . the results suggest that the cisternal oxygen tension to some degree reflects the average oxygen tension of the surrounding brain tissue and besides reflecting the available free oxygen to the brain it registrates changes of short

duration in the cerebral blood flow .

.I 238

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ventricular septal defect with prolapsed aortic valve and outflow tract obstruction .

a case of ventricular septal defect combined with aortic valvular lesion and infundibular pulmonic stenosis is described . the right coronary cusp of the aortic valve, protruding through the ventricular septal defect, was demonstrated by right ventricular angiocardiology as a polyp-like mass in the right ventricular outflow tract . cardiac catheterization and angiocardiology showed progressive right ventricular outflow obstruction .

.I 239

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functional adaptations of the right ventricular outflow tract in congenital heart disease .

functional adaptations in the right ventricular outflow tract have been discussed in relation to the development of acquired /pulmonary stenosis/ .

it is concluded that physical forces as well as structural abnormalities may greatly influence both the clinical picture and the life history of many patients with congenital heart lesions .

the importance of further serial haemodynamic studies to provide a fuller understanding of the natural course of many lesions is stressed, so that better advice about prognosis and the optimal time for surgical treatment may be given .

.I 240

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mitral atresia associated with pulmonary venous anomalies .

pulmonary venous anomalies were observed in 5 among 29 specimens with mitral atresia . in 4 of these 5 the anomalous pulmonary veins took the form of anomalous pulmonary venous connexion . in the remaining case the pulmonary venous anomaly was represented by cor triatriatum . in 3 (group i), mitral atresia and premature closure of the foramen ovale coexisted . the anomalous pulmonary venous connexions in this group provided collateral routes for the flow of pulmonary venous blood, and can be understood as developing in response to obstruction at the foramen ovale when the mitral valve is atretic . in the remaining 2 (group ii) no such causative factor could be invoked . in one of the latter group total anomalous pulmonary venous connexion coexisted with a common atrium . in the other, cor triatriatum coexisted with a patent foramen ovale .

pulmonary venous obstruction occurred in each of the 5 cases .

.I 241

.W

basal metabolic rate after cardiovascular surgery .

the basal metabolic rate and respiratory equivalent of patients were determined during 8 days of convalescence from cardiovascular surgical operations performed with or without cardiopulmonary bypass . the results were compared in patients who had undergone operation for different diseases . metabolic rate in the majority of cases was increased but was commensurate with body temperature . some patients, particularly those requiring open operation on the aortic valve, had raised metabolic rates which could not be explained solely by pyrexia .

all types of patients in this series had elevated respiratory equivalents which persisted throughout convalescence . these equivalents were greater in patients treated with cardiopulmonary bypass than in patients treated without bypass .

.I 242

.W

surgical treatment of ventricular septal defect .

the surgical technique of closure of ventricular septal defects in 80 cases (37 cases of isolated defects and 43 cases of tetralogy of fallot) is discussed in the light of the follow-up results . the use of a patch for closure has reduced the incidence of recurrence to 4 percent, compared with 18 percent when direct suture was performed . the incidence of heart block also decreased from 15 percent, when direct suture was used, to 4 percent with a patch . the transatrial approach is preferred for isolated ventricular septal defects,. the ventricular approach is preferred for cases with tetralogy of fallot . in cases combined with aortic insufficiency only small defects are closed through the aorta . larger defects are closed in the usual way at a first stage operation, and a total valve prosthesis is introduced at a second operation . there was an operative mortality of 6 percent in isolated ventricular septal defects, compared with 27 percent in cyanotic patients with tetralogy of fallot .

.I 243

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some hemodynamic observations in congenital heart disease with special reference to pressure curves in ductus arteriosus .

hemodynamic observations in 100 congenital heart disease cases are

made based on data in the department of pediatrics, kyoto university
between may 1961 and december 1963 . we have classified these 100 cases
according to the malformation from the hemodynamic view point . our
cases were classified into the following groups .

(1) ventricular septal defect	35 cases
small ventricular septal defect	20
moderate ventricular septal defect	9
marked ventricular septal defect	4
ventricular septal defect with pulmonary stenosis	2
(2) patent ductus arteriosus	21
(3) atrial septal defect	19
atrial septal defect	14
atrial septal defect with pulmonary stenosis	5
(4) pulmonary stenosis	5
(5) tetralogy of fallot	14
(6) aortic stenosis	3
(7) aortic insufficiency	3
aortic insufficiency with ventricular septal defect	2
aortic insufficiency with pulmonary stenosis	1

in some small ventricular septal defect, we tried the vasoactive
drugs . phenylephrine was injected slowly into the right ventricle via
the catheter, a rapid rise in femoral arterial pressure associated with
bradycardia and intensification of the systolic murmur was observed .
after the administration of amyl nitrite, a rapid fall in femoral
arterial pressure associated with tachycardia and softening of the sys-
tolic murmur was observed .

in patent ductus arteriosus, when the cardiac catheter is withdrawn

slowly from the aorta into the pulmonary artery, the outstanding pressure curve is recorded in ductus arteriosus . the systolic pressure curve in the ductus arteriosus is the same as the systolic pressure in the aorta and the diastolic pressure curve in the ductus arteriosus has a diastolic dip followed by a late diastolic pressure peak .

in patent ductus arteriosus, when the cardiac catheter is withdrawn from the left pulmonary artery to the right ventricle, the pressure curve reveals a considerable characteristic rise in pulmonary arterial pressure which is regarded as an effect of the transmission of systemic pressure through the ductus arteriosus .

.I 244

.W

a study on the direction of inscription of the vectorcardiographic t-loop in left and right ventricular hypertrophy .

(1) frank lead vectorcardiogram was recorded in 30 normal persons and in 323 cases with hypertension and acquired and congenital heart disease the t-loop was classified into 8 types according to the directions of inscription in 3 planar projections . frequently observed types were examined with the direction of the maximal t vector .

(2) in majority of normal cases, the t-loop was inscribed counterclockwise in horizontal and clockwise in sagittal planes .

(3) in left ventricular hypertrophy, abnormal inscription of the t-loop was observed with abnormal rightward and superior deviation of its maximal vector and the t-loop oriented more than 120 in horizontal plane was usually accompanied by abnormal inscription . percentage of abnormal inscription was higher in cases with cardiac complaints .

(4) in right ventricular hypertrophy, directional change of the t-loop

was relatively small but changes in inscription of it were common . the t-loop was always inscribed abnormally in cases with abnormal inscription of the qrs-loop .

(5) the concept of the polar vector was found to be valuable in studying the inscription and the direction of the t-loop . significance of changes in inscription of the t-loop was discussed .

.I 245

.W

pulmonary vascular plexiform lesion pathogenetic studies .

an attempt was made to test the theory that in pulmonary arterial hypertension, the plexiform lesion is a jet lesion beyond points of arterial stenosis resulting from nonspecific intimal thickening .

in 39 subjects with such congenital communications as are associated with pulmonary arterial hypertension, the lungs were studied histologically . in each, there was an additional element of pulmonary venous obstruction . it is likely that in the absence of pulmonary venous obstruction, adult patients with only the congenital communication would have developed plexiform lesions .

in the three adult patients in the study, no plexiform lesions were identified . among the 36 infants or children, one subject showed plexiform lesions, a 53-day-old girl with mitral atresia, ventricular septal defect, and patent ductus arteriosus .

while the findings in the three adult subjects support the theory regarding the genesis of plexiform lesions, the findings in the one infant with plexiform lesions appear to contradict it .

.I 246

.W

renal hemosiderosis (blue kidney) in patients with valvular heart disease .

anatomic evidence of intravascular hemolysis, i.e., renal hemosiderosis, was found at necropsy in 4 of 132 patients who died of severe valvular heart disease . the aortic valve in each of these 4 patients was heavily calcified, immobile, and portions of the calcific deposits were in direct contact with the blood . hemolysis in each patient was attributable to direct trauma to erythrocytes traversing the stenotic valve, and the frequency of trauma was increased by an associated regurgitant flow . renal hemosiderosis was not observed in any patient with isolated mitral valve disease, or in those with combined mitral and tricuspid valve malformations .

.I 247

.W

tumor scanning with radioactive cesium .

fourteen patients with cancer were scanned 10 minutes to 48 hours after injection of radioactive cs. and satisfactory scans of the tumors were obtained in seven . positive scans were obtained in large, superficial tumors, in a pulmonary lymphoma, and in a carcinoma of the upper third of the esophagus . the negative scans were all in abdominal tumors . correlations were made with data obtained from external counting and by well scintillation counting of biopsy specimens . two modes of uptake are suggested.. (a) early uptake due to vascularity and probably not proportional to stable cesium content.. and (b) a later uptake based upon greater alkali metal content of tumors than of normal tissue .

.I 248

.W

lung scanning with colloidal risa .

the use of colloidal risa injected intravenously in a particle size of 10.50 microns followed by lung photoscanning offers a practical, atraumatic method of visualizing pulmonary artery occlusions in the dog the fact that the particles have a relatively short biological half-life appears to decrease the radiation dose delivered and the duration of occlusion of pulmonary capillaries as compared to ceramic microspheres . work is in progress to apply this technique to the study of pulmonary artery occlusion in the human .

.I 249

.W

multivariate comparison of results of treatment in chronic lymphocytic and chronic granulocytic leukemia .

the results of several clinical trials have been analyzed by multivariate procedures which rely completely on laboratory findings and do not involve scoring specific changes or subjective evaluations . statistically significant differences among drugs after three months of therapy were demonstrated . a relationship between the multivariate method and the subjective evaluation was demonstrated which indicates that if the subjective evaluation is an estimate of the physiologic state or prognosis of the patient, then so are the completely objective techniques used here .

.I 250

.W

oxacillin--apparent hematologic and hepatic toxicity .

bone marrow depression and hepatocellular dysfunction developed in an

allergic woman receiving 3.0 gm. of sodium oxacillin by mouth daily for nearly three months . discontinuing the drug and administering corticosteroids and antibiotics resulted in apparent recovery . the toxic potentialities of oxacillin should be appreciated .

.I 251

.W

drugs and neonatal jaundice .

this paper is not intended as an exhaustive review of bilirubin metabolism nor of the many factors which may result in exaggerated physiologic jaundice.. for such a review the interested reader is referred to the excellent articles by zuelzer and brown . brief mention has been made of the mechanism by which certain drugs may contribute to the development of hyperbilirubinemia . a few drugs, the water-soluble vitamin k derivatives, sulfasoxazole (gantrisin), the salicylates, and novobiocin have been unequivocally shown to affect adversely the newborn infant's ability to handle bilirubin . in time other compounds will definitely be incriminated .

it is important to remember that the administration of a drug to a mother just prior to delivery may result in appreciable concentrations of the compound in the infant's serum, and that drugs administered to the nursing mother may be excreted in breast milk and thereby absorbed by the infant . careful consideration of the drugs given not only to the newborn but also to the mother is therefore essential if we are to avoid what may be termed iatrogenic hyperbilirubinemia .

.I 252

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amputation in patients over 80 years of age .

although patients over 80 years of age can be expected to have poor physical reserve and many co-existing diseases, our observations show that nevertheless they can be subjected to surgical procedures without undue mortality . the mortality rate can be maintained at a minimum if the surgeon considers the factors that contribute to its increase in the elderly . this necessitates.. 1) careful evaluation of the patient and treatment of any pre-existing or co-existing disease, 2) proper control of electrolytes, 3) avoidance of infection, 4) prompt correction of any postoperative hypotension, 5) postoperative pulmonary ventilation and tracheal cleansing, and 6) avoidance of prolonged surgical procedures .

a group of 26 patients past the age of 80 years underwent amputation of a lower extremity, without undue mortality (9 deaths) .

lumbar sympathectomy is not considered advisable in these aged patients .

the standard mid-thigh operation can be questioned in the younger patient, but it is the procedure of choice for removal of a gangrenous extremity in patients over 80 years of age .

.I 253

.W

radical operation for ventricular septal defect in infancy .

ventricular septal defect is the most common congenital anomaly of the heart in infancy, and has a poor prognosis . we have operated upon 18 infants all under one year of age for ventricular septal defect . there has been successful repair in 16 cases .

at present, hypothermia with a surface cooling method has proved to be superior to the artificial heart-lung machine because of the simplicity and the good operative results with its use . in addition, early

operation during the infantile period will cause less psychological impact on infants . these advantages are sufficient for us to advocate radical operation of ventricular septal defect in infancy, even including the severely ill children .

.I 254

.W

specific suppression of tumor growth by isolated peritoneal macrophages from immunized mice .

methods were presented by which macrophages may be isolated from the peritoneal cell population of mice . these cells, and for comparison peritoneal lymphocytes and lymph node cells, were tested for immunologic activity by injecting a mixture of the test cells and tumor cells subcutaneously into irradiated mice . each cell type, when obtained from immunized mice, was capable of suppressing the growth of the specific tumor cells . the results are discussed with respect to a possible specific immunologic function for macrophages in graft rejection .

.I 255

.W

effect of heterologous antiserum and complement on glycolysis of tumor cells .

the effect of heterologous antiserum and complement on glucose metabolism of rat ascites tumor cells was examined to clarify the mechanism of the cytotoxic effect of antibody .

1. lactate-production of the target cells was inhibited by the cooperation of antiserum and complement, while no inhibition was observed when the cells were subjected to either antiserum or complement alone . the inhibition of lactate-production was observed under both

acrobic and anacrobic conditions . no effect of the antiserum and complement was observed on the oxygen consumption of the cells .

2. the amount of antiserum necessary for the inhibition of lactate-production of the cells was determined in the presence of a definite amount of complement, and it was found that the degree of inhibition was not in parallel with the concentration of antiserum beyond a certain threshold . on the other hand, a parallelism was observed between the amount of complement and the rate of inhibition of lactate-production when different amounts of complement were added to a definite amount of antiserum .

3. similar inhibitory effects of the antiserum and complement on lactate-production of the cells from glucose, fructose-1, 6-diphosphate, and pyruvate suggested that the inhibition occurred toward the final step of glycolytic process of the cells .

.I 256

.W

soluble tissue antigens in human brain tumor and cerebrospinal fluid .

an a-2 globulin antigen present in human glioblastomas and immunologically identical with antigens present in human brain, liver, spleen, and metastatic carcinoma cyst fluid has been described . this protein antigen is not present in plasma, wbc, or normal csf . it has been demonstrated in the csf of three of 27 patients with tumors of the central nervous system . when present, it may represent a specific tissue protein fraction contributed by either the tumor itself or the adjacent cns tissue . the major protein components of normal and abnormal csf are derived from, or, at least, antigenically identical to, the plasma proteins .

.I 257

.W

the apparent immunofluorescence of tissue mast cells .

both rat mast cells and rat eosinophils exhibited fluorescence in blue violet light after treatment with FITC-conjugated rabbit anti-rat γ -globulin and in each cell this fluorescence was immunologically nonspecific .

whereas eosinophils fluoresced after treatment with fluorescein alone, mast cells fluoresced only after treatment with a protein conjugate containing γ -globulin .

the phenomenon was observed in cells from different organs and the fluorescence was seen to be associated with the cytoplasmic granules normally present in these cells .

.I 258

.W

the determinants of cerebrospinal fluid P_{O_2} the effects of oxygen and carbon dioxide breathing in patients with chronic lung disease .

the lumbar cerebrospinal fluid P_{O_2} of some hypoxemic hypercapnic patients with chronic lung disease is the same as that of patients without chronic lung disease . breathing 95% oxygen with 5% carbon dioxide increased lumbar cerebrospinal fluid P_{O_2} more than breathing 95% oxygen with 5% nitrogen . the change in cerebrospinal fluid P_{O_2} is closely related to the change in arterial P_{CO_2} , and this relationship is similar to the relationship between arterial P_{CO_2} and cerebral blood flow in patients with and without hypercapnia . interpretation of these observations must be qualified by the following.. cisternal cerebrospinal fluid P_{O_2} differs from lumbar cerebrospinal fluid P_{O_2} in

its response to breathing oxygen with carbon dioxide,. regulation of blood flow to the spinal cord and nerve roots is not known to be comparable to that of the brain,. and factors other than blood flow may have contributed to the changes of cerebrospinal fluid po2 .

.I 259

.W

the behavior of lymphocytes in primary explants of human lung cancer in vitro .

the activity of lymphocytes within outgrowths from explanted tissue fragments of 20 human lung cancers has been studied . the study included cancer-bearing tissue explants from all cases and noncancerbearing lung tissue from 4 of the 20 cases . five major categories of lymphocytic behavior were derived from the study, namely.. (1) emigration and migration of lymphocytes from the explant,. (2) clustering of lymphocytes around /target/ cells,. (3) ameboid transformation of lymphocytes,. (4) lymphocytic congregation,. and (5) emperipolesis . criteria for these different lymphocytic activities have been amplified or introduced .

findings of particular interest were.. (1) the frequency of both viable and nonviable lymphocytes within the vacuoles of other cells . this observation is considered to be an absolute criterion for the recognition of emperipolesis . a subsequent /inclusionbody/ appearance of the dead lymphocytes has been observed . (2) the intimate relationship of ameboid forms of lymphocytes to selected cells, resulting in a juxtannuclear and frequently unipolar crowding of one cell by numerous lymphocytes while nearby cells were totally devoid of ameboid lymphocytes . reasons are given to support the impression that this

phenomenon is related to sensitization . there is also the possibility that the phenomenon may indicate that the lymphocyte is /conditioned/ . (3) the apparent entry of the lymphocyte into the cell has been recorded by timelapse cinematography .

a lymphocyte relationship to cancer cells was infrequently found although explants of 15 of the 20 cases produced identifiable cancer cells and lymphocytes emigrated from the explants of all 20 cases . it is not apparent from this limited study whether this is a significant finding .

.I 260

.W

ventricular septal defect with aortic insufficiency a clinical and hemodynamic study of 18 proved cases .

eighteen patients with the combination of ventricular septal defect and aortic insufficiency were studied . nine also had infundibular pulmonary stenosis . seventeen were treated by open-heart operations .

the physical findings were those of a typical ventricular defect murmur and thrill together with an aortic insufficiency blow and a wide pulse pressure . a systolic murmur at the upper left sternal border with thrill is strongly suggestive of the additional lesion of infundibular pulmonary stenosis, but the presence or absence of infundibular pulmonary stenosis was indicated most accurately at cardiac catheterization and on inspection at operation . it was not of sufficient severity for signs of additional right ventricular hypertrophy to appear on the electrocardiogram .

retrograde aortography serves to demonstrate the severity of the aortic regurgitation .

the problem of the surgical correction of these lesions will be the subject of a separate communication .

.I 261

.W

radioisotope photoscanning as a diagnostic aid in cardiovascular disease a safe, simple method for diagnosing pericardial effusion and aneurysm .

radioisotope scanning is a safe, simple, and useful method for the diagnosis of pericardial effusion and aortic aneurysm . the whole-body radiation dose, approximately 25 millirads from 300 of i 131-sodium iodipamide, is no greater than the dose received from a standard posteroanterior chest roentgenogram or a blood volume determination . there are no side effects or complications from the procedure, and it is well tolerated by the patient . the scan can be repeated at intervals to assess progress of the disease or response to treatment . cardiovascular scanning with radioactive isotopes can be recommended as a useful and safe diagnostic tool .

.I 262

.W

studies of hematology and bone marrow morphology in vitamin e-deficient pigs .

forty-four pigs were used in two experiments whose purpose was to produce a deficiency of vitamin e . the anemia and changes in bone marrow morphology occurring in the vitamin e-deficient state are described . the hematologic disorders include low hemoglobin and hematocrit values, leucocytosis and granulocytosis . nuclear abnormalities were observed in the erythroid precursors in the bone marrow, many of the cells being multinucleated . giant multinucleated

cells of megakaryocyte type were frequently found .

.I 263

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significance of blood groups in homotransplantation of marrow in the dog
ten dogs were given 1,500 r whole-body irradiation and an infusion of
allogeneic marrow from a donor matched with respect to six erythrocyte
antigens . methotrexate was given to reduce secondary syndromes . four
dogs survived . in a similar experiment with 10 dogs, in which no effort
was made to match donors and recipients, three dogs survived . it was
concluded that matching of donor and recipient for these six red cell
antigens did not increase significantly the longterm survival rate of
lethally irradiated dogs with allogeneic marrow grafts .

.I 264

.W

radioautographic studies of bone marrow lymphocytes in vivo and in
diffusion chamber cultures .

radioautography with tritiated thymidine has been utilized to examine
the turnover rate and origin of small lymphocytes in the bone marrow of
the guinea-pig .

very few marrow lymphocytes were initially labeled by a single
injection of tritiated thymidine, but thereafter the number of labeled
lymphocytes rapidly increased to high maximum levels at 3 days .
analysis of the labeling curves and grain counts indicates that the
population of marrow lymphocytes is maintained in a dynamic steady state
with an average turnover time of 3 days or less .

suspensions of bone marrow cells were isolated from the circulation
within intraperitoneal diffusion chambers after short-term labeling with

tritiated thymidine in vivo . although very few small lymphocytes were labeled when introduced into the diffusion chambers, a considerable percentage became labeled during the subsequent culture period .

tritiated thymidine was also administered intravenously whilst excluded from one hind limb by the application of an occlusive compression bandage for 20 minutes . very few labeled small lymphocytes were found after 72 hours in the tibial marrow of the initially occluded limb, whereas the normal high percentage was labeled in the control tibial marrow .

these experiments do not demonstrate any large-scale influx of small lymphocytes from the blood stream into the marrow parenchyma . they suggest that newly formed small lymphocytes appear in the marrow as a result of the division of locally situated precursor cells, but the mechanism of intramedullary lymphocytopoiesis is uncertain .

/transitional/ cells, intermediate in morphology between blast cells and small lymphocytes, synthesize dna and are actively proliferative, but they do not appear to account fully for the rate of lymphocyte production .

certain large, undifferentiated labeled cells appeared in the bone marrow as a result of hematogenous migration . some implications of these findings are discussed .

.I 265

.W

autoradiographic study on the origin and fate of small lymphoid cells in the dog bone marrow.. effect of femoral artery clamping during in vivo availability of h3-thymidine .

the origin and fate of small lymphoid cells in the dog bone marrow

were studied autoradiographically by observing the effect of clamping of the femoral artery during in vivo availability of h3-thymidine . heavily labeled small lymphoid cells appeared in the bone marrow of the clamped leg 3 hours after injection of the tracer and increased in number up to 6 days . the labeling indices of these cells, however, were significantly lower than those of control marrow . a possible interpretation is that dog bone marrow contains two populations of small lymphoid cells, one migrating into the marrow via the blood stream, the other originating from local precursor cells within the marrow . there was no evidence for a transformation of migrated small lymphoid cells into erythroblasts during the first 48 hours after injection of h3-thymidine .

.I 266

.W

the lymphocyte in guinea-pig bone marrow .

the structure and distribution of lymphocytes in the bone marrow of normal 400 g guinea-pigs have been studied by means of light microscopy, electron microscopy, and radioautography . the study of structural organization by all three techniques confirms the morphological identity of the marrow small lymphocytes with small lymphocytes in other situations and affords added proof of the presence of a series of cells transitional in appearance between small lymphocytes and blast cells . unlike the small lymphocytes, transitional cells show evidence of dna synthesis . marrow small lymphocytes and transitional cells are diffusely scattered throughout the parenchyma, often situated in close proximity to the sinusoidal endothelium . they are also found characteristically concentrated within some of the sinusoids,. this is

termed /lymphocyte loading/ .

the findings are discussed with particular reference to the possible origin, interrelationship and fate of these cells .

.I 267

.W

surgical treatment of atrial septal defect under hypothermia .

the technique of inflow occlusion under 30 c. hypothermia was adopted for direct visual correction in 133 consecutive cases of atrial septal defect of the secundum variety and the associated anomalies .

the use of extracorporeal circulation combined with hypothermia was reserved for the repair of two cases of ostium primum defects .

the over-all operative mortality was 4 .

post-operative evaluation showed that the results have been good in almost all patients, including those with pulmonary hypertension .

since an ostium primum defect requires cardio-pulmonary bypass for its closure, the pre-operative recognition of the defect is highly desirable in the selection of patients for operation and in planning the procedure itself .

the information derived from the clinical examination and appropriate diagnostic studies has been found to be consistently accurate in the pre-operative differentiation of the primum from the secundum defect . therefore, the unexpected discovery of a primum defect at operation was not a problem .

in our experience, open-heart surgery under 30 c. hypothermia for the repair of an atrial septal defect of the secundum type and the associated anomalies is a safe and practical technique and effectively corrects the anomaly with minimal risk .

.I 268

.W

internal cooling for general hypothermia .

a further presentation is offered on the advantageous use of intragastric temperature control as an adjunct in general hypothermia . a device is described which accomplishes this end with no encountered deleterious side effects, minimal technical involvement, and minor expense . observations are recorded on rates of temperature change according to sex, weight, and type of surgery performed .

.I 269

.W

late effects of regional renal hypothermia .

in summary, one can safely conclude that no deleterious effects were created in dogs observed over a period of 3 years following renal ischemia of 6 hours' duration protected by hypothermia . the blood pressure failed to climb, there was no evidence of azotemia, and careful microscopic studies failed to reveal histological evidence of renal, vascular or cardiac damage . renal function, as demonstrated by creatinine and pah, was preserved and there was no delay in wound healing .

.I 270

.W

mesenteric vascular response to hypothermia .

1. total and segmental resistances were studied in the mesenteries of 37 dogs, and the effects of hypothermia, changes in blood viscosity and epinephrine on these resistances were compared .

2. cooling to 15 c. caused an increased mesenteric resistance in 94

per cent of animals with approximately 90 per cent of the resistance rise contributed by the arterial segment . small vessel resistance increased in 52 per cent . there was no evidence of venous constriction

3. blood viscosity appeared to play a minor role .

4. it is suggested that hemorrhagic necrosis of the bowel wall is due to intense vasoconstriction in the precapillary vessels with subsequent distal anoxia and cellular damage .

.I 271

.W

the response of dogs to perfusion and arrest of circulation at near zero cerebral temperatures .

1. twenty-six dogs were cooled by a whole body, closed chest perfusion technique to end perfusion brain temperatures of 14.1 to 0.2

c. inclusive .

2. there were no deaths in the group of six dogs in which the end perfusion brain temperature was 10.0 c. or higher .

3. in the 17 dogs cooled to brain temperatures of 5.0 c. or less there were nine deaths, of which five occurred quickly from cardiovascular failure, while four resulted from gross neurologic disturbances .

4. there was no evidence of aortic incompetence during whole body, closed chest hypothermic perfusion .

5. the lower the temperature of the brain at the end of the cooling perfusion, the greater was the passive transfer of heat from the environment .

.I 272

.W

effects of graded hemorrhage on cardiopulmonary functions of hypothermic

dogs .

experiments were conducted on anesthetized dogs subjected to moderate hypothermia (28 c.) and then bled in percentages of the estimated blood volume . respiratory work was not influenced by the degree of hemorrhage pulmonary ventilation, respiratory rate and tidal volume were not influenced significantly as a result of blood withdrawal . physiologic dead space as a percentage of tidal volume increased with hemorrhage . oxygen consumption decreased as the hemorrhage was made more severe, whereas carbon dioxide production was unchanged, indicating a shift in the respiratory exchange ratio . cardiac output decreased 78 per cent from control level when 35 per cent of the estimated blood volume was withdrawn . systemic arterial pressures decreased markedly but heart rate was not changed as a result of blood withdrawal . comparison of responses to hemorrhage in hypothermia and normothermia is discussed .

.I 273

.W

hypothermia in management of acute renal failure .

1. prolonged hypothermia begun in the period immediately following the infusion of epinephrine into the renal artery appears to give partial protection against renal damage .

2. shorter periods of hypothermia do not appear to be beneficial .

3. prolonged hypothermia at 28 to 30 c. has a mortality rate of 50 percent to 60 percent .

.I 274

.W

2803. effect of dosage on endotoxin-induced changes in the reticuloendothelial

system of rabbits

tissues were removed from rabbits 4

and 24 hr. following an i.v. injection of 5,

25, or 200 ug of endotoxin. explants of

tissues from normal and injected animals

were grown in a coagulated plasma medium

and in medium containing 1 ug/ml of

endotoxin. the migration and growth of cells

were observed during the following week

of incubation. the inhibition or stimulation

of cells of the reticuloendothelial system

(res) at different host sites after endotoxin

administration depended on the dosage

and on the known capacity of different organs

to take up circulating endotoxin. macro-

phage migration was suppressed in cultures

of spleen removed 4 hr. after a dose of

hibited by 200 ug, but macrophages in

lymph node, testis, and thymus showed an in-

crease in numbers, in extent of migration

and in phagocytic activity. widespread

res stimulation was seen in tissues removed

24 hr after the largest dose. in ad-

dition to the restoration of re cell activity in

spleen and lung there was a marked

increase in the migration of large phagocytic

cells from bone marrow, as well as

other organs. macrophages from endotoxin-injected animals were as sensitive as normal macrophages to added endotoxin in vitro.

.I 275

.W

3075. vaccinia pneumonia in mice. a light and electron microscopic and viral assay study

swiss white mice between 2 and 4 days of age developed generalized vaccinia viral infection 2 to 7 days after intranasal inoculation.

gross and histologic evidence of pneumonia was seen in more than 80% of approximately 300 mice. virus was recovered in relatively high titers from the lungs (10⁶ pfu per g) during the period when pneumonia developed; viremia was also present, but virus titers in the blood stream remained much below those in the lungs. histologically, vaccinia pneumonia was characterized by large swollen mononuclear cells giving rise to marked widening of alveolar septa. only scattered neutrophils were noted, usually in association with cell necrosis. exudation of edema fluid and red cells into alveoli was considered the result of viral replication and cytopathic effect on cells

comprising alveolar septa. various forms of vaccinia virus were observed by electron microscopy within both 'type i' and 'type ii' alveolar lining cells, capillary endothelial cells, and interstitial cells within alveolar walls. these infected interstitial cells were probably derived from fixed macrophages and were noted also around bronchioles. virus particles were similarly observed in bronchiolar epithelium and surrounding smooth muscle cells. the earliest pathologic ultrastructural change noted in virus infected cells was intracellular edema, evidenced by low electron density of the background cytoplasmic material and dilatation of the endoplasmic reticulum. more extensive changes resulted in cell necrosis with release of virus particles into the extracellular space.

.I 276

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1161. electron microscopy of the bovine lungs lattice and lamellar structures in the alveolar lumen in an electron microscopic study of samples from the lungs of 20 normal cattle, and from 4 with high mountain disease, lattice and lamellar structures were obser-

ved free in the alveolar lumens in 25% of the normal cattle and in 100% of those with high mountain disease. in one specimen, a lattice and lamellar structure was observed in a vacuole within an alveolar epithelial cell. all others were extracellular. the shape and dimensions of these lattice and lamellar structures were similar to those described by other workers in experiments involving intratracheal injections of silicon and oleic and linoleic acid. this is the first report of the structures free in the alveolar lumens of apparently normal cattle.

.I 277

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1162. electron microscopy of the bovine lungs the blood-air barrier in acute pulmonary emphysema
electron microscopic studies of experimentally induced acute pulmonary emphysema in 2 cows yielded the following findings
alveolar epithelial edema and cytolysis, endothelial 'thinning' and cytolysis, excessive elastic and collagenous alveolar wall fibrosis, hyperplasia of alveolar wall smooth muscle, numerous intra-alveolar lattice and lamellar bodies, hyaline membrane formation, hypertrophied

endothelial perikaryons, numerous alveolar macrophages, and alveolar epithelial secretion of an electron-dense amorphous mass. it was postulated that the lattice and lamellar bodies were a result of degenerating alveolar epithelial cells.

.I 278

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1560. the ultrastructure of the lungs of lambs. the relation of osmiophilic inclusions and alveolar lining layer to fetal maturation and experimentally produced respiratory distress the lungs in 69 fetal and newborn lambs were studied. osmiophilic inclusion bodies first appeared at about 121 days gestation and their total number increased with maturation. normal surface activity of lung extracts was detectable a few days following the appearance of inclusion bodies. the excretory nature of the type ii alveolar epithelial cell, the phospholipid nature of the inclusion body content, the decrease in the number of inclusion bodies and their loss of density associated with respiratory distress and with the loss of normal surface activity of lung extracts provide strong evidence that inclusion bodies are the source of pulmonary

surfactant. a dense osmiophilic alveolar lining layer in mammals is described. since the presence of such a layer is well correlated with surface tension values and the number of inclusions, it is suggested that this layer consists of surface active substances. the difficulty in detecting such an osmiophilic layer in other mammals is thought to be, at least in part, due to species differences in the composition of materials constituting the pulmonary surfactant. cytologic immaturity exists until lamb fetuses reach 135 days gestation. this is considered to be the basis for the susceptibility of immature lambs to respiratory distress. fibrin with 230 a periodicity is a component, although a small one, of hyaline membranes in lambs. in view of the fact that mature fibrin appearing as bundles of fibrils is rarely found, it is suggested that the bulk of the hyaline membrane is not a mature fibrin, but probably consists of polymers of fibrinogen and serum protein.

.I 279

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1685. differentiation of exfoliative broncho-alveolar disease from desquamative

interstitial pneumonia

three cases are presented of the pulmonary disease described by liebow and associates and named by them desquamative interstitial pneumonia. the cases support the existence of the entity and the contention that it had not been previously described.

a differential diagnosis between exfoliative bronchoalveolar disease and desquamative interstitial pneumonia is submitted. clinical, roentgenologic and histopathologic manifestations are tabulated for each condition and the differences between them are emphasized. additional symptoms, changes and phenomena not previously recorded are introduced. the most distinctive differences between the 2 diseases were found in the histopathologic manifestations.

.I 280

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3831. lysosomes in the rat sciatic nerve following crush peripheral nerves undergoing degeneration are favorable material for studying the types, origins, and functions of lysosomes. the following lysosomes are described (a) autophagic vacuoles in altered schwann cells. within these vacuoles the myelin

and much of the axoplasm which it encloses in the normal nerve are degraded (wallerian degeneration). the delimiting membranes of the vacuoles apparently form from myelin lamellae. considered as possible sources of their acid phosphatase are golgi vesicles (primary lysosomes), lysosomes of the dense body type, and the endoplasmic reticulum which lies close to the vacuoles.

(b) membranous bodies that accumulate focally in myelinated fibers in a zone extending 2 to 3 mm distal to the crush.

these appear to arise from the endoplasmic reticulum in which demonstrable acid phosphatase activity increases markedly within 2 hours after the nerve is crushed.

(c) autophagic vacuoles in the axoplasm of fibers proximal to the crush. the breakdown of organelles within these vacuoles may have significance for the reorganization of the axoplasm preparatory to regeneration.

(d) phagocytic vacuoles of altered schwann cells. as myelin degeneration begins, some axoplasm is exposed. this is apparently engulfed by the filopodia of the schwann cells, and degraded within the phagocytic vacuoles thus formed. (e) multivesicular

bodies in the axoplasm of myelina-

ted fibers. these are generally seen near the nodes of ranvier.

.I 281

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2431. histochemistry of surface epithelial and pleural mucins in mammalian

lung. the demonstration of sialomucin in alveolar cuboidal epithelium

sialo- and sulfomucins have been demonstrated

histochemically in the surface

layer of the lung and pleura from rabbit,

syrian hamster, guinea pig, mouse, and

man. sialomucin predominates in the distal

bronchial tree and covers the alveolar

epithelial surface. the possible significance

of these observations is discussed.

.I 282

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617. maturation of postnatal human lung and the idiopathic respiratory distress

syndrome

maturation and pathologic alterations of the lung

in 19 newborn infants who died of idiopathic respiratory

distress syndrome were studied by light-and electron

microscopy. normal lungs from 6 fetuses and 11 new-

borns served as controls. in all infants with idiopathic

respiratory distress syndrome, respiratory bronchio-

les and alveolar ducts usually presented the histologic

pattern of mature lungs, i.e. they were predominantly

lined by type i cells, which also formed the epithelial

component of most blood-air barriers. well expanded alveoli exhibited a similar pattern, whereas collapsed alveoli were lined by numerous type ii cells which participated in the formation of poorly developed blood-air barriers. the capacity of type ii cells to produce inclusion bodies seemed to increase with survival beyond the 14th hr of age. secretion of inclusion bodies and presumably surfactant into alveolar spaces did occur but only in the lungs of infants older than 2 days. however, this process was not accompanied by reduction in the number of type ii cells per alveolus as in the normal lung. the distribution of pathologic changes in idiopathic respiratory distress syndrome appeared to be determined by the degree of maturity of the air sacs. structurally mature air sacs were associated with damage of epithelial lining and hyaline membrane formation. in contrast, collapsed alveoli revealed an intact epithelial lining and marked septal edema but were free of hyaline membranes. the findings of this study suggested that transudation of plasma through well developed blood-air barriers was responsible for epithelial damage and hyaline-membrane formation in air sacs. they also suggested that alveolar collapse and presumably lack of surfactant were related to abnormal maturation of the epithelial lining and to septal edema.

.I 283

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903. lattice structures and osmiophilic bodies in the developing respiratory tissue of rats

osmiophilic inclusions have been observed in the lungs of rats particularly in the 20-day rat embryo and newborn up to 3 days post partum. these inclusions are present in the large alveolar cells as dense laminated structures of variable size and configuration. they generally consist of concentrically arranged membranes and have the appearance of myelin figures, usually with a dense center. these osmiophilic inclusions are frequently seen in direct contact with the cell membranes and the alveolar space. the alveolar space contains numerous osmiophilic myelin figures which are thought to originate from the intracellular osmiophilic inclusions. they may extrude through a channel formed inside the cell or by rupture of the cell membrane. secretion materials may occasionally be seen in the cytoplasm of the large alveolar epithelial cells. these cells appear to be in the process of degeneration. their cell surfaces are disrupted and the cytoplasm is continuous with materials in the air space. the lattice structure in the alveolar space may originate from the cytoplasmic secretion material. the cytoplasmic secretion material in the cell and the lattice structures in the air space disappear after the rats are 3 days old. (i,t*)

.I 284

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454. xanthogranuloma (xanthoma) of choroid plexus. the origin of foamy (xanthoma) cells

a case of a 3-month-old infant with intense proliferation of choroidal epithelium with foamy cells, a second similar case in a 9-month-old infant with generalized glycogen storage disease and a case of a 51-year-old male with bilateral xanthogranuloma of choroid plexus and proliferation of the choroidal epithelial cells are discussed. the pathogenesis of the foamy xanthoma cells in the stroma of the choroid plexus, particularly, is discussed. the authors believe that the origin of foamy cells and the mode of formation of such a xanthogranuloma can be explained by the proliferative capability and the phagocytic activity of the choroid epithelium. choroidal epithelial cells can be regarded as fixed macrophages which becomes wandering phagocytes after detachment. disintegration of these foamy cells then releases the lipid content into the interstitium and provokes a response of macrophages and multinucleated giant cells of the foreign-body type. hemorrhage is also considered as a factor involved in the formation of xanthogranuloma.

.I 285

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4. mixed hematopoietic and pulmonary origin of 'alveolar macrophages' as demonstrated by chromosome markers
the origin of alveolar macrophages was investigated in mouse chimeras in which the hematopoietic cells

could be identified by marker chromosomes. by chromosome analysis it was found that in both normal lungs and in lungs exposed to an irritant, approximately two-thirds of the dividing cells which could be recovered by lung washing arose from the hematopoietic system and one-third were of pulmonary origin.

.I 286

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632. pulmonary alveolar proteinosis. a study using enzyme histochemistry, electron microscopy, and surface tension measurement lung biopsies from 4 patients with pulmonary alveolar proteinosis were studied using histochemical methods, electron microscopy, and surface tension measurement. the lipid-rich intraalveolar fluid contained material with the staining reactions and ultrastructure of phospholipid. although many alveoli were lined by enzymatically active, secreting granular pneumonocytes, extracts of proteinotic tissue were not surface active, and, in fact, inhibited normal surfactant. some of the cells free in the intraalveolar material were degenerating sloughed granular pneumonocytes. at the margins of the lesions were lipid-filled macrophages which appear to play a role in the removal of the material. these observations indicate that alveolar proteinosis is not a primary overproduction of surfactant and are consistent with the concept that the alveolar clearing process is defective in this disease.

.I 287

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1688. surface phenomena in lungs in health and disease

in summary, the authors have attempted to bring together the multiple observations which seem germane to the understanding of surface phenomena in lungs in health and disease. to this end, the contributions of anatomists and pathologists on the fine structure of alveolar cells and their lining are fundamental. the concepts of alveolar stability required the special insights of physiologists who were concerned with the causes of bubble stability as they related to the particular problems posed by a lung of several millions of bubbles arranged in parallel. soon the contributions of the chemists became significant as methods of identification and assay of the alveolar lining material were of interest. clinicians asked what relevance these studies had to atelectasis as it occurs in disease, and soon the question of when the surfactant appeared in development occurred to those concerned with premature infants. students of metabolism began to focus on the lung as a site of phospholipid synthesis,

and their tools seem most promising at this time in unearthing possible errors in metabolism which may express themselves in disease. surgeons who undertake perfusion of the isolated lung ask the requirements of that organ with respect to the nutrients and environment of the alveolar cells, and anesthesiologists inquire into the possibilities of mechanical injury to the alveoli during artificial respiration. the problems posed to the reviewers of a subject which touches so many disciplines are obvious. doubtless some pertinent studies have been omitted although unintentionally; others may have been misinterpreted through lack of qualifications as specialists in all specialties. the authors hope they have provided evidence that the forces of surface tension cannot be ignored in an organ with an air-liquid interface of some 70 m². they further hope they have described some of the properties of the film at the alveolar-air interface which operate to produce stability of the alveoli. they hold the belief that study of the metabolism of the alveolar lining layer will further their understanding of a number

of disease processes in which it may be altered. and lastly, they hope for much closer communication between workers in many disciplines who can elucidate this remarkable subject best through cooperative studies.

.I 288

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1689. alterations in pulmonary surface active lipids during exposure to increased oxygen tension
the syndrome of progressive respiratory distress, pulmonary edema, and increased pulmonary surface tension was induced in 8 dogs by exposure to oxygen tensions greater than 550 mm hg for 44.5 and 52 hours. pulmonary surfactant was extracted by endobronchial washing for measurement of lipid composition and surface activity. five dogs developed respiratory distress without pulmonary edema. in these dogs endobronchial wash surface tension was normal or slightly increased, and total lipid distribution was essentially normal. esterified fatty acids in the lecithin fraction were consistently altered with a reduction in palmitate and total saturated fatty acids. three dogs developed pulmonary

edema with increased surface tension, increased total lipid and protein, and relatively decreased total phospholipid in the endobronchial washings. esterified fatty acids in the lecithin fraction were markedly altered with palmitate levels about 1/3 normal. esterified arachidonate was present that was attributed to intra-alveolar plasma. electron micrographs of the lung after oxygen exposure showed thickening of alveolar basement membrane and alterations in the structure of the lamellar bodies of the type ii alveolar epithelial cells.

.I 289

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3805. cisternal fluid oxygen tension in man
measurement of cerebral oxygen tension in man has been hampered by technical difficulties. the authors present a method in which a beckman microelectrode was introduced into the cisterna magna and oxygen tension measured, the hypothesis being that measurement of oxygen tension in a fluid which equilibrates with the average cerebral oxygen tension should give reliable measure of cerebral oxygen tension. in their subjects, inhalation of

pure oxygen produced an increase in the oxygen tension in the cisternal fluid as well as in the arterial blood without any alteration of the oxygen tension in the bulb of the internal jugular vein, whereas inhalation of 95% oxygen and 5% carbon dioxide increased the oxygen tension in the cisternal fluid as well as in the arterial and venous blood. 5% carbon dioxide in air produced an increase in the cisternal oxygen tension; a fall in arterial blood pressure associated with the introduction of the suboccipital needle was accompanied by a decrease in cisternal oxygen tension which then rose simultaneously with the increase in arterial blood pressure that followed infusion of dextran. intravenous injection of xanthinol niacinate induced in all patients a more or less pronounced fall in arterial blood pressure and at the same time the cisternal oxygen tension fell; administration of aramine was associated with a rise in arterial blood pressure plus a rise in cisternal oxygen tension.

.I 290

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4181. cerebrospinal fluid in man native to high altitude

csf ph was shown in a prior report to remain essentially constant during 8 days of acclimatization to 3,800 m. in order to further evaluate the possible role of csf acid-base equilibria in the regulation of respiration, 20 peruvian andean natives were studied at altitudes of 3,720-4,820 m. in 10 subjects at 3,720 m, means were csf ph 7.327, pco, 43, hco₃-21.5, na+136, k+2.6, cl-124, lactate 30 mg/100 ml. arterial blood ph 7.43, pco, 32.5, hco₃-21.3, na+136, k+4.2, cl-107, hematocrit 49, sao, 89.6. in 6 subjects at 4,545 m and 4 at 4,820 m csf values were not significantly different; mean arterial pco, was 32.6 and 32.3, respectively. the only significant variations with altitude were the expected lowering of pao, to 47 and 43.5 mm hg, and of sao, to 84.2 and 80.7, and increase of hematocrit to 67% and 75%, respectively. the natives differed from recently acclimatized sea-level residents in showing less ventilation (higher pco,) in response to the existing hypoxia, and less alkaline arterial blood. the difference appears to relate to peripheral chemoreceptor response

to hypoxia rather than central medullary chemoreceptor.

.I 291

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1116. na, k, ca, mg, and cl concentrations in choroid plexus fluid and cisternal fluid compared with plasma ultrafiltrate in 7 cats the concentrations of na, k, ca, mg, and cl were measured in plasma ultrafiltrate, newly formed choroid plexus fluid, and cisterna magna fluid. the choroid plexus fluid did not differ from plasma ultrafiltrate in cl and k concentration but contained higher na, markedly higher mg, and lower ca concentrations than the ultrafiltrate. cisterna magna fluid differed from the ultrafiltrate with respect to all 5 electrolytes, containing higher concentrations of cl, na, and mg and lower concentrations of k and ca. it differed from choroid plexus fluid in containing a higher concentration of cl but lower concentrations of k, ca, and mg. hco₃-concentration, calculated on the basis of the charge balance, was 7 mm/kg h₂o higher in choroid plexus fluid than in cisterna magna fluid, suggesting an elevated ph at the former site. without

measurement of the potential difference between the csf and plasma, definitive conclusions could not be drawn as to which cations were actively transported. the fact that the distribution ratio between cerebrospinal fluid and ultrafiltrate of one divalent cation was in the opposite direction from that of the other, and that this was also true of the monovalent cations, was taken as evidence that the mechanisms involved in cation transfer are quite selective. though not proven, active transport was considered the most likely explanation of these findings. the data suggest that these specific transfer mechanisms subserve a homeostatic function with regard to mg and k in the cerebrospinal fluid.

.I 292

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3230. cerebral hemodynamics, blood gases, and electrolytes during breath-holding and the valsalva maneuver continuous recordings of arterial and internal jugular blood oxygen tension, oxygen saturation, carbon dioxide tension, ph, sodium and potassium, together with paco₂, blood pressure, and electroencephalogram were obtained to compare the

effects of inspiratory and expiratory breath-holding and the valsalva maneuver on the cerebral circulation and cerebral oxygen availability in man. during the interval of tolerated breath-holding for 69 seconds or less, jugular venous oxygen tension was increased owing to increased cerebral blood flow resulting from an increase of arterial carbon dioxide tension. there was a statistically significant correlation between changes in $j\text{pO}_2$ and paco_2 , which proved to be more or less linear for both increases and decreases of paco_2 4 mm. above and below control levels. no threshold was found for changes in paco_2 altering effective cerebral perfusion and cerebral venous pO_2 , extremely small changes in paco_2 (less than 1 mm. hg) altered cerebral oxygen availability within 10 to 20 seconds. during the valsalva maneuver a consistent reduction of jugular oxygen tension was found associated with the sudden fall in arterial blood pressure and reduction of arterial carbon dioxide tension. the rapid changes in cerebral hemodynamics and cerebral oxygen availability during the procedure

are briefly discussed.

.I 293

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2344. respiratory and cardiovascular changes during rapid spontaneous variations of ventricular fluid pressure in patients with intracranial hypertension

in patients with intracranial hypertension

the ventricular fluid pressure (vfp)

curve is characterized by 3 main forms

of spontaneous variations. two of these

forms are of a rhythmical nature, and

are here called 1-per-minute waves and 6-per-minute waves, respectively, in

accordance with the dominating frequency.

the third form - irregularly appearing

waves of large amplitude and duration -

is called plateau waves in accordance

with the usual shape of the fluctuations.

respiratory and cardio-vascular changes

accompanying these variations of the vfp

were studied by simultaneous recording,

in various combinations, of the vfp, the

pulmonary ventilation, the pco₂ of the

expiratory air, the arterial and the venous

blood pressure, and the pulse frequency.

it was found that the rhythmic vfp variations of the 1-per-minute type occurred

synchronously with the respiratory periods in cheyne-stokes breathing. synchronously appearing variations in systemic blood pressure, in pulse frequency, as well as in consciousness and in muscular tone of the limbs were also noted. the respiratory midposition shifted towards the inspiratory side during the periods of hyperpnoea. the 6-per-minute waves were entirely synchronous with variations in the systemic arterial blood pressure of the traube-hering-mayer type. long sequences of these waves were observed only when the vfp level was considerably elevated. the plateau waves were not accompanied by corresponding elevations of the arterial or venous systemic blood pressure. simultaneously with the crests of the plateau waves sudden changes often occurred in the pulse frequency (from bradycardia to tachycardia), and in the respiratory pattern, sometimes also in the degree of consciousness and in the muscular tone. there were also long sequences of 6-per-minute waves. the deep, irregular breathing seen in this stage induced a considerable hypocapnia preceeding

the final critical fall in the vfp ending the plateau wave. in most instances, however, this fall did not begin until several minutes after the appearance of the hypocapnia.

.I 294

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82. central nervous system lesions in rats exposed to oxygen at high pressure
adult female rats paralyzed by repeated exposures to oxygen at high pressure were found to have CNS lesions of 2 types (1) focal necrosis of individual neurons within certain nuclear groups, and (2) complete or partial necrosis of nuclear groups with frequent damage to myelin, axons, and glia in the area involved. both types were usually bilateral and symmetrical. lesions of the first type were found consistently in the superior olivary complex, ventral cochlear nuclei, and nuclei of the spinal tract of cranial nerve V. lesions of the second type were found consistently in the substantia nigra and globus pallidus, were frequent in the rhinencephalon, and never occurred in the neocortex.

.I 295

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747. electrode size and tissue PO_2 measurement in rats exposed to air or high pressure oxygen
a comparison has been made of values of

po₂ recorded in several rat tissues with 60- μ or 330- μ flexible gold electrodes. although qualitatively both sizes of electrodes give similar results, the quantitative values of po₂ differ. such large differences as are found in some cases between electrodes varying only in physical dimensions are thought to reflect the amount of trauma caused in the tissue under investigation due to electrode insertion. errors in po₂ estimations due to tissue damage are considered to outweigh any other errors such as those due to electrode calibration. soft, highly vascular tissues, such as liver, kidney and spleen, which show macroscopic bruising over quite a large area when electrodes are inserted, show the greatest difference in estimations of the po₂ value. recordings of tissue po₂ were made while animals breathed air and when compressed to 4 or 5 atm. in pure oxygen, and the pattern of response of tissue po₂ to such exposure of the animal to high pressures of oxygen is described.

.I 296

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3384. adrenergic effects in splenic po₂ of rats in air or oxygen

at 5 atmospheres
oxygen tensions have been measured
in the spleens of rats breathing air and during
exposure of the animals to 5 atm abs
of oxygen (hpo). the response of splenic po₂
to compression was complex, usually
reaching a peak value immediately after com-
pression, then falling to a lower value.
this form of response has been termed a
hump response. after adrenalectomy
or bretylium tosylate injection the hump res-
ponse of po₂ after compression was
almost abolished, and the values of splenic po₂
at 5 atm were considerably higher
than in control animals. a combination of adrena-
lectomy and bretylium tosylate also
markedly reduced the number of hump responses,
but unexpectedly significantly lowered
splenic oxygen tensions, both when the ani-
mals were under ambient conditions
or at 5 atm of oxygen. cardiac rate and blood
pressure were studied in an attempt
to find the explanation of this latter effect, and
while blood pressure was the same
in adrenalectomized rats and control rats after
bretylium injection, adrenalectomy
potentiated the bradycardia produced by brety-

limum tosylate.

.I 297

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10642. the effects of antioxidants on high pressure oxygen toxicity

several commonly used antioxidants have been tested for their effect against poisoning due to high pressures of oxygen (ohp).

the tests used were preclusive pe-

riod and survival time of mice at 5 atm

absolute oxygen, lung damage in rats ex-

posed to 5 atm oxygen for 1 hr., and post

ohp paralysis in rats following deep

pentobarbital-na anesthesia and ohp at 4

atm for 30 min. 2,5-bis (1,1-dimethyl-

propyl) hydroquinone gave excellent

protection against ohp toxicity in all tests,

and several other antioxidants also

protected against ohp toxicity but their potency

and effectiveness varied for the

different criteria of oxygen poisoning tested in the

experiments.

.I 298

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3716. glycolytic control mechanisms. i. inhibition of glycolysis

by acetate and pyruvate in the isolated, perfused rat heart

acetate or pyruvate had similar effects

on the over-all metabolism of glucose. gly-

colytic flux was decreased in both the presence and absence of insulin, glucose oxidation was greatly decreased, and the conversion of glucose to glycogen and lactate was promoted. glucose phosphorylation was decreased in the presence but not in the absence of insulin. hexokinase, phosphofructokinase, glyceraldehyde phosphate dehydrogenase, and pyruvic kinase are far displaced from equilibrium, while the other enzymic steps of glycolysis are maintained either at equilibrium or fairly close to equilibrium. in different metabolic situations, glycolytic flux may be affected by those steps which are far displaced from equilibrium. increased levels of the hexose monophosphates, and decreased levels of the other glycolytic intermediates between fructose 1,6-diphosphate and pyruvate after the addition of 10 mm acetate indicate that glycolytic flux was decreased by inhibition of phosphofructokinase. after the addition of 10 mm pyruvate, fructose 1,6-diphosphate, and triose-phosphate accumulated as a result of an inhibition of either glyceraldehyde phosphate dehydrogenase or phosphoglyceric kinase.

acetate had little effect on the total content of oxidized or reduced di- or triphosphopyridine nucleotides, but slightly decreased the ratio of nad to nadh₂ in the cytoplasm, as estimated from the ratios of lactate to pyruvate and α-glycerophosphate to dihydroxyacetone phosphate. pyruvate increased the total content of nadh₂ and nadph₂ as shown both by an increase of fluorescence in the intact heart, and by tissue analyses, but the ratio of nad to nadh₂ in the cytoplasm was greatly increased. these results demonstrate compartmentation of pyridine nucleotides between cytoplasm and mitochondria in the intact cell. after the addition of acetate, citrate was the only intermediate of the citric acid cycle which increased greatly in amount, while oxaloacetate levels decreased. after the addition of pyruvate, the levels of citrate, α-ketoglutarate, malate, and oxaloacetate were all greatly elevated. the glutamic-oxaloacetate transaminase reaction as measured from the total contents of the reactants in the tissue remained close to equilibrium. changes in the concentrations of the adenine nu-

cleotides were insufficient to account for the inhibition of phosphofructokinase, but the results are consistent with control at this step being mediated by citrate.

.I 299

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244. oxygen tension in human malignant disease under hyperbaric conditions

oxygen tensions were recorded continuously in tumours and normal tissues of 34 patients pressurized in pure oxygen to 4 atmospheres absolute. mean rises to 620 mm. hg and 320 mm. hg for tumours and normal tissues respectively were recorded. with patients breathing air at atmospheric pressure 22/90 (24%) of tumour electrodes registered po₂ values of less than 4 mm. hg compared to only 2/39 (5%) of normal tissue electrodes. the results obtained suggest that oxygen polarography as a method for determining po₂ in 'solid' tissues in vivo is complicated by many artefacts - particularly tissue damage due to electrode trauma - which reduce its value to clinical research concerned with accurate information of absolute po₂ values in intact tissues.

.I 300

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7839.cortical ph and the blood-brain barrier

a method was described for measuring

the ph, dc and ac potentials concurrently

on the cerebral cortex of the adult cat,

under conditions of controlled ventilation.

kittens and rabbits were also studied.

the cortical ph response to i.v. nahco₃

was acidic and was accompanied by a

dc negativity, while the blood became alkaline.

such an acidic response was present in

the rabbit and kitten. it was not present

in a number of other tissues in the cat,

including the dura. the cortical acidic

response was not affected, qualitatively,

by i.v. acetazolamide, prolonged hypoxia

or 10% (v/v) co₂. it was reduced reversibly

by 20% (v/v) co₂. it was not affected

by removal of the arachnoid membrane.

the cortical ph response to an i.v. nh₄⁺

salt solution was complex. nh₄cl did not

produce an alkaline response. the cortical

ph response to an alkaline or an acidic

sodium phosphate solution was augmented

but not changed in its direction following

treatment of the cortex with n-butanol.

the results were interpreted in terms of a restriction of HCO_3^- by the blood-brain barrier, through which CO_2 can pass. this restriction is probably non-specific for inorganic ions, and perhaps for other substances. it does not appear to be related to a low cerebral extracellular space, and is independent of substantial oxidative metabolism.

.I 301

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7083. brain damage and paralysis in animals exposed to high pressure oxygen - pharmacological and biochemical observations
single exposures of high pressure oxygen (ohp) at 30-66 gauge pressure caused cns damage and paralysis in rats and mice but guinea-pigs, rabbits, and man did not show such sequelae. the cns damage in rats was greatly increased by cns-depressant drugs (pentobarbital, paraldehyde, N_2O and phencyclidine) given before exposure to ohp. the cns lesions were also potentiated by raised respired PCO_2 , by acetazolamide and by NH_4Cl , whilst protection was afforded by methaemoglobinemia by tham, by 2,4-dinitrophenol and by serotonin against the barbiturate and CO_2 potentiation of ohp brain damage.

ohp-induced brain damage was not modified by hypothermia (cp2), electroconvulsive shock treatment during ohp, cerebral x-irradiation, adrenalectomy or cortisone, slow decompression rates, spinal block with local anaesthetic, 'conditioning' of rats to ohp, hyper- and hypoglycaemia, or alterations in tissue histamine levels.

the results are discussed in relation to possible biochemical mechanisms and theories of oxygen poisoning.

.I 302

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8914. the effect of hypoxia on oxygen consumption of cerebral cortex, liver slices and of diaphragm in vitro during post-natal development of the rat

oxygen consumption of slices from the liver and cerebral cortex and of the cut diaphragm was determined in rats aged 5, 10, 14, 20 and 25 days and in adult animals.

under hypoxic conditions (gas phase 10% oxygen, 90% nitrogen) oxygen consumption of liver slices and diaphragm is decreased by about 25% in all age groups. hypoxia, however, did not affect oxygen consumption of slices of the cortex from 5-day-old rats and its inhibitory effect only appeared

later as the normal oxygen consumption started to rise. the inhibitory effect of hypoxia was greatest in adult animals.

.I 303

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5407. hypoxic-hypercapnic interaction in subjects with bilateral cerebral dysfunction

to analyze cerebral influences modifying autonomic respiratory responses, the authors compared normals and patients with bilateral pyramidal tract disease for their ventilatory response to hypoxia and hypoxia-hypercapnia. during eucapnia, the 2 groups showed similar hypoxic responses. during hypercapnia, the ventilatory response to hypoxia was greater in the brain-damaged subjects. this apparent augmentation, however, was due entirely to anoxia interacting with an abnormally facilitated carbon dioxide sensitivity compared with normals, brain-damaged patients at p_{aO_2} 90-100 mm hg showed an 85% greater CO_2 response, and at p_{aO_2} 50mm hg showed a 79% greater CO_2 response. since cerebral dysfunction facilitated the ventilatory response to hypoxia-hypercapnia combined but not the response to hypoxia

alone, the results imply that the 2
respiratory stimuli interact centrally rather than
peripherally.

.I 304

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3917. plasma free fatty acid and blood sugar levels in newborn
infants and their mothers
simultaneous plasma free fatty acid (ffa)
and blood sugar levels were determined
for fasting newborn infants during the first
24 hours of life, for their cord bloods,
and for their mothers at delivery. the
following observations were made. in con-
trol infants the mean ffa level rose about
three times the cord level after birth
and was accompanied by a 25% drop in the
mean blood sugar level. thereafter, the
mean blood sugar level remained relatively
constant, but the mean ffa level varied
from 2.5 to 3 times the cord level. there
was no significant correlation between the
length of maternal fasting prior to delivery
and the infant ffa level; there was,
however, a significant negative correlation
between the length of maternal fasting
prior to delivery and the infant blood sugar
level at 24 hours of age. high ffa levels

occurred in the infants of obese mothers and low levels were observed in infants with delayed respirations, in infants of preeclamptic mothers, and in infants of diabetic mothers.

.I 305

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2933. the essential fatty acid requirement of infants and the assessment of their dietary intake of linoleate by serum fatty acid analysis the content of polyunsaturated fatty acids in serum total fatty acids was related to the dietary intake of linoleate in 243 infants two to four months of age and in 197 infants eleven to twelve months of age. the curves relating triene tetraene ratio to dietary linoleate indicated approximately 1 per cent of total calories as minimal linoleate requirement. the exponential equations relating dienoic, trienoic and tetraenoic acids to dietary linoleate were derived by computer methods. these yielded constants from which the minimal nutrient requirement could be calculated. the best estimates were obtained from the triene and tetraene data for two to four months' old infants and were found to be

approximately 1.4 per cent of the caloric intake. the nutritive status with respect to linoleate may be estimated by means of logarithmic regression equations. the equation for two to four months' old infants is $\log_{10} \text{dietary linoleate} = -1.087 + 0.0432$ (di - tri + tetra). the data for eleven to twelve months' old infants were found to have greater scatter and give lower triene tetraene ratios at comparable linoleate intakes. the scatter and displacement are considered to be due to supplements of solid food to the basic diet not considered in the calculated dietary linoleate.

.I 306

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74. analytic study of the a- and b-lipoprotein micellar groups and of nonesterified fatty acids of the plasma in normal pregnancy
 an analytical study has been made on 39 patients, using a chemical method which allows the simultaneous detailed evaluation of the lipidic and a- and b-lipoprotein fractions of the plasma. in addition the non-esterified fatty acids have been titrated, the b-proteins and the uric acid assayed, and numerous indices and deducible ratios made from the data obtained. the existence

of quantitative dyslipidemia has been proven, starting gradually, especially in the 4th-5th month of pregnancy, and mostly regarding the b-lipoproteins, prevalently the low subfractions, greater increase of glycerides than phosphatides and cholesterol, but with a non-proportional increase of b-proteins (lower proteinic content). it has, moreover, been noted that there is a prevalent rise of free cholesterol in the fraction of b-lipoproteins with a reduction of the total esterification coefficient. the morphological picture of the lipidic rate in pregnancy shows characteristics which, according to the authors, are like those to be seen in the lipidic rate of male presenility.

.I 307

.W

75. behavior of polyunsaturated fatty acids in physiological pregnancy by the enzymatic lipoxidase method of macgee et al., the author measured polyunsaturated fatty acids (p.f.a.) in healthy pregnant women at full term of pregnancy. before labour there are in the blood 75-95 mg.% of p.f.a., i.e. 10-15% more

than in non-pregnant women; during labour

p.f.a. increase very much, 100-137

mg.%, about 50% more than before labour.

.I 308

.W

5196. effects of nutritional deficiency of unsaturated fats on

the distribution of fatty acids in rat liver mitochondrial phospholipids

the fatty acid composition of liver mitochondrial

phospholipids from rats rendered

deficient in essential unsaturated fatty acids

has been determined, and compared

with that of rats fed a diet containing corn oil.

in addition to marked reductions in

the amounts of linoleic and arachidonic acids

esterified at the b-position of ethanol-

amine-, inositol-, and choline glycerophosphatides,

the deficiency resulted in ex-

tensive changes in the distribution of saturated

acids at both the a- and b-positions.

palmitoleic and oleic acids were increased in

amount in fat deficiency, and large

amounts of docosatrienoic acids appeared in

these 3 phospholipids. the fatty acids

of the sphingomyelins were not altered as a

result of essential fatty acid deficiency.

the data demonstrate that each phospholipid

is unique in the way in which its fatty

acid moieties change in response to feeding

a fat deficient diet.

.I 309

.W

3204. interventricular septal defects with aortic insufficiency

sanchez f.-villaran e.

the coincidence of these 2 malformations

permits their diagnosis provided that a

careful evaluation is made of the hemodynamic

and oximetric data, on the basis of

specific auscultatory features. even then, a

differentiation from other cardiopathies

patent ductus arteriosus with/without pulmonary

hypertension, aortopulmonary sep-

tal defect, interventricular communication,

truncus arteriosus, aneurysm of the

sinus aortae ruptured into right cavities - is

not simple. for this an analysis of the

course of the syndrome together with the

information supplied by phonocardiography,

catheterization, angiocardiography, radiology

and ecg (in this order of importance)

are indispensable. an analysis is made of 5 cases

in which, in the absence of ana-

tomical confirmation, concrete data were obtained

on which to base the diagnosis.

.I 310

.W

2579. measurement of aortic regurgitation by upstream sampling with continuous infusion of indicator

a direct and theoretically valid method

for the measurement of aortic regurgitation

involves the recording of indicator concentrations

from the left ventricle and a down-

stream site during aortic root injection. however,

this method has yielded erratic

results when applied to man in the authors'

laboratory when using the sudden in-

jection technique. therefore, the upstream

sampling method, using continuous in-

fusion of indicator, was evaluated in 18 patients

with aortic regurgitation during

retrograde aortic and transseptal left ventricular

catheterization. the continuous

infusion technique was compared with the technique

of sudden injection in 10 patients

and with aortic valvulography in 14 patients.

measurements of forward flow obtained

with continuous infusions into the aortic root

were not significantly different from

measurements obtained with sudden injections

into the pulmonary artery. recordings

of indicator concentrations from the left ventricle,

during continuous infusions into

the aortic root, demonstrated readily evident equilibrium plateaus. the resultant measurements of regurgitant flow were highly reproducible and not impaired by nonsimultaneity of upstream and downstream sampling. the percentage error of estimate at 95% confidence limits was 22% of the measurement for regurgitant flow, 13% for total flow, and 9% for the regurgitant fraction of total flow. the corresponding errors of estimate for the sudden injection technique were 4 times larger. regurgitant flow by the continuous infusion method ranged from 0.8-30.0 l/min, total flow from 3.0-36.0 l/min, and the regurgitant fraction of total flow from 12-86%. ranking of patients by the magnitudes of regurgitant and total flow did not correspond to ranking by angiographic criteria of severity. however, an excellent correlation prevailed between angiographic grade and the regurgitant fraction of total flow, demonstrating that this variable is the most meaningful expression of severity. the correlation (0.997) between the angiographic grade and the regurgitant fraction measured by the continuous infusion technique was

clearly superior to that obtained with the sudden injection technique (0.894). mild regurgitation was equivalent to a regurgitant fraction of <25%, moderate regurgitation to a fraction of 25-50%, moderately severe regurgitation to a fraction of 50-75% and severe regurgitation to a fraction of >75%. it is concluded that the upstream sampling method during continuous infusion of indicator, because of its sensitivity, reliability, applicability to multiple measurements, and validity in the presence of mitral regurgitation is the most useful method for quantifying aortic regurgitation in man.

.I 311

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2950. aortico-left ventricular tunnel. a cause of massive aortic regurgitation and of intracardiac aneurysm the clinical, roentgenographic, hemodynamic and pathologic findings in a 14-year-old boy with aortico-left ventricular tunnel are presented. the accessory channel between the aorta and left ventricle resulted in massive aortic regurgitation, and the portion of the tunnel which traversed the ventricular septum was aneurysmal,

displaced the posterior wall of the right ventricle and caused severe obstruction to right ventricular outflow. the presence of associated cardiovascular anomalies, in this and previously reported cases, suggests that the malformation is congenital rather than acquired. the clinical and hemodynamic manifestations of aortico-left ventricular tunnel are indistinguishable from those observed with the more common forms of aortic regurgitation, and the correct diagnosis can be established only by thoracic aortography. the malformation is usually recognized in childhood; since aortic regurgitant flow can be abolished by simple closure of the aortic ostium, and without aortic valve replacement, the indications for operative treatment differ from those which apply in aortic regurgitation due to a valvular anomaly.

.I 312

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502. the haemodynamic implications of the bisferiens pulse
a bisferiens carotid arterial displacement pulse
was recorded in 10 patients with
severe aortic valvular disease. the braunwald
test indicated that moderately severe,

severe, or gross aortic regurgitation was present in each. the absence of a peak systolic aortic pressure gradient in certain cases, particularly in those with the most severe regurgitation, suggested their freedom from an element of stenosis.

the anacrotic wave and the peak of the aortic pressure pulse were found to coincide with the percussion and the tidal waves of the simultaneously recorded carotid arterial displacement curves. it is suggested that amplitude of the peak of the anacrotic wave is proportional to the rate of change of momentum of the ejected blood, and that the amplitude of the corresponding percussion wave of displacement is modified by the distensibility of the artery. the depth and shape of the trough between the two peaks is thought to depend upon the magnitude and slope of the two waves rather than upon a venturi effect. it is suggested that the condition of the arterial wall, the diastolic blood pressure, and the stroke volume can influence the pulse sufficiently to preclude its use as a simple guide to the nature of the aortic valve lesion.

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2753. left ventricular function following replacement of the aortic valve. hemodynamic responses to muscular exercise evaluations of left ventricular myocardial function were carried out in 14 patients 4-16 mth after stenotic or regurgitant malformations of the aortic valve had been corrected by valve replacement. the circulatory responses to exercise, judged by the increases in cardiac output in relation to the increases in oxygen consumption, were normal or only mildly reduced in 12 patients. in 5 patients the relationships between the change in the left ventricular end-diastolic pressure and the alteration in the stroke volume were also normal, a fall or an increase in left ventricular end-diastolic pressure of less than 3 mm hg being accompanied by an increase in stroke volume. in 8 patients, however, abnormal increases in the left ventricular end-diastolic pressure occurred during exercise, and in 4 the left ventricular end-diastolic pressure was increased to levels above 12 mm hg. variable alterations in the stroke volume accompanied these increases in end-diastolic pressure. it is

suggested that in the 3 patients who exhibited simultaneous increases in left ventricular end-diastolic pressure and stroke volume, the changes were either a manifestation of the frank-Starling mechanism, or primarily the result of a positive inotropic influence. In the 5 patients who exhibited increases in left ventricular end-diastolic pressure, but no change or a fall in stroke volume, it is proposed that a distinct depression of left ventricular performance was present. Thus, while the cardiac output response was adequate to meet the stress of exercise in the majority of the patients studied following aortic valve replacement, determination of the relationship between the left ventricular end-diastolic pressure and the stroke volume permitted the detection of abnormalities in the function of the left ventricle.

.I 314

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2497. pulmonary atresia with intact ventricular septum when the pulmonary valve is atretic and the ventricular septum intact, the right ventricle usually consists of a small chamber with a very thick wall capable of de-

veloping high pressure. this pathologic picture is associated with clinical findings similar to those in tricuspid atresia-cyanosis, decreased pulmonary flow, left ventricular preponderance on the electrocardiogram, and early death. the diagnosis may be confirmed by heart catheterization and selective angiocardiography with injection into the right ventricle, but the risk is great. surgery has never been successful in the past; but because of the equally hopeless prognosis on medical treatment, attempts should continue to be made. anastomosis of the superior vena cava to the right pulmonary artery appears to offer hope of success in the future.

.I 315

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1635. intra-atrial pressure measurement and electrocardiography in the detailed diagnosis of atrial septal defect after discussing the possibilities and limitations of different methods for identifying the anatomical type of atrial septal defect, the authors suggest a more useful new method. this consists in simultaneous recording of both the pressure curve and endocavitary electrocardiogram during

withdrawal of the catheter from the left into the right atrium. in the ostium primum type, the septal foramen has no inferior margin, and the point of the catheter during retraction (unlike in the ostium secundum type) rests on the intermediate section of the atrioventricular septum. the endocavitary electrocardiogram in the zone of passage between the two atria shows the typical pattern of the intermediate section of the atrioventricular septum; the pressure curve may show a pattern of the atrial of intravalvular type.

.I 316

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1636. ventricular septal aneurysms. a report of two cases
two cases of ventricular septal aneurysm are reported, one in the membranous and one in the muscular portion. the diagnosis was made by selective left ventricular angiography. it is suggested that these cases represent spontaneous closure of a ventricular septal defect with weakness and aneurysmal formation due to the high left ventricular pressure. both are asymptomatic and hemodynamically within normal limits. surgical repair of the aneurysms is not considered necessary.

.I 317

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1642. electrode catheters and the diagnosis of ebstein's anomaly
of the tricuspid valve

the successful surgical treatment of ebstein's
anomaly calls for accurate pre-operative assessment of the nature and severity of
the tricuspid valvular lesion. the

increased risk of cardiac catheterization in this
condition has been matched by increased experience of intracardiac techniques,
and provided the examination is in

skilled hands, patients with ebstein's anomaly
should be investigated in the same
way as those with any other serious congenital
heart lesion for whom surgery is con-

templated. the diagnostic value of electrode
catheters is discussed, and the intracardiac electrocardiographic features of ebstein's
anomaly are illustrated. false

positive and false negative records are demonstrated
and the mechanism of their

production is explained. it is concluded that, though
helpful, intracardiac electro-

cardiographic evidence should be regarded as confirmatory
rather than diagnostic.

records made with electrode catheters during cardiac

catheterization should be considered only along with the other clinical, electrocardiographic, and radiological features of the case, and should not be relied upon as the definitive method in the diagnosis of Ebstein's anomaly.

.I 318

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3326. Unusual aneurysm of the membranous interventricular septum
The case of a patient with a huge aneurysm of the membranous interventricular septum is presented. This is believed to be the first such patient to have undergone successful resection.

.I 319

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934. Laevocardia with situs inversus. A case report and a review of literature
A case of levocardia, with inversion of the chambers of the heart and transposition of the great vessels and situs inversus, has been described. Gross cyanosis and clubbing were present and were due to a veno-arterial shunt through a right-sided superior vena cava open-

ing into the arterial atrium and
passage of venous blood
into the aorta through a ventricular
septal defect. the
case was complicated with right-sided
hemiplegia and
with the development of a liver abscess.
a review of the
literature with prognosis and possible
etiology of the
condition has also been made.

.I 320

.W

1831. postoperative aneurysm of the right ventricle
twelve patients with postoperative aneurysm
of the right ventricular outflow tract
after corrective surgery for pulmonic valvar
stenosis, ventricular septal defect and
tetralogy of fallot are reported. the literature
is reviewed and the pathogenesis is
discussed. different diagnostic tests are evaluated
stressing the role of roentgen
examinations and the importance of careful follow-up
by intercalative chest roent-
genography.

.I 321

.W

1991. ventricular septal defect with aortic regurgitation.

medical and pathologic aspects

thirty-four patients with ventricular septal defect

and aortic regurgitation, repre-

senting less than 5% of the patients with ventricular septal defect, are discussed.

a loud, systolic murmur, characteristic of ventricular septal defect, is noted dur-

ing infancy, whereas evidences of aortic regurgitation (protodiastolic murmur and

wide pulse pressure) does not usually appear until some time between 2 and 10

years of age. clinical and catheterization data indicate that the principal hemody-

namic load is aortic regurgitation, whereas the ventricular septal defect does not

usually result in a large pulmonary blood flow or high pulmonary arterial pressure.

in about 50% of the patients, a significant pressure gradient across the right ven-

tricular outflow tract exists. detailed pathologic studies indicate that the ventricular

septal defects are high and anterior and encroach to a greater or lesser degree on

the membranous bulbar septum. the right coronary cusp is the one most severely

involved, and, by its prolapse, causes aortic

regurgitation; the noncoronary cusp is always less severely affected. the anatomic basis of the pressure gradient observed across the right ventricular outflow tract is not always clear.

.I 322

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2431. the natural history of arrhythmias following septal defect repair the repair of 191 atrial and ventricular septal defects between 1955 and 1961 was reviewed to determine the incidence and prognosis of arrhythmias related to operation. cases included 90 ventricular septal defects, 61 atrial defects of the ostium secundum type, and 40 of the ostium primum variety. nodal rhythms, second degree blocks, complete heart block, and flutter or fibrillation that persisted after completion of operation were analyzed, while intermittent ectopic beats, sinus tachycardia, and bundle branch blocks were excluded. fifteen per cent of the patients with ventricular defects, 17% with ostium primum defects, and 35% with ostium secundum defects developed abnormal rhythms associated with repair. of 18 patients whose arrhythmias began during operation, there were 8 deaths; no fatalities occurred in the 24

patients who developed arrhythmias in the postoperative period. seven deaths were associated with complete heart block and one with second degree block. although only one half of the patients who developed arrhythmias had pulmonary artery pressure greater than 30 mm. hg systolic, all fatalities occurred in this group. four of the deaths followed surgery with the use of the pump oxygenator in children under 30 months of age. thirty-eight per cent of the abnormal rhythms that began in the postoperative period were nodal. flutter and fibrillation were common following repair of atrial secundum defects in patients over 15 yr. of age but did not occur in younger patients. deaths from heart block occurred in the first 30 days following operation except one, 5 months later. survivors of complete heart block reverted to a less serious arrhythmia or normal rhythm within 3 months.

.I 323

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1021. left ventricular angiocardiology in the study of ventricular septal defects
sixty-five cases of ventricular septal defect were studied by left angiocardiology.

the left ventricle was entered by retrograde arterial catheterization with a catheter having a j-shaped tip. this procedure appears to be little, or no more, hazardous than right-sided angiocardiology. ventricular septal defects may be divided into 5 types, depending on their location in the ventricular septum. the anatomic and radiological features of the septum and septal defects are described. selective injection of contrast material into the left ventricle opacifies the blood passing through the defect in the septum and permits preoperative localization of the defect in relation to identifiable anatomic landmarks. multiple defects of the septum are well demonstrated. such information may be of considerable value to the surgeon undertaking repair of the septum. left ventriculography, often combined with supravascular aortography, has been used, when indicated, to differentiate between mitral insufficiency and ventricular septal defect and in the detection of other cardiac anomalies whose manifestations are marked by those of the septal lesion. this technique is well suited to the postoperative study of

patients following repair of the septal defect and for follow-up studies in patients not operated upon to clarify the natural history of defects in different portions of the ventricular septum.

.I 324

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4105. free fatty acid metabolism in chinese hamsters

in normal chinese hamsters (*cricetulus griseus*) the mean concentration of free fatty acids (ffa) in serum varied from group to group, but was (1) consistently 4 to 9 times greater than in rats, dogs, or man; (2) slightly higher than in syrian hamsters; (3) two- to four-fold higher than in fasting or alloxan-diabetic rats. the epididymal adipose tissue of the chinese hamster (1) had initial concentrations of ffa comparable to those in the rat and syrian hamster; (2) released, in the same time interval, 8- to 10-fold more ffa in vitro than this tissue of the rat; (3) had higher concentrations of ffa after incubation than the incubated tissue of the rat. the retroperitoneal (perirenal) adipose tissue of the chinese hamster was less active in release of fatty acids in vitro than the

epididymal, but was, however, more active than the epididymal adipose tissue of the rat. these characteristics of ffa metabolism in the chinese hamster were apparently attributable to species, not to age, diet, or sex. in the chinese hamster, the weight of the epididymal adipose tissue per gram of body was relatively high. it appears that in this species the rate of release of fatty acids from adipose tissue is great, leading to high ffa concentrations in serum. in chinese hamster and rat adipose tissues in vitro, glucose and insulin (separately) reduced the rate of release of ffa and the amount of ffa in the tissues, but glucose and insulin together produced the greatest reduction. the net reduction in ffa release by glucose and insulin in vitro was greater in tissue from the chinese hamster. insulin markedly increased glucose uptake by the adipose tissues of both species. the possible relation of the results to spontaneous diabetes in the chinese hamster is discussed.

.I 325

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95. changes in serum non-esterified fatty acid levels in spon-

taneous and in oxytocin induced labour
the nonesterified fatty acid (nefa)
concentration of serum rises progressively
during the course of normal labor.
the rise appears to be related to the duration
of labor. the use of oxytocin to induce
and stimulate labor does not alter the normal
pattern of rise in nefa provided it is
given in physiologic dosage. the levels of
nefa in the umbilical vein and the
umbilical artery at delivery are comparable and
always significantly lower than the
maternal level. the maternal/fetal ratio varies
between 1.7 1 and 3.9 1 in this series.
following delivery the nefa levels begin
to fall almost immediately. the rate
of fall is 10-30% of the delivery value in the 1st
hour, 30-50% within 18 hr. and 50-70% within 36 hr.

.I 326

.W

1545. the effect of combined glucose and insulin infusions on
the lipoid and carbohydrate metabolism of the parturient
woman and of the fetus
the infusion of glucose with insulin during delivery
was used by the authors pri-
marily in order to determine, whether the utilization
of glucose can be enhanced

under these conditions. they wanted to investigate, whether the increase of unesterified fatty acids in the cord blood which takes place after a sole glucose infusion in the mother, could be caused by the low capability of glucose utilization in the fetus. the infusion during delivery which consisted of the application of 500 ml of 10% glucose and 16 u of insulin over a period of 30 min. brought about a greater decrease of unesterified fatty acids in the parturient woman as compared with the infusion of glucose exclusively. the reason for this result is thought to be due to a better utilization of glucose which is favorably influenced by insulin. during the infusion of glucose with insulin, an increase in the values of lactic and pyruvic acid took place in the parturient women; this was probably due to an accelerated glycolysis and an increased production of lactic acid, but not caused by a higher share of the anaerobic metabolism. in the cord blood, there were likewise increased values of lactic and pyruvic acid as a reflection of the higher values of these substances in the mother. the formation of these products of metabolic

breakdown by the fetus, however, was not significantly increased. after infusion of glucose with insulin, the other investigated parameter values, including those of the levels of unesterified fatty acids are found in the cord blood in similar amounts as after infusion of glucose alone. these results cannot reliably prove the passage of insulin through the placenta especially after a continued study of the metabolic values in newborns. as a proof of the passage of insulin through the placenta could not be established, it is possible that after an intake of insulin the increase of unesterified fatty acids in the cord blood could be caused by a relative insufficiency of the insular apparatus of the fetus. the most probable reason for the increase of unesterified fatty acids is the different deposition and metabolism of unesterified fatty acids in the course of intrauterine life.

.I 327

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1547. glucose and nonesterified fatty acid levels in maternal and cord plasma
the authors established in 44 healthy women

at the moment of delivery the contents of glucose and free fatty acids in the blood of the mother and of the umbilical cord. the concentration of both substances was significantly higher in the mother than in the infant. the relation for free fatty acids was 1.7 1, that for glucose 1.3 1. the relation glucose fatty acids in the mother was significantly different from that in the infant.

.I 328

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3294. epinephrine infusions in normal and toxemic pregnancies.

ii. plasma glucose, nonesterified fatty acid, and epinephrine-norepinephrine alterations

seven controls and 9 preeclamptic patients were infused with different amounts of epinephrine. plasma nefa, glucose and catecholamines were determined before, during and after epinephrine infusion. the toxemic patient responds to the metabolic effects of infused epinephrine in a manner similar to that of the normal pregnant patient. the increased levels of nefa in pregnant patients are explained by a complicated biochemical mechanism involving an increased availability of cortisone-like

steroids, slightly increased amounts of thyroid, hormones, etc., resulting in an alteration of carbohydrate utilization. the study leads to the conclusion that epinephrine is not an etiologic agent in toxemia of pregnancy.

.I 329

.W

766. a lipid-mobilizing substance in the serum of pregnant women, of probable placental origin
a substance capable of inducing free fatty acid (ffa) release was found in the sera of 12 from 13 pregnant women. the rat epididymal fat pad was used for bioassay. this substance circulates in late pregnancy and disappears within 5 days post partum. it is present in crude placental extracts and is removed by their deproteinization. it is nondialyzable. application of pituitary extraction procedure to placentae yielded active fractions where pituitary growth hormone is usually found. in accordance with these facts a hypothesis concerning a part of metabolic changes occurring during pregnancy was pronounced as follows. the described substance diminishes maternal glucose consumption through the elevation of plasma free fatty acids, or by direct in-

hibition of glucose uptake, or both. this permits a preferential shunting of glucose to the fetus. at the same time, increased plasma free fatty acid levels would serve as the alternative maternal energy substrate. elevated maternal insulin levels during late pregnancy stabilize the degree of maternal lipid mobilization. the contrainsulin properties of a substance capable of mobilizing free fatty acids and inhibiting maternal glucose utilization would pose a diabetogenic challenge, and in the face of compromised maternal insulin reserves, provoke overt or worsen existing diabetes mellitus.

.I 330

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3682. metabolism of free fatty acids during perinatal life of lambs

there is a rapid rise of free fatty acids in blood plasma after birth in newborn lambs. this study confirms this rise, caused by an augmented mobilization of these acids from the tissues. norepinephrine easily mobilizes free fatty acids in adult ewes. in newborn lambs this special effect is lacking, though cardiovascular responses are clearly demonstrable. blocking

the sympathetic nervous system in newborn lambs inhibits the rapid rise of free fatty acids after birth. this is compatible with the concept, that increased activity of these sympathetic nerves after birth is an important factor for free fatty acids mobilization. during intrauterine life there is an ample study of carbohydrates and the organism uses them as an energy source. hypoglycaemia resulting from sudden carbohydrate deprivation at birth, demonstrates with rising free fatty acids the change-over to (tissue) fat as main source of energy.

.I 331

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1163. the effect of glucose infusions on the lipid and the carbohydrate metabolism of the parturient woman and the fetus in 20 parturient women who were given glucose infusions during the expulsive stage of labor, the authors were able to observe an unusual hyperglycemia and a decrease in unesterified fatty acids (uefa). the uefa-level usually increases regularly during delivery. likewise, the values of esterified fatty acids (efa) showed an in-

crease above the normally present levels in women who had received a glucose infusion during the expulsive stage of labor. the results show that during delivery both hyperglycemia and the increase in lipoids are predominantly due to the energy demands of the organism. however, there is also evidence that other, hitherto unknown factors may play a role. in the fetus, the infusion of glucose leads to an increased glucose retention. the infusion, however, does not bring about a decrease, but, contrary to the expectations, an increase in the uefa-values. in general, such a reaction is not found in any of the subsequent periods of life. further investigations were conducted in order to find an explanation for the paradox uefa-reaction. as shown by an analysis of the lactic acid and the pyruvic acid values, the increase in the uefa can most probably not be attributed to an impairment in the fetal metabolic conditions. the administration of physiological saline infusions to 10 parturient women under equal conditions revealed that the cause for the uefa-increase can apparently neither be found in

hemodynamic changes due to the infusion
nor in changes of the electrolyte balance, but
rather in an adaptation insufficiency
of the fetal islet cells, respectively in a different
fat mobilization or fat deposition.

.I 332

.W

1320. the plasma free fatty acid composition and blood glucose
of normal and diabetic pregnant women and of their new-
borns

the blood glucose and plasma ffa content
and composition of the newborns of
normal women, gestational diabetics, and
insulin-dependent diabetics were analyzed.

normal maternal ffa levels were twice the
fetal values; by 2 hr of age ffa in-
creased 4-fold over initial values in normal
infants, while infants of gestational
diabetics had a 3-fold rise, and those of
insulin dependent diabetics only 2-fold.

blood sugar at the same time decreased and
there was an inverse relationship be-
tween blood glucose in the normal infants and
ffa. this relationship is altered in
the infant of the diabetic mother. gas
chromatography of plasma indicated a higher
ratio of unsaturated to saturated ffa in

mothers compared to infants. no pattern differences were noted between the normal and diabetic mothers, except that the latter had higher oleic acid. in the initial 2 hr of life, the patterns changed, although no differences were noted between infants of diabetic mothers and normals. the observations suggest (1) the metabolic interrelationships of glucose and ffa in the normal infant are different from those in the infant of the diabetic mother, the latter infant having a state of physiologic hyperinsulinism; (2) plasma ffa in the fetus is derived from both fetal fat synthesis as well as placental transfers; (3) the infant of the diabetic mother does not differ from the normal as regards ffa composition.

.I 333

.W

3107. lipids of human placenta
the chloroform-methanol-soluble components of 4 human placentae were isolated by rubber membrane dialysis and gas chromatography, and analysed. two thirds of the total lipids consisted of phosphatides with lecithin as the main component

(22.5%), colamine cephalin (13%) and sphingomyelin (7.5%). free cholesterol formed 14% of the total lipids, while cholesterol esters accounted for 6% and triglycerides for 13%. investigation of the phosphatide fatty acids by gas chromatography showed a content of 60% saturated, 27% simple unsaturated and 12% polyunsaturated acids. the fatty acids of the triglycerides consisted of about 50% saturated and 25% each of simple and polyunsaturated acids. the polyenoic acids (30%) of the cholesterol fatty acids had a high content of linoleic acid, about one quarter that of the total acids.

.I 334

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377. experimental study of sensitization to nickel sensitization was effected by epicutaneous application of nickel sulfate in 15 guinea-pigs. it was confirmed by the appearance of eczematiform lesions in skin tests with nickel sulfate. for maintenance of the animals in good general condition it was necessary to add vit. c and antiinfective agents to the diet. for this reason the allergenicity of the ni

salt had to be augmented by the use
of adjuvants (freund's complete adjuvant or alum).
such adjuvants act by
stimulating the res. the method for
sensitization of guinea-pigs to metal salts
having been worked out, it is now proposed
to study the mechanism of such
sensitization, the biological disturbances
involved and the possible existence
of cross-sensitizations.

.I 335

.W

2285. some remarks on the nickel dermatitis
by non-occupational contact
this dermatitis represents 2% of the
skin diseases observed at the
allergologic outpatients department of
the dermatological clinic of milan.
the disorder is more frequent in women
and prefers the thighs (girdles, keys)
and the wrist (watch); its incubation
period is generally long and a peculiar
papulo-vesicular follicular and lichenoid eruption often follows.

.I 336

.W

3200. studies on the binding of protein by nickel.
with special reference to

its role in nickel sensitivity

the reaction between nickel and proteins

was studied using the technique of

equilibrium dialysis. in most of the experiments

crystalline bovine serum

albumen was used. the nickel-protein complex

was of low stability, the quantity

of nickel bound by the protein being dependent

on the concentration of free

nickel ions, the ph, and the particular protein used.

the sites of binding of

the nickel ions were primarily carboxyl and amino

groups. the author concluded

that it was unlikely that nickel behaved as a

haptens capable of initiating an

allergic response.

.I 337

.W

2596. experimental nickel contact sensitization in man

in 16 of 172 male prisoners contact-type

delayed hypersensitivity was induced

experimentally by repeated application of

25% nickel in a 0.1% sodium lauryl

sulphate solution on the skin. test reactions

with 5% nickel with occlusion

were found to be irritating. no experimentally

sensitized subject demonstrated

clinical sensitivity to the metal in his environment.

.I 338

.W

1013. hand eczema

the clinical aspects of 106 cases of hand eczema are reviewed. the clinical types are defined nummular eczema, nickel allergy, atopic dermatitis, hyperkeratotic dermatitis of the palms, hand eczema post partum, mycotic eczema, contact dermatitis, occupational eczema and idiopathic eczema. the results of the patch tests, the influence of psychological and psychiatric factors, the effect of water and cleansers, the diagnosis, treatment and prognosis are discussed. in 39% no significant causative factor could be found. in many cases where causative factors could be identified these were probably no more than contributory, superimposed upon an underlying idiopathic eczema.

.I 339

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670. steroid aerosol spray in contact dermatitis. prophylactic use with particular reference to nickel hypersensitivity

proper use of topical aerosol dexamethasone (decadron) spray affords complete protection to patients with nickel sensitivity. this clinical result is confirmed by the results of patch testing nickel-sensitive patients with a 5% nickel sulfate solution and nickel coins. a combination of dexamethasone and an isopropylmyristate film is necessary for successful prophylaxis; the individual components alone do not protect these patients. clinical and patch test results indicate that a moderate degree of protection is afforded to patients with paraphenylenediamine sensitivity. patch test results indicate that the spray does not protect against poison ivy and ragweed oleoresin, potassium dichromate, certain rubber accelerators, and monobenzyl ether of hydroquinone. it affords a moderate protection against formaldehyde. no tests were done with patients with formaldehyde hypersensitivity. a fair degree of protection was obtained by the use of the spray in housewives eczema presumably due to irritants present in soap and detergents.

.I 340

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2078. the pathogenesis of contact eczema due to detergents for domestic use the thesis is maintained that eczema due to household detergents is pathogenically linked with allergic contact sensitization to metallic salts, especially chromium and nickel. in a series of 20 cases of contact eczema attributable to detergents, the existence of sensitization to these metals was demonstrated by the patch test. likewise, in the analysis of 9 samples of different detergents used for washing, in all of them chromium and nickel were found to be present in a proportion which, for either of these metals, varied between 1 and 5 p.p.m.

.I 341

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4010. studies of nickel carcinogenesis. the subcellular partition of nickel in lung and liver following inhalation of nickel carbonyl wistar rats were exposed by inhalation to nickel carbonyl either once only at a concentration of 80 ppm for 60 minutes

(0.60 mg ni(co)4/l.air), or
repeatedly at 4 ppm (0.03 mg ni(co)4/l. air)
for 30 minutes 3 times weekly
for 1 year. they were killed 24 hours after
(the final period of) exposure.
nuclear, mitochondrial, microsomal and supernatant
fractions were isolated
from lung and liver homogenates and measurements
of the nickel, nitrogen
and rna-content of each subcellular fraction
were made. the greatest ratios
of nickel to nitrogen were in the nuclear
fractions of both liver and lung,
but increased amounts of nickel were also found
in the microsomal and
supernatant fractions of both liver and lung
and in the mitochondrial
fraction of lung.

.I 342

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188. studies of nickel carcinogenesis;metastasizing pulmonary tumors in rats
induced by the inhalation of nickel carbonyl
in a combined series of studies, 6 out of 409 rats (n.b. only 195 survived for
more than 3 wk.) exposed to nickel carbonyl developed pulmonary carcinoma
with metastases. the lesions included the common types of pulmonary cancer,
squamous cell carcinoma, adenocarcinoma and anaplastic carcinoma. all of
the pulmonary lesions were found between 24 and 27 mth. after the initial

exposure to nickel carbonyl. the amount of nickel found capable of inducing lung cancer in the rat was comparable to the amount of nickel inhaled by persons smoking less than 15 cigarettes per day for a period of a year. the mean weight of rats chronically exposed to nickel carbonyl was found to be consistently less than that of the control rats throughout the entire 3-year period of study.

.I 343

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189. influence of age, sex and glandular extirpation on muscle carcinogenesis in rats

the carcinogenic effect of a single intramuscular injection of nickel sulphide in an aqueous suspension to which penicillin g had been added was compared in male and female castrated, hypophysectomized or intact, rats of different ages. the response seemed most marked in intact females injected when 2 mth. old. castrated or hypophysectomized 2-month old females were less responsive. one-month old intact males were more responsive than 2-month or 3-month old intact males, 1-month old castrated males, or 1-month old intact females. more data would be required before firm conclusions could be drawn from these results.

.I 344

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3176. studies of trace metal metabolism electron paramagnetic resonance of manganese in ribonucleic acids

the electron paramagnetic resonance spectrum pattern of manganese was readily detected in all of the samples of rna. the resonance patterns indicate that manganese is present in rna in a divalent state and suggest that manganese is located at the center of a distorted octahedron of oxygen

atoms. from the intensity of nominally forbidden resonances, the crystal field splitting parameter d was estimated to be 0.02 cm^{-1} .

.I 345

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4790. metal chelates as potential reactivators of organic phosphate poisoned acetylcholinesterase

as part of a study to investigate metal chelates as possible reactivators of phosphate poisoned acetylcholinesterase, it is shown that chelates act as inhibitors of the enzyme. in addition, copper and nickel chelates of 2-pyridinealldoxime catalyze the decomposition of dfp and sarin. compared to 2-pam, however, these chelates are very poor reactivators, probably because of an improper alignment of the oxine oxygen in the chelate-enzyme complex.

.I 346

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3446. effect of NiCl_2 on an isolated ranvier node

an attempt was made to explain the extreme prolongation of the nodal potential by $0.1\text{-}1.0 \text{ mm}$ NiCl_2 in terms of the ionic theory. the effects of NiCl_2 at room temperature are similar to those of temperature reduction decreased maximum rate of rise of the action potential, lengthened action potential duration, elevated threshold, increased tendency for repetitive activity; in addition, the amplitude of the action potential is slightly increased. the long-lasting plateaus of the responses obtained under the combined influence of NiCl_2 and temperature reduction are shortened by cathodal polarization, strong anodal polarization and decrease of $(\text{Na})_0$. the plateau can be prematurely terminated by short anodal pulses of critical amplitude; short cathodal pulses reduce the duration of the plateau gradually with increasing pulse strength. increased $(\text{K})_0$ prolongs plateau duration; the

steep repolarization phase which normally terminates the plateau is replaced by a long lasting after-depolarization with stepwise potential decline.

the amplitude of k-depolarization is not influenced by NiCl_2 or temperature reduction. 1.0 mm NiCl_2 changes the relation between maximum rate of rise and steady-state polarization; the potential change required for 50% sodium inactivation is +8mv in normal Ringer's solution and +16mv in the presence of 1.0 mm NiCl_2 (22 c.). 1.0 mm NiCl_2 increases the time constant of delayed rectification as measured in Na-poor solutions at 4 c. by a factor of about 2. the decrease of action potential under cathodal polarization is slightly delayed by NiCl_2 . it is concluded that prolongation of the nodal action potential by NiCl_2 is due to delayed and reduced inactivation of Na permeability and delayed increase of K permeability; part of the NiCl_2 -effect could be explained by assuming competition between Ni^{++} and Ca^{++} for specific sites at the membrane.

.I 347

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2302. the carcinogenic activities of n-hydroxy-2-acetylaminofluorene and its metal chelates as a function of retention at the injection site

the carcinogenic activities of s.c. administered

n-hydroxy-2-acetylaminofluorene

(n-hydroxy-aaf) and a variety of its metal chelates indicate that greater activity locally is associated with a longer retention of the chelates at the site of injection with a slow release of n-hydroxy-aaf to the surrounding tissue. no tumors were obtained at the sites of 4 injections of n-hydroxy-aaf (3.2 mg. /injection), but 4 and 16 of 20 rats developed sarcomas at the sites of 8 and 16 injections, respectively. the nickelous, cobaltous, ferric,

or cupric chelates induced moderate to high incidences of sarcomas with 1 or 4 injections; in these cases one-half of the administered n-hydroxy-aaf was retained at the injection site for 4-50 days. the manganous and zinc chelates and the potassium salt were less active at the injection site; the half-retention times for these ranged from 2.5 hr. to 2.5 days. the comparable half-retention time for n-hydroxy-aaf was about 2 hr. injection of the metal derivatives s. c. with short half-retention times resulted in higher incidences of mammary tumors than injection of the derivatives with half-retention times of 4 or more days. when administered in the food the cupric chelate of n-hydroxy-aaf induced the same spectrum of tumors as n-hydroxy-aaf, but the incidences were lower. while the prolonged retention of the material at the injection site may account for the greater carcinogenic activities of the metal chelates, serious consideration must also be given to the possible importance of chelation of carcinogens or their metabolites to cellular constituents.

.I 348

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12083. generation of action potentials in single ranvier's nodes of isolated frog nerve fibres under the influence of nickel and cadmium ions (russian) by experimenting on single ranvier's nodes of frog isolated nerve fibres it was shown that, along with a marked prolongation of the repolarization phase of the action potential (ap), ni and cd ions also caused a rise of the critical membrane depolarization level and an increased ap amplitude with somewhat reduced steepness of its ascending phase. ni and cd ions restored the ap generation in the nodes of ranvier altered by a 0.01% procaine solution, by an excess of potassium ions 00mm/1. of kcl) or by slight mechanical injury during dissection. it was only with a reduced na

concentration in the medium that the restoration of ap could be achieved. ni and cd ions considerably slowed down and weakened the cathodal rise of the critical level and the ap reduction. cysteine (10^{-2} to 10^{-3} m) eliminated all the effects of the mentioned ions. a suggestion is made that by binding the sh-groups of the nerve fibre proteins, nickel and cadmium reduce the rate of inactivation and the increase of potassium permeability in depolarization and also weaken the initial inactivation and the increase of potassium permeability in depolarization, as well as weaken the initial inactivation of the membrane (i-h), whenever this happened to be raised by previous influences.

.I 349

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1287. agnostic alexia and constructive apraxia with regressive evolution in a child of 12 yr. of age after an acute encephalopathy, the etiology of which could not be determined, a boy of 11 yr. and 10 mth. of age developed a syndrome of agnostic alexia and constructive apraxia which was remarkably pure. the intellectual functions were normal as determined by iq tests, speech was not disturbed either. the child could not read or copy a text, but was fully able to write (both freely and dictated). the patient could not read what he had written. this shows the characteristic features of agnostic apraxia. motor activity and performance were normal, but the child had extreme difficulty in constructing geometric forms, even elementary, either spontaneously or by copying. this remarkable syndrome disappeared, and during its involution it was followed up.

.I 350

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1288. the symptomatology of the parietal cerebral syndrome of the dominant hemisphere. parietal dyslexia and conduction aphasia

this is a very comprehensive study on a patient. in the beginning there was a pronounced gerstmann's syndrome, with autotopagnosia for parts of the face, dyspraxia and constructive apraxia and dyslexia. the autotopagnosia and mild left-right disturbances showed marked regression. actual hemianopsia was not observed, but tachistoscopia revealed that perception of the right field of vision was poor. audiometric examination showed a conduction deafness and disturbed binaural word synthesis. the disturbances were examined meticulously and tested for symptom relationships, which became evident in the various factors concerned with creative ability.

.I 351

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4544. observations on colour agnosia

a 56-year-old right-handed man, following the formation of a left posterior subdural hematoma developed 'spelling dyslexia' and impaired picture interpretation, which resolved, and color agnosia, which persisted. the latter impaired the use both of color information and of the names of the colors. this may be explained as a disorder impairing the recollection and formation of associations between color names and other types of information, with resulting interference in any task in which colors or their names have to be placed in a specific context. the alternative views of willbrand (1887) that here a limited dysphasia, and of sittig (1921) that a recognition defect is simultaneously present, cannot be excluded. in the present and in previously reported cases the causative lesion seems to have been posteriorly located in the dominant hemisphere, in the borderland between the area receiving visual input and the language or verbal recording area.

.I 352

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652. bitemporal hemianopia

two stages can be distinguished in the development of bitemporal hemianopia in hypophyseal tumors. the first stage is the consequence of direct pressure of the tumor on the lower side of the chiasma. hence its start with upper quadrantic field defects. in this stage the visual disorder is amenable to prompt and complete restoration. with progressing growth of the tumor the second stage follows as consequence of constriction by the circle of vessels. in this stage nerve fibers are being destroyed. therefore, after pressure relieving operation no restoration occurs, or to a limited extent only.

.I 353

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387. ophthalmic manifestations of bilateral non-occipital cerebral lesions

twelve patients are described with neuro-ophthalmic symptoms resulting from bilateral cerebral lesions in areas other than the occipital lobes. the symptoms and signs are categorized as follows group i those showing predominant disturbances in visual object recognition (visual agnosia) and disturbances of visual spatial localization. group iia those having defects in voluntary control of eye movements (ocular motor apraxia). group iib those with persistent palsies of conjugate gaze. although these symptoms may be present to some extent with unilateral lesions, they are much more profound and less able to be compensated with bilateral lesions. the evidence in the present cases suggests a biparieto-temporal localization for the lesions causing visual agnosia, disturbances of spatial localization, and ocular motor apraxia, and a more frontal localization for the lesions causing prolonged paralysis of conjugate gaze.

.I 354

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1774. the speed of reading. basis for a clinical function test
as an easily comprehensible measure for the capability of reading, the author recommends the determination of the reading speed for supplementation of the ocular function tests. the method in question constitutes a senso-motor efficiency test which is of value in the appraisal of haemianopias, paracentral and central defects of the visual field, in squint amblyopias and in spontaneous nystagmus.

.I 355

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1303. the problem of visual agnosia
this is a critical assessment of the ancient and modern theories on visual agnosia. an original description of the subjective world of these patients is also given. visual agnosia is a rare disorder, but it has led to comprehensive discussions, for instance, by the fact that the problem of normal visual perception is always involved. bay's view, which denies the existence of agnosia as a separate phenomenon in perception disorders, is especially dealt with. it is affirmed that no case has been described in the literature in which visual agnosia is decidedly a pure and isolated phenomenon.
mostly there are also disturbances in the intellectual interpretation of visual data. often there is metamorphopsia or asthenopia. there is no localized prestriate gnostic center for visual impressions. the older concept of higher and lower levels of perception and perception disorders is also criticized.
visual perception is not a passive, but a very active process, in which neurophysiological and psychological aspects are involved.
each of these can be

disturbed, leading to various degrees of visual perception disturbance.

.I 356

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2496. dysbarism among hyperbaric personnel

a survey of the effects of hyperbaric exposure on 62 medical personnel exposed to 1,516 compressions and decompressions revealed no case of permanent ill effect. pain in the ears or sinuses was the most common symptom but could often be ameliorated or avoided by the valsalva technique of forced insufflation with the nostrils occluded. the most serious symptoms encountered were 3 episodes of transient homonymous hemianopsia. the classic symptoms of decompression sickness extremity pains (the 'bends'), pulmonary or substernal distress (the 'chokes'), and skin dysesthesias occurred only rarely, and were so mild or so fleeting as to require no treatment. a further reduction in symptoms without increase in decompression time may be obtained by the inhalation of 100% oxygen during decompression stops at pressures below 26.8 pounds per square inch gauge (psig).

.I 357

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2996. visual static agnosia with special reference to literal agnosic alexia

this is a report of 2, right-handed adults who had 'visual agnosia (with predominance of literal alexia)'. recognition of letters was poor or nonexistent when the patient simply viewed the material (static method) but if the letter was slowly developed for them, they were able to identify it (dynamic method). one patient had vascular pathology which was considered to involve both occipital lobes and the 2nd patient had the surgical removal of the left occipital lobe for an angioma.

1388. optic agnosia semeiological and pathogenetic aspects

the authors discuss the classical concept of agnosia and make a survey of pathogenetical factors which determine its phenomenology. the original and traditional concept of such a term implied the loss of the capacity to recognize objects, when the functions of sense organs are undamaged. the psychological studies on perception and the modern physiology of vision allow to avoid the dichotomy between sensation and perception and to affirm their identity. cortex and receptors are closely bound and function in unison.

every cortical alteration is thus reflected in sensorial functions; it is therefore that on practical semeiological grounds it is possible to obtain a congruous information of the corresponding cortical functionality through an exploration of sense organs carried out by suitable means. since we are confronted with functional changes, exploration methods must be fit to evaluate dynamic aspects of perception in connection with the temporalization and spatialization of stimuli. such methods are now quite numerous and often complex a particular stress is laid on local adaptation, flicker fusion, and tachistoscropy on account of their significance and suitability. by such methods it is possible to show those functional deficits or pathological disturbances of sensorial functions which are also behind the pathology of visual recognition. fluctuation, extinction, alteration in the perception of movement, both real and apparent, changes in adaptation to light and darkness are all phenomena which can be detected instrumentally and which, at the same time, may be of determinant importance for the onset of 'agnosic' behaviour. the complexity of the latter, on the other hand, cannot always

be explained by sensorial disturbances only other mechanisms, with a function complementary but not less indispensable to the dynamics of perceptive processes, may intervene and interfere in it. on the basis of the latest neurophysiological data the attention is called to ocular motility and proprioceptivity, centrifugal innervation of sensorial receptors, and vestibular afferences. a particular clinico-pathogenetical significance is attached by the authors to the association of lateral visual disturbances with altered proprioceptive and kinesthetic information from the corresponding half-body such association in fact is nearly always present among the factors responsible for the most strictly 'spatial' errors of 'agnosic' pathology. in the light of these pathogenetical considerations as well as of suitable semeiological findings, the authors deem it convenient to divide their cases into 3 categories with distinct clinical features (a) cases in which altered visual behaviour may be related to changes of the visual function and of its complementary mechanisms; (b) cases in which hemianopia is associated with a homolateral deficit of somatic proprioceptivity; (c) cases in which the changes in behaviour are chiefly, but not only, due to a dissolution of the symbolic sphere.

.I 359

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2568. clinical observations on hemianopia (japanese)

the clinical findings in 19 cases of hemianopia were analyzed. hemianopia was caused most frequently by vascular lesions of the central nervous mianopsia, and by tumors. willbrand's prism sign, which is generally taken as evidence of an optic tract lesion, was positive in one case with a parietal lesion. no case showed a cogwheel movement of the eyeball. optokinetic nystagmus was positive in 3 cases, one of which proved to have a parieto-occipital aneurysm.

the etiological factor could not be identified in the remaining 2 cases. macular sparing was found to be symptomatic of an occipital lobe lesion. incongruity of the 2 fields was observed in 2 cases with an occipital lobe lesion. as for the prognosis, hemianoptic field defects remained stationary in cases of vascular lesions. on the other hand perfect recovery of the visual field defect occurred in cases with an occipital lobe tumor and in hypophyseal hypertrophy caused by pregnancy. the visual acuity of hemianoptic patients was fairly good and no deterioration occurred during the observation period of about 4 years. only one patient out of the present series died. these results suggest that a favorable vital prognosis can be accorded to hemianoptic subjects.

.I 360

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1384. importance of campimetry and carotid and vertebral angiography in thrombosis of the posterior cerebral artery
the authors report a case of thrombosis of the posterior cerebral artery which presented only lateral homonymous hemianopia and stress the importance of campimetry and of carotid angiography beside vertebral angiography.

.I 361

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375. hemianopsia and glaucoma
after a discussion of the bibliographic references to the few observations on the simultaneous occurrence of hemianopsias and glaucoma the author states on the basis of his experiences the following points homonymous hemianopsias occasionally take place in glaucoma, although no direct relation can be established between the former and the glaucoma. it has to be pointed out, however, that in other older patients, for example in those with retinal

detachment, neuritis, etc. who are likewise subjected to repeated and exact perimetry, such hemianopsias do not occur, or are to be found at a lesser rate than in glaucoma. a homonymous hemianopsia has to be taken into consideration also in the event of a sudden impairment of the visual field in a glaucomatous patient or when the hemianopic defect supervenes in addition to the visual field defect due to glaucoma. in cases of binasal hemianopsia, the simultaneous presence of glaucoma is not a rare incident. whether the binasal hemianopsia is the result of the gradual development of a glaucomatous visual field with nasal defects or whether it constitutes an independent symptom to a certain extent, cannot always be clarified in the individual case. obviously the condition of the basal cerebral vessels plays a certain role in the development of glaucoma, even if this role cannot be clearly defined as yet. in cases of binasal hemianopsia, a glaucoma has to be ruled out before radical diagnostic and therapeutic measures are carried out.

.I 362

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1131. disorders of oculomotor functions in lesions of the optic pathway at the parieto-occipital level and their significance in topical diagnosis
paresis of ocular movements to the hemianopic side is described in 9 patients with acute vascular lesions in the parieto-occipital region. in 7 cases the paresis was of the dissociated type with inability to follow the moving finger, while ocular movement in a verbally stated direction was quite normal. in the remaining 2 patients in whom the oedema extended into the frontal region there was complete paresis of all conjugate movements. conjugate paresis receded hand-in-hand with the parietal symptomatology even if the hemianopia persisted. the oculomotor disorders referred to have never been observed in

lesions which did not extend beyond the occipital region. conjugate paresis has in all cases drawn attention to the presence of hemianopia unobserved by the patients and this has led to a more accurate topical diagnosis.

.I 363

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2333. binocularity in anomalous retinal correspondence

patients with anomalous retinal correspondence demonstrate complete bitemporal or binasal hemianopia when tested for binocular vision; exotropes have a binasal suppression and esotropes a bitemporal suppression. this is contrary to the prevailing concept of the function of the peripheral retina in anomalous retinal correspondence. 6 references.

.I 364

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2120. thioguanine in the treatment of certain autoimmune, immunologic and related diseases

the therapeutic effectiveness of 6-thioguanine has been evaluated over the past 3 years in 19 patients with diverse syndromes. only patients with severe debilitating disease unresponsive to conventional therapy were treated. remissions occurred in 2 of 5 patients with systemic lupus erythematosus, in 1 patient each with dermatomyositis and necrotizing angiitis, 2 patients with psoriasis and 2 of 4 patients with atopic disease. improvement occurred in other patients with these diseases and in 2 of 4 patients with neurodermatitis. two patients with scleroderma experienced only equivocal benefit. significant toxicity attributable to the drug was observed in 5 patients. assessment of the eventual value of these agents in therapy requires further study. hypotheses regarding the

mechanism of action of these agents and the significance of clinical response are discussed.

.I 365

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2469. the nature of collagen disease, particularly of systemic lupus erythematosus (sle), with special reference to renal lesions (japanese) from the results of examination of 161 autopsy cases of collagen diseases, rheumatic fever and polyarteritis nodosa (pn) are considered as diseases of hyperergic nature, showing pronounced specific manifestation in particular organs. as the reactivity becomes lower, this specific localization becomes less significant and many organs become affected in sle. it may accordingly be supposed that sle is not a disease of hypersensitivity but one occurring in a state of exhaustion of reactivity after prolonged sensitization. moreover, a sle-like syndrome arises not only in the end stage of parasepsis, nephritis, nephrosis and some cases of prolonged sensitization by myco.tb but also in pn,pss,dm and rheumatism. it may therefore be conceivable that sle is a syndrome rather than a separate entity. it is most important to consider whether sle-like symptomatology may be regarded as a process equal to an auto-immunization and whether the key to morphological elucidation of the auto-immune phenomenon may lie hidden in this problem.

.I 366

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420. therapy of lupus nephropathies by 6-mercaptopurine corticosteroid therapy improved the general prognosis of sle, but has no detectable effect on the nephropathy and this is actually the main cause of death. a new therapeutic method is presented using 6-mp purinethol (leupurin) which produced 2 remissions in 6 consecutive cases total and in 4 cases

with severe nephropathy definite remission. it should be emphasized that 5 of the cases reported had definite npn elevation, accordingly they are considered hopeless.

.I 367

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2475. lupus erythematosus with fatal hemorrhage into the liver and lesions resembling those of periarteritis nodosa and malignant hypertension.

immunocytochemical observations

a firmly established case of lupus erythematosus with histologic

characteristics of periarteritis nodosa and fatal hemorrhage is presented.

immunocytochemical studies were done to explore the possibility of the vascular

lesions being immunological in type. by immuno-fluorescent techniques

γ-globulin, human serum complement, albumin and fibrinogen were demonstrated in

the vascular lesions. γ-globulin in the renal glomeruli was associated only

with complement. the conclusion is that lupus erythematosus is primarily an

immunological disease with complex auto-immune mechanisms operative.

.I 368

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198. early experiences with azathioprine in ulcerative colitis. a note of caution

azathioprine was administered to 10 patients with ulcerative colitis classified

as 'very severe' in 2, 'moderately severe' in 7 and 'relatively mild' in 1

patient, in conjunction with 'standard' therapy and adrenal corticosteroids in

8 of the 10 patients. the possible beneficial therapeutic effects of

azathioprine in this small series cannot be evaluated definitively because of

the concurrent medication and the preliminary uncontrolled observations.

however, clinical improvement was apparent in 8 of the 10 patients; and in 2

patients, the favorable course occurred in the absence of steroid therapy. in 2 additional patients, the favorable course was maintained during the administration of azathioprine following the discontinuance of prolonged steroid therapy. in 1 patient, the administration of azathioprine was associated with amelioration of an arthritis and pyoderma gangrenosum which did not respond to the use of steroids and other medication. immuno-suppressive observations were limited. the established delayed hypersensitivity response, as reflected in various skin tests, was unchanged during the administration of azathioprine. azathioprine had no discernible toxic effects upon the kidneys or the liver in 2 patients, 1 with postnecrotic cirrhosis and the other with serum hepatitis. gastro-intestinal symptoms (anorexia, epigastric discomfort, and nausea) occurred in 8 patients. mild to moderate leukopenia developed in 8 patients and, in 2 individuals, was accompanied by thrombocytopenia. temporary alopecia occurred in 1 woman. the hematopoietic effects developed within 2 or 3 wk of therapy with azathioprine at a dosage level of 4-6 mg/kg/day. azathioprine does not exert the rapid beneficial effect in ulcerative colitis noted with corticotropin and adrenal corticosteroids. therefore, its use in severe ulcerative colitis requiring intensive therapy probably is undesirable. azathioprine, on the basis of these initial observations, may be considered for moderately severe ulcerative colitis, under circumstances permitting controlled and prolonged therapeutic trial as adjunct medication, but with careful supervision for prevention of toxicity, especially leukopenia.

.I 369

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1281. effect of fluoropyrimidines on delayed cutaneous hypersensitivity
the ability to express delayed cutaneous hypersensitivity was assessed in 51 patients with carcinoma. evidence is presented that 5-fluorouracil and

5-fluoro-2'-deoxyuridine paradoxically potentiate this parameter of immune responsiveness.

.I 370

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248. data on etiology, pathogenesis, treatment results and survival period in 560 patients with cirrhosis of the liver

statistics were compiled from a total of 560 cases chosen at random, of cirrhosis of the liver. the figures refer to the age and sex of the patients, as well as to the etiology and the hepatic morphology. as the date of death of 304 of the subjects was known, it was possible to calculate the survival time after the diagnosis was made. only 36% survived the time of diagnosis by 1 year, 16% by 3 years, and 8% by 5 years. these figures show that modern therapy of liver cirrhosis has up to now not succeeded to prolong the life of the majority of the victims. in many cases, however, it is possible to a large extent to relieve the patients' suffering by improving the appetite and the general condition and by eliminating ascites and periods of hemorrhage and stupor. particular attention should be paid to the prophylaxis of the disease and, by studying the survival time assessments and therapeutic reports, to the method of selection of the subjects.

.I 371

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897. chronic renal diseases and pregnancy a review

a review is given of the reciprocal relationships between chronic renal disease and pregnancy. after a short review of the most important changes in renal function due to normal pregnancy, the diagnosis of chronic renal disease is discussed. subsequently, the following complications of pregnancy are discussed individually chronic pyelonephritis, chronic glomerulonephritis,

lupus erythematosus, the nephrotic syndrome, diabetic nephropathy and polycystic disease of the kidney. the paper is concluded by a discussion on the influence of pregnancy on the different renal affections.

.I 372

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4193. the occurrence to cytomegalovirus infections in childhood leukemia. report of three cases

cytomegalic inclusion disease (cmid) presented the following clinical findings in three children with acute leukemia persistent high temperature, cough, vomiting, diarrhea, hepatosplenomegaly, rales, and terminal icterus.

pancytopenia was present in all, including two children in leukemic remission.

roentgenographic evidence of pneumonia did not appear until the third week after the onset of symptoms. abnormalities in liver function tests were late

findings. intranuclear inclusions were seen in urine sediments of two

patients. in neither of these patients were intranuclear inclusions

demonstrable in the sputa. virus culture from urine was done in one of these

patients and cytopathogenic changes characteristic of cytomegalovirus (cmv)

were demonstrated. cmid was the cause of death in these three children, all

of whom had received chemotherapy with agents known to have immunosuppressive properties.

.I 373

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. on chorea, lupus erythematosus, and cerebral arteritis

a woman aged 33 developed chorea 10 yr after the onset of systemic lupus erythematosus (sle). she had experienced an asymptomatic interval of

8 yr. the abnormal movements persisted for 5 mth, but then subsided

after short-term administration of 6-mercaptopurine. there are 11 previous

descriptions of chorea patients with sle. in 3 out of 4 autopsied cases, extensive cerebral lesions due to diffuse arteritis were found. the cns changes were quite similar to those found in chorea minor.

.I 374

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1878. pharmacologic actions on cellular immunity

the following chapters of interest in the field of drugs and immunity processes are included manifestations of cellular immunity. states of reduced immunologic reactivity. present status of pharmacologic immunosuppression. tests for susceptibility of tuberculin reactions to pharmacologic action. tests for susceptibility of transplantation immunity to pharmacologic action. comparative susceptibilities of tuberculin and skin homotransplantation reactions to pharmacologic action.

.I 375

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2625. chromosome aberrations in human cells following treatment with imuran
five women with various collagen diseases were studied. bone marrow aspirates were obtained from each patient before and 12 to 24 days after start of imuran (azothioprine) therapy. fifty metaphases from each sample were counted. in patients nos. 1 and 2 the increase in cells with structural abnormalities during therapy is significant. the aberrations found were mostly breaks of the chromatid and chromosomal type. a few abnormal chromosomes were seen, among which a ring chromosome. in patient no. 1 chromatid exchanges were seen in three cells.

.I 376

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3645. autoimmune hepatitis

in 30% of 301 patients with cirrhosis, the cause was uncertain. of these 90 cases the clinical picture of active chronic hepatitis could be recognized in 69, and 26 of these were characterized as lupoid hepatitis. the relationship between active chronic hepatitis, lupoid hepatitis and sle was studied in 3 groups of 25 cases each. a comparison was then made between the possible etiological factors, the systemic manifestations, the survival rate, the histological appearances, the biochemical tests, the autoimmune reactions and the results of the immunosuppressive drugs. from this study a concept emerged according to which a proportion of cases of cirrhosis occurring in adequately nourished individuals can be attributed to the end result of an autoimmune reaction.

.I 377

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766. a comparison of the effects of selected cytotoxic agents on the primary agglutinin response in rats injected with sheep erythrocytes
a comparative study was made of the effects of several cytotoxic agents, given at maximally tolerable doses, on the primary agglutinin response in rats immunized with sheep erythrocytes given intraperitoneally. antigen was given before, at the beginning, or in the middle of a 5-day course of drug treatment. chlormethine (mechlorethamine), 5-fluorouracil, and 5-fluoro-2'-deoxyuridine did not suppress the primary response significantly. methotrexate, 6-mercaptopurine, 6-mercaptopurine riboside and 2-amino-6-((1-methyl-4-nitro-5-imidazolyl) thio) purine prolonged induction time and suppressed peak titer maximally when immunization was performed one to three days prior to drug treatment. vinblastine did not affect peak titer, but did prolong induction time when antigen was given 2 days prior to drug treatment.

cyclophosphamide markedly prolonged induction time and suppressed peak titer irrespective of the time of antigen administration. the antimetabolites appeared to suppress maximally the intermediate stage of the primary response. cyclophosphamide appeared to suppress all stages.

.I 378

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1959. analysis of mechanism of immunosuppressive drugs in renal homotransplantation

dammin g. j.

a long-term study of the mechanism of action of immunosuppressive drugs has been completed in bilaterally nephrectomized dogs with kidney homotransplants. over 1,000 test animals with 24 different drug protocols have been analyzed. increasing numbers of long surviving animals have posed many questions regarding the status treated host. the current drug protocol of azathioprine and diazoacetylserine ('azaserine') has produced 90% 50-day survivors and 50% 100-day survivors. the following observations have been documented all animals on prolonged drug therapy are immunologically competent; drug therapy can be stopped successfully in some but not all animals; long surviving kidneys apparently are protected in some way in the new environment because a second donor kidney can be rejected while the first survives; retransplantation of a long surviving kidney back to its original host did not lead to a decrease in renal function; long surviving kidneys successfully retransplanted back to their original donors are rejected when transplanted to third party, non-drug treated recipients; immune paralysis does not account for the prolonged survival because the second donor kidney which constitutes a double dose of antigen is rejected while the first continues to survive; absorption or metabolism of the drug does not account for the variation in results because

two kidneys, each from separate donors, can be rejected differentially in the same drug treated host; and all hosts are sensitized against the recipient and this sensitization continues even in those animals successfully weaned from drugs. additional analyses of the relationship of skin homografts and kidney homografts reveal the following skin homografts are universally rejected within 20 days by hosts treated with the drug regimen which protects kidney homografts sometimes permanently. when skin and kidney homografts from the same donor are placed simultaneously skin survival is prolonged while kidney survival is shortened. this paradoxical effect probably is explained by the production of antibodies by skin which are absorbed by the rejecting kidney. additional observations indicate that drug-treated animals, male and female, are fertile and that multiple rejection processes can produce generalized immunological picture in the host similar to an autoimmune disease process.

.I 379

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3083. myocardial toxicity of contrast agents used in angiography

the myocardial toxicity of many current and some experimental contrast agents has been studied in dogs, by use of a previously unreported method of occlusion retrograde coronary venography as well as the familiar technique of selective coronary arterial catheterization. the following conclusions appear justified in the light of the experiments not only the iodine-containing radicals with which the contrast agents are so often identified (acetrizoates,

diatrizoates, iothalamates, etc.), but also the final salification products appear to be responsible for the widely divergent degrees of myocardial toxicity of contrast agents, to the point that different salts of the same compound behave as entirely different agents both chemically and biologically. the results seem to indicate the dominance of sodium ion and/or the protective effect of methylglucamine salts with respect to the myocardial toxicity of current radiopaque media. reported, yet unexplained, electrocardiographic changes occurring within one to two seconds from the beginning of massive caval high-pressure injections appear to find a causal relationship in the myocardial irritability induced by the distention of the coronary veins and the myocardial infiltration which is intentionally enhanced with our retrograde injection techniques. a peculiar trait, shared in varying degrees by all radiopaque agents tested, is their ability to increase coronary blood flow. the clinical significance of this phenomenon, however, remains to be established. these studies re-emphasize the limita-

tions of the standard toxicity studies conducted in animals. it should be clear from the results reported that agents to be administered into the coronary circulation demand investigation in regard to their potential toxicity by the methods described herein or variations thereof. in fact, similar tests should be carried out for all organs to be subjected to radiographic examination via the vascular bed. the authors hope that this presentation will stimulate renewed investigation, particularly in view of the growing clinical applications of selective cardiovascular opacification techniques.

.I 380

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2476. studies on cardiac dimensions in intact, unanesthetized man. i. description of techniques and their validation. ii. effects of respiration. iii. effects of muscular exercise
a method is described which permits measurement of relative changes in the external dimensions of individual cardiac chambers throughout the cardiac cycle in intact, unanaesthetized man. it consists of suturing multiple radiopaque silver-tantalum

clips to the surface of the heart at the time of cardiac operations. in the postoperative period, cineradiograms are obtained and the distances between clips are measured on each individual frame.

this technique has been found to be safe and has been employed in 68 patients without any complications. as a result of studies in 8 patients utilizing biplane serial exposures, the effects of rotation of the heart in the sagittal plane during the cardiac and respiratory cycles were determined precisely.

if clips were properly placed on the heart, the possible errors resulting from such rotation were found to be quite small.

during inspiration right ventricular dimensions increased, while the opposite occurred during expiration and during the valsalva manoeuvre. left ventricular dimensions

exhibited little change during normal

respiration. during deep, slow inspiration,

the changes in dimensions of the left

ventricle lagged behind those of the right

ventricle by 1 to 5 (generally 2 or 3) cardiac

cycles; the magnitude of the changes in

the dimensions of the left ventricle was

smaller than that which occurred in the right

ventricle. the effects on ventricular dimensions of light muscular exercise performed in the supine position were studied in 9 patients. the end-diastolic dimensions decreased by an average of 6.0% of control in the right ventricle, and by an average of 5.1% in the left ventricle. end-systolic dimensions decreased by an average of 5.6% of control in the right ventricle and by an average of 6.5% in the left ventricle. these decreases are considered to approximate one-half of the resting stroke volume. in the 4 patients in whom the rate of right ventricular pressure rise was determined continuously, exercise resulted in an elevation of dp/dt while ventricular end-diastolic dimensions decreased. these data are interpreted to indicate that an increase in myocardial contractility occurs during muscular exercise in man.

.I 381

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3765. radioactive isotope determination of myocardial blood flow by surface counting and ratio formula wilkinson d.

the results presented here have a large scale error and a large scatter, so that

the authors recommend that further clinical use of this method should not be attempted. if the coronary portion of the flow rate curve exists, then a change in the present instrumentation is needed to allow use of the technique of sevelius and johnson in defining a coronary portion of the flow rate. an attempt is made to evaluate the possible source of errors.

.I 382

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1379. risa-ventriculography and risa-cisternography
some general experience of the authors with risa-ventriculography and risa-cisternography is related. they conclude that the former technique may be particularly useful in detecting intraventricular tumors and internal hydrocephalus as well as assessing the efficiency of surgical shunts; the latter technique may be useful in the study of normal csf circulation as well as in cases of csf leaks, arachnoiditis and external hydrocephalus.

.I 383

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3485. measurement of the cardiac output and ventricular volumes by radiocardiography

cardiac output was measured by external counting after injection of radioisotopes (rihsa and erythrocytes-cr51). the results in 113 subjects, including 16 normals, are presented and compared with the results by other methods. cardiac output at rest and after exercise was compared in 65 subjects. the principle of ventricular volume measurement by radioisotope-cardiography is discussed. the results of measurement of the ventricular volume in 17 normal subjects and 90 patients, and of measurement of the ventricular volume in 57 patients, are presented.

.I 384

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3762. aberrant left coronary artery
five cases of aberrant coronary artery are presented, with emphasis on the angiographic features and differentiation from endocardial fibroelastosis. clinical and electrocardiographic features may suggest the proper diagnosis, but only angiography can conclusively demonstrate the continuity between the pulmonary artery and the left coronary artery. in these cases, blood flow was from the pulmonary

artery to the coronary artery (forward) in 2 cases, and from the coronary artery to the pulmonary artery (retrograde) in the other 3. when the diagnosis of aberrant coronary artery is suspected, selective left-sided angiocardiology should be the angiographic procedure of choice. the differentiation from endocardial fibroelastosis and other myocardopathies is usually not a problem with such a study, but may be more difficult with intravenous angiocardiology. with this latter type of study, the coronary arteries are not generally visible, but a persistently thin lateral aspect of the left ventricular wall should suggest the proper diagnosis. subsequent confirmation by a left-sided injection is advisable.

.I 385

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4159. detection of heart shunts by means of ^{125}I external scintillation detection of a pure dilution curve originating in the right ventricle has been pursued by investigators for many yr. the use of the soft photons of ^{125}I offers an improved method of determination by allowing excellent collimation through 2 mechanisms (1) a small half value layer

of 2 cm in tissue, and (2) unidirectionality, in part due to all-or-none photoelectric absorption of these photons as compared with the pluridirectionality due to Compton scatter in the case of ^{131}I

i. In 30 normal individuals, externally detected dilution curves from the right heart ventricle and arterial dilution curves obtained by arterial puncture are compared.

Five hundred microcuries of ^{125}I are injected into an antecubital vein. The amount of radiation absorbed from a 500 μCi dose in an adult of 70 kilos is 1000 to 2000 mrad when injected in the form of ^{125}I iodide. The use of ^{125}I orthoiodohippurate is advised due to its short biological half-period and the integrated whole-body radiation exposure is decreased 100-fold in comparison with the ^{125}I iodide. The

shape of the right heart curve is very similar to the arterial dilution curve with a

13–5% excess of counts originating outside the right ventricle area. The descending segment of the right ventricle curve has a minimum count rate of only 12–2% of the peak of the curve as compared with the arterial curve of 10–2.5%. A mean $t_{1/2}$

of the descending down slope of the right ventricle is 1.52

0.45 sec. for the right

heart curve and 2.4 0.65 sec. for the arterial curve.

the clinical usefulness of this

procedure in 20 patients with atrial septal defects and 9

patients with ventricular sep-

tal defects is analyzed. it seems possible to perform selective

right-heart radiocardio-

graphy by means of external precordial detection of 125 i. the

method is simple and

reproducible.

.I 386

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4160. clinical applications of quantitative radiocardiography. i.

results in normal subjects and changes with age

a technique is described for routine determinations

at the bedside of blood volume,

cardiac output and pulmonary blood volume by means

of the method of quantitative

radiocardiography. the instrumentation is simple,

the technique is easy to perform

and causes little trouble to the patients, only one

injection of about 50 uc of rihsa

being needed. thirty-nine patients aged 17-83 yr.,

free of cardiovascular or re-

spiratory disorders, were studied. the results

obtained are in close agreement with

previous reports. only the cardiac index showed a significant decrease with age, while the reduction of blood volume and of pulmonary blood volume was slight. a close statistical correlation was found between pbv and sv, and was interpreted as a dependence of pbv on sv.

.I 387

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2725. demonstration of myocardial infarction by photoscans of the heart in man intravenously injected radioiodinated oleic acid was incorporated into heart muscle in sufficient concentration to permit recording photoscans of the heart in man. in 3 fatal cases of massive septal myocardial infarction, injection of the radioiodinated fatty acid (rifa) was made during life; at necropsy photoscans of the excised heart showed a discrete area of absent radioactivity corresponding to the infarcted interventricular septum. photoscans of the heart were made during life in 42 patients, 9 of whom had suffered recent myocardial infarction. there were definite areas of decreased radioactivity corresponding to the location of the infarction,

judged by the electrocardiogram, in 4, and probable areas of decreased radioactivity in 2, of the 9 cases of myocardial infarction. the technic as presently employed just approaches the limits of definition of infarction in acute cases. modification of the biochemical principles or further development of the y-camera may bring the method to a level of diagnostic usefulness.

.I 388

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2716. γ -angiocardiology recordings were made, simultaneously with the γ -cardiogram, of a pulmonary angiogram by means of a collimator placed in the left scapular region and of carotid angiogram by a collimator centered on the axis of the external auditory canal. the 3 curves yielded very interesting information on the chronology of the various cardiac cycles. the pattern of the pulmonary and carotid γ -angiograms was valuable in several pathologic conditions. it is more logical to measure the cardiac output on the carotid curve than on the γ -cardiogram, especially if there are shunts. the pulmonary curve allows rectification of the time

constant of emptying of the left cavities of the heart. as regards chronologic information on cardiac cycles, attention is drawn to the fact that in the pulmonary circulation long and short circuits can be demonstrated. the characteristic times can be measured. between the time that the radioactive material appears in the left cavities and the time that it leaves the carotid, there is an interval of 3-4 systoles, which represents the time necessary for left circular filling. the validity of calculation of the cardiac output with the stewart-hamilton formula is discussed. this is valid if the collimator covers a small volume of the principal channel. it remains to be shown if such a calculation is valid for larger cavities, or for 2 cavities, through which the radioactive material passes successively, and which have different $c(t)$ functions as well as for all tissue 'seen' by the collimator, some of which are not yet irrigated with the radioactive blood, while in other areas recirculation has already started. these aspects, and their application to the pulmonary angiogram, are discussed in detail. with the

authors' technique, y-angiogram is especially valuable, as correction for the time constant of the decrease of the left peak is based on the lengthening of this curve. this again serves as a basis for determining the left ventricular volume.

.I 389

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2717. the value of quantitative radiocardiography in the study of hemodynamics six normal subjects and 7 patients with mitral stenosis were studied. quantitative radiocardiographic investigations (rihsa) were performed according to donato's method. the stroke volume as well as the cardiac output were found to be decreased in mitral stenosis, the right ventricular evacuation ratio diminished, and the pulmonary circulation time prolonged. the results pertaining to diastolic right ventricular capacity, right ventricular resting blood volume and pulmonary blood volume proved inconclusive.

.I 390

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3056. the localization of aortic shunts developed by a precordial

registration of ^{131}I injected into the aorta at different levels

a technique for localizing shunts of aortic origin

is described, based on the analysis

of precordial records of ^{131}I injected at different

aortic levels. seven patients with

patent ductus arteriosus (pda), 1 with a

coronary av fistula, 2 with ventricular

septal defect (vsd), 1 with atrial septal defect

(asd), 3 with mitral regurgitation,

2 with aortic regurgitation and 2 with systemic

hypertension were studied. retro-

grade arterial catheterization by seldinger's

technique was performed in all the

patients, as well as right-sided catheterization

in those with congenital cardiopathies,

and transseptal catheterization in those with

valvulopathies. a dose of 5-15 μCi of na

^{131}I was injected at the levels of the aortic root,

the ascending aorta, the aortic arch,

the origin of the left subclavian artery (ductus

level) and the descending aorta (post-

ductus level). precordial curves were obtained by

means of a 2-inch thallium-acti-

vated nai crystal focused over the 3rd left intercostal

space at the sternal margin.

the shunt outlet can be detected by obtaining

simultaneous venous dilution curves

from the right chambers and the pulmonary artery.
the latter technique was used
in 2 patients with pda, 1 with coronary av fistula
and 1 with vsd. these curves
were obtained by continuous withdrawal of blood which
had flowed through a well
scintillation counter. the crystal pulses were carried
to ratemeters which worked
with the following time constants 0.01-0.15 sec for the
precordial curves and 0.5
sec for the venous curves. a direct recorder with a
5-mm/sec paper speed was
used. normal precordial curves after injecting above
the aortic valve were obtained
in patients with arterial hypertension, mitral regurgitation
and asd and vsd. a
swift downslope which fell down near the baseline level and
the recirculatory area
was observed.

.I 391

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1671. the use of 99m tc pertechnetate in cardiac scanning
technetium 99m pertechnetate has been utilized
in the aas' laboratory for scanning the
cardiac blood pool. the delineation of the heart
pool and surrounding vasculature
is comparable to that obtained with the standard

^{131}I compounds now in use. In the authors' hands $^{99\text{m}}\text{Tc}$ had the following advantages since they routinely utilized $^{99\text{m}}\text{Tc}$ for brain and thyroid scans, it is available, eliminating the purchase and shelf decay of other materials. Three to 5 mCi quantities may be administered with relatively low patient radiation dosage. The associated high count rate permits rapid scanning. The identification of pericardial effusions is enhanced by the radioactivity in the stomach which in some cases becomes abnormally separated from the cardiac blood pool.

.I 392

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2012. The use of technetium $^{99\text{m}}\text{Tc}$ as a clinical tracer element the physical properties, metabolism and radiation dose of $^{99\text{m}}\text{Tc}$ are discussed and compared with those of ^{123}I , ^{125}I , ^{131}I and ^{132}I . It is shown that with $^{99\text{m}}\text{Tc}$ the highest 'in vivo' counting rates are obtained for a given internal radiation dose, so that measurements of high statistical accuracy may safely be made. The γ -ray energy is near optimum for scanning and the observation of transients allowing light-weight collima-

tors to be used. while ^{99m}Tc tagged albumin is considered superior to ^{131}I for applications such as brain scanning, placentography and the measurement of cardiac output, ^{123}I if it becomes available will be preferable for thyroid scanning.

.I 393

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2626. a study of central arteriovenous shunts by precordial recording of radioalbumin dilution curves
precordial dilution curves of 185 patients were studied, 56 of them without cardiovascular disease, 48 with central arteriovenous shunts and 45 with various cardiac diseases. collimation was not used, allowing only minimal quantities of radioactive material (0.5-2.2 μCi of ^{131}I -tagged albumin) to be utilized. the precordial focusing zone was a critical factor in this technique. the application of different discrimination factors, among them the ratio between the minimal concentration and the latter -an index proposed here - made possible the diagnosis in 46 of the 48 patients with shunts. this method was shown to be as sensitive as classical oximetry done during cardiac catheterization. the curves in pure valvular

stenosis do not show similar changes to the shunts. on the other hand, these changes are shown in certain valvular regurgitations. this fact becomes the most important limiting factor in the diagnosis of central arteriovenous shunts. cardiac failure does not preclude the diagnosis, providing one can exclude valvular regurgitation by other means. the method is thus, in spite of its limitations, of extreme value in diagnosing central arteriovenous shunts, especially when the results are analyzed together with clinical

.I 394

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information.

2724. primary epidermoid cancers of the lung. electron microscopic study

an electron microscopic study was made of 8 squamous cell, 3 undifferentiated, and 3 alveolar carcinomas of the lung on biopsy specimens embedded in methacrylate. the squamous cell carcinomas were found to contain cylindrical cells with glycogen granules, scanty mitochondria, a reticular endoplasm which was chiefly vesicular, numerous free ribosomes,

and bundles of confluent fibrils in the desmosomes. the authors also observed in the center of the tumor nodes, cells richer in tonofibrils which enveloped the nucleus, and cells in which all the cytoplasmic organelles had almost disappeared except for tonofibrils or cells packed with keratohyalin and even lipid granules sometimes arranged in lamellar formations of the myelin type. the picture as a whole was that so often seen in the optic microscope tumor foci formed of slightly differentiated cells at the periphery which became more differentiated as one approaches the center. the undifferentiated cells resembled more the intermediate bronchial cells than the basal cells. the paper does not describe the undifferentiated and alveolar carcinomas.

.I 395

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1375. loss of neoplastic properties in vitro. ii. observations on kb sublines
ten sublines of the kb cell line obtained from a number of different laboratories were reexamined with respect to chromosome number and heterotransplantability

to the syrian hamster cheek pouch. twelve clonal cultures derived from 2 of these sublines were similarly examined. three sublines differed from one another and from the kb cell line originally studied, which was heterotransplantable with inocula of circa 10^4 cells. only 2 of the sublines could be heterotransplanted with inocula of less than 10^4 cells; 5 were heterotransplantable with inocula of 10^4 - 10^6 cells; and 2 failed to heterotransplant, even with inocula of 10^6 cells. similar differences in heterotransplantability were observed among the clonal derivatives of 2 of these sublines. although the modal numbers of these sublines and clonal derivatives were basically similar, ranging from 73 to 80, a few lines had a chromosome of sufficiently distinctive morphology to serve as a marker. there was, however, no apparent correlation between these minor karyotypic differences and heterotransplantability.

possible differences between non-heterotransplantable and heterotransplantable sublines with respect to the pattern of variability in cytoplasmic protein and cytoplasmic ribonucleic (rna) content per cell

remain to be studied in detail. for i of this

series of articles see exc. medica cancer, 1965, abstr. no. 2378.

.I 396

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1377. establishment of a tissue culture strain jtc-14 from actino-

mycin-induced ascites sarcoma, and its biological characters

cell line jtc-14 has been maintained for more

than 2 yr. and subcultured 93 times.

cells from the 10th subculture on subcutaneous

injection into mice produced tumors

identical with those produced by the original

cells. judged by the time taken to kill

mice on intraperitoneal injection the tissue

culture cells were not as malignant as

the original tumor cells. after passage in

animals the cells were easily re-established

in culture in vitro.

.I 397

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1378. microcinematographic study of the mechanism of cancerous

invasion in cultures of normal tissue combined with malignant cells

normal myocardium of newborn c3h mice was

cultivated in vitro in contact with

homologous sarcomatous cells (strain n1 and

strain nctc) and studied by micro-

cinematography for 22 days. it was found that

the tumor cells tend to move apart,

and with more vigorous and rapid movements
some of them called 'commando's'
make their way into the group of normal
cells but are arrested wherever they meet
a compact group of these cells. this then
demonstrates, on the one hand, direct
aggressivity of the tumor cells and, on the
other, the 'group' defence of the normal
cells.

.I 398

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2413. the presence of lymphocytes in long term cultures of
newborn mouse thymic epithelium
thymic epithelial cells derived from newborn
mouse thymic fragments were cultured
in vitro for over 22 mth. subcultures were
started by transferring minute cell
sheets obtained by mechanical scraping of
the original culture when it was 14 mth
old or older. lymphocytes, many of them
with the morphological appearance of
plasma cells, were seen in the subcultures.
intact lymphocytes, as well as mitotic
figures were seen within cytoplasmatic vacuoles
of the epithelial cells. the possible
bearing of these observations on the origin of the
thymic lymphocytes is briefly

discussed.

.I 399

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3748. four separate tumour clones derived from a transplantable pleomorphic carcinoma of the lung in a heterozygous mouse
a metastasising pleomorphic adenocarcinoma
in the lung of an untreated heterozygous male mouse was successfully
transplanted to 4 brothers by the 'plating'
technique of henderson and rous. by
'plating' multiple small grafts in air bells in
the subcutaneous tissues of the new hosts
it was possible to select 4 different clones
of transplantable tumour for further study.
the histological peculiarities of
different parts of the original tumour
were reproduced in the different clones a i,
ii, iii, and b. retrospective study
of the primary tumour and of its metastases
provided some interesting clues to routes
of metastasis and the selective survival of
malignant cells. it is concluded that by
the cloning of transplantable cells, at the
first serial passage, valuable information
about the histogenesis and potential
malignancy of the primary tumour can be
obtained. lastly, the highly malignant

character of 4 clones of tumour cells apparently derived from the familiar clinically benign adenoma of the mouse lung may be of some interest, from the point of view of prognosis based on histology.

.I 400

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2379. in-vitro culture of pulmonary tumors in hamsters caused by adenovirus 12

it is known that the adenoviruses 12 and 18 provoke malignant tumors in the new-born hamster. the authors made a study of the histogenesis of these tumors and examined the specific changes brought about in the cells by the virus infection malignancy, presence of viral antigen, reactions to superinfection. when new-born hamsters were inoculated in the chest with adenovirus 12, malignant tumors developed in one or two months, in 16 animals out of 22. these tumors presented an epithelial aspect and were of bronchiolo-alveolar origin. they were transplantable in vivo; if they were cultured in vitro, they consisted in the first few cultures of macrophages, fibroblasts and epithelium. in subsequent passages, there was a progressive disappearance of the macrophages

and fibroblasts. in some cases, the culture after seven passages was of a purely epithelial nature, and when it was reimplanted into hamsters at this time it gave rise to the rapid development of an epithelial tumor. in the tumor cultures, no adenovirus could be demonstrated. nor could cultures of the pulmonary tumors, or cultures of normal hamster lung be infected with adenovirus. it appears that the lung of the hamster in an organotypical culture constitutes a means of choice for the malignant transformation of adenovirus 12.

.I 401

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133. demonstration, purification, and partial characterization of abnormal (hsl) antigens in stable human cell lines
the existence of abnormal human stable line (hsl) antigens common to a number of stable human cell lines, but absent from normal human tissues and normal human diploid cell strains in tissue culture, was demonstrated by agar gel microimmunodiffusion. hsl was detected in hela-sj, hela-mba, hela-s3, chang conjunctiva, syverton's embryo

esophagus, Chang liver, and J-III. It was not detected in Henle's human intestine or Detroit-6. It was absent from two normal diploid strains, WI-38 and SJ-DHL, and was not found in a variety of concentrated extracts of fresh human organs. HSL was not associated with contamination by pleuropneumonia-like organisms (PPLO) of cell lines. The purest HSL preparations obtained from HeLa-SJ by ammonium sulfate fractionation yielded absorption spectra characteristic of protein and were inactivated by trypsin. Sephadex chromatography indicated a particle weight of approximately 150,000; HSL was not sedimented at 125,000 x g. In 0.02 M PO₄ buffer, activity was virtually completely eliminated after 2 minutes at 50 °C, 8 minutes at 45 °C, or 80 minutes at 40 °C. Preliminary studies with fluorescent anti-HSL globulin indicated that HSL was not a surface antigen; rabbit antisera to purified HSL fractions were not cytotoxic to HeLa cells. The best preparations of HSL still contained a trace of common human antigen and appeared to consist of multiple

components active in immunoprecipitation.

electrophoresis indicated the in-

homogeneity of this material.

.I 402

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1696. further comparative studies on two isogenic cell lines of autologous

origin, one of which is tumor-producing

a single explant of normal lung tissue

from an adult female mouse c57bl provided

2 cell lines. one remained normal

and is referred to as pg, the other became

malignant and is designated as

pt. with successive in vitro passages by tryp-

sinization the tumour-inducing capacity

of the pt line considerably decreased its

tumour-producing capacity as well

as its aerobic glycolysis coefficient, while the

pg line showed no appreciable

change. results of chromosome studies are de-

scribed, but proved inconclusive.

similar experiments were also carried out on

cell lines derived from the pt line

and their results are discussed.

.I 403

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1202. characteristics of human adenovirus type 12 induced hamster tumor

cells in tissue culture

characteristics of a human adenovirus type 12 induced hamster tumor serially propagated in vitro are described. these include small cell size, epithelioid appearance, rapid growth rate, resistance to superinfection with a-12, and transplantability to weanling hamsters. these cells grew either as monolayers or as balls of aggregated cells detached from the glass, depending on whether calf serum or horse serum was added to the eagle's medium. attempts to demonstrate virus activity by subculture of supernatant fluids and lysed cells into hela cells, mixed culture with human and hamster cells, electron microscopy, and inoculation of newborn hamsters with irradiated tumor cells were negative.

.I 404

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142. trials of heterotransplantation of human cancer in rabbits and kleisbauer a.

trials of transplantation of human tumours (some 20, almost all carcinomas) in the pleural cavity of large rabbits (6 months old flanders, weighing 3 kg.) gave negative results also when cortisone treatment was associated with it, though in

the cortisone treated animals the
necrosis of the tumours was less massive.
examination of the grafted tumour
was carried out at different times (from 8 to
365 days after transplantation) and
was also controlled by radiographic examina-
tions. detailed description of the
giant cell reactions around the tumours and in
the adjoining lung.

.I 405

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1207. solitary mast cell granuloma (histiocytoma) of the lung.

a histopathologic, tissue culture and time-lapse cinemato-
graphic study

a pulmonary histiocytoma in a 57-year-old

woman was studied intensively histo-

pathologically and by other techniques.

abundant mast cells were found within the

lesion, a previously unreported finding.

tissue culture studies suggested that the

process is reactive rather than neoplastic.

some plasma-cell granulomas of the

lung may be mast cell histiocytomas.

.I 406

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2773. the value of fluorescence cytology for the cytodiagnosis

of pulmonary cancer

the paper discusses the test results of 527 tissue samples sent in for the cytodiagnosis of lung cancer and compares the method of ao-fluorochromation with other methods of preparation. by means of applying ao-fluorochromation, the rate of erroneously positive findings could be reduced. the rate of erroneously negative findings was somewhat higher but the total diagnostic precision of 93% was 3% higher than in all other methods applied.

.I 407

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2774. pitfalls in the clinical and histologic diagnosis of bronchogenic carcinoma
a necropsy study of 380 cases of extrathoracic carcinoma revealed that pulmonary metastases occurred in almost 50% of the cases and bronchial metastases in over 25%. there were 39 cases (10.3%) in the series with clinical features simulating bronchogenic carcinoma and in 24 (62%) of these cases there was cytologic and/or histologic confirmation. carcinomas of the pancreas presented the greatest source of diagnostic error accounting for more than one-third of the 39 cases; the primary

site second in frequency was carcinoma of the kidney. bronchial metastases were chiefly responsible for the clinical, cytologic, and histologic findings compatible with the diagnosis of bronchogenic carcinoma. secondary growths in the lungs may present roentgenologically as solitary tumors indistinguishable from primary lung cancer. metastatic lesions in lymph nodes, bronchi, and lung may exhibit pleomorphic features simulating squamous cell carcinoma. the diagnosis of bronchioloalveolar carcinoma in resected lung tissue is a presumptive conclusion inasmuch as the identical morphological features may be reproduced by metastases from duct or glandular carcinomas. the simulation of bronchogenic carcinoma by metastatic tumors occurs with sufficient frequency to challenge the diagnostic accuracy of deaths certified as bronchogenic carcinoma with necropsy exclusion of other primary sites.

.I 408

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4396. effects of arginine deprivation, ultraviolet radiation, and x-radiation on cultured kb cells. a cytochemical and ultrastructural study

cultured kb cells (derived from a human oral carcinoma) grown in monolayers were injured by one of three agents: starvation by arginine deprivation or treatment with high doses of either ultraviolet radiation or x-radiation. the different agents produced changes in nucleolar structure and varying accumulations of triglyceride and glycogen. all three agents produced an increase in number and size of lysosomes. these were studied in acid phosphatase preparations, viewed by both light and electron microscopy, and, occasionally, in vital dye, esterase, and aryl sulfatase preparations. ultrastructurally, alterations in lysosomes suggested that 'residual bodies' developed in a variety of ways, i.e., from the endoplasmic reticulum, multivesicular bodies, or autophagic vacuoles. following all three agents, the endoplasmic reticulum assumed the form of 'rough' or 'smooth' whorls, and, after two of the agents, arginine deprivation or ultraviolet radiation, it acquired cytochemically demonstrable acid phosphatase activity. near connections between the endoplasmic reticulum and lysosomes

raise the possibility that in kb cells, at least when injured, the endoplasmic reticulum is involved in the formation of lysosomes and the transport of acid phosphatase to them.

.I 409

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1106. the simultaneous use of extracorporeal circulation and hypothermia in the surgery of the heart

the operative technique of cardiac

surgery under conditions of deep hypothermia with

simultaneous use of a pump oxygenator

and cardiopulmonary bypass is described. in

the majority of cases the patients were

cooled with water at 2 c. and the perfusion

volume was reduced by more than 50%

during hypothermia. in others, a gradient of

10 c. between blood and water was

maintained and the perfusion volume was reduced

by less than 50%. the data presented

show that neither technique leads to hypoxic

changes in the cerebrum and internal

organs, provided the mean arterial pressure

is kept between 70 and 90 mm. hg during perfusion.

the overall mortality in the

authors' 168 cases - most of which

had congenital heart disease - was 14.8%. in 53

cases of tetralogy of fallot - most
of them cyanotic - the vsd was closed by taking
a flap of tissue from the crista supraventricularis.
in this group mortality was 24.5%.

.I 410

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464. cardiac performance in hypothermia. an experimental study of left
ventricular power, oxygen consumption, and efficiency in dogs
multiple cardiac parameters have been measured
in 30 dogs cooled to 20 c. aortic
blood temperature. the parameters have been
expressed both as absolute values
and as percentages of normothermic values.
at normothermia, dogs with closed
chest had an ascending aorta flow of 154%
and a left ventricular external power of
183% of the corresponding values for dogs
with open chest. both ascending aorta
flow and left circumflex coronary artery flow
were reduced to 25% of normothermic level
at 20 c. aortic arch mean pressure was
reduced to 50% of normothermic level
at 20 c. total peripheral resistance was
increased to 205% of normothermic level
at 20 c. left ventricular external power
was decreased to 11% of normothermic
level at 20 c. left ventricular oxygen

consumption was decreased to 31% of normothermic level at 20 c. mechanical efficiency of the left ventricular myocardium was decreased to 39% of normothermic level at 20 c.

.I 411

.W

3270. tolerance of dogs to deep hypothermia. controlled and maintained with a pump oxygenator

the advantages of hypothermia of below 10 c for 2 hr, induced and maintained by

extracorporeal circulation of 200 min.,

were compared to partial bypass of the same duration during normothermia.

in the normothermic group 9 dogs out of 12

lived. in the hypothermic group 6 dogs

out of 15 (40%) survived when perfused at

the high flow of 55 cc/kg/min. eleven

dogs out of 15 (70%) survived when the flow

rate was reduced to 25 cc/kg/min when

the temperature was below 10 c. the death

in the high flow group were due mainly

to postperfusion lung changes even when low

pulmonary venous pressure was assured

by venting in the left atrial chamber. metabolic

acidosis occurred in all groups;

though greater in the high flow, with the

low flow intermediate between the former

and the normothermic group. this change
to a great degree, can be explained by the lung changes.

.I 412

.W

1593. bleeding tendencies associated with profound-hypothermia technics in
neurologic surgery

forty-three patients with bleeding intracranial
aneurysms were operated on under
deep hypothermia and with the aid of extracorporeal
circulation. the open-thorax
method was used in 18 cases and the closed-thorax
method in 25. the following
points are made (1) the closed-thorax method
is considered superior to the open-
thorax method in several respects; (2) meticulous
hemostasis is essential to control
the oozing that occurs during extracorporeal
circulation under profound hypothermia
until the heparin antagonist can become
effective and body temperature can return
to normal; (3) significant thrombocytopenia
may develop during extracorporeal cir-
culation, and inhibition of the thrombin-fibrinogen
reaction by factors other than
heparin may cause a major coagulation defect
and may also, by mimicking the he-
parin effect, lead to the excessive use of

heparin antagonists; (4) pathologic changes in microcirculation during extracorporeal circulation may be determinants of a hemorrhagic tendency.

.I 413

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4088. the use of hypothermia and dehydration in the treatment of severe cerebral hypoxia

the rational for using hypothermia or cerebral dehydration is to suppress or reverse progressive or delayed cerebral damage after hypoxia. it is suggested that damage of this nature results from injury to the astroglia and oligodendroglia, especially the former. experimental and clinical evidence favors lowering of the body temperature immediately after any episode of hypoxia accompanied by important damage to the brain. the rational for using dehydration is insecure and its results are uncertain. this treatment should probably be reserved for cases in which a raised cerebrospinal fluid pressure has been proved, and in which other measures, especially hypothermia, are either not available or have failed.

.I 414

.W

7828. selective cerebral hypothermia physiology and technic

a safe, suitable technique for producing

selective brain cooling by a perfusion

method is described. of 15 dogs, 7 survived.

the salient features aiding survival

are discussed. the use of a direct vasodilator

(papaverine) in the perfusate to

relieve vasospasm markedly reduced cooling time

and represented the most signi-

ficant technical advance over previously

described methods. an acid base analysis

utilizing the siggaard-andersen curve nomogram

was performed on 4 dogs and no

significant acidosis noted during selective brain

cooling. a definite arteriovenous

lactic acid difference developed at hypothermic

temperatures indicating the brain

may metabolize this substance in preference to

glucose at lowered brain tempera-

tures, the reasons for which were discussed.

the rate of disappearance of physi-

cally dissolved oxygen (po_2) was measured

in the brain following ischemia at dif-

ferent temperatures. the average rate of

disappearance at 20 c. was 40% of the

rate at 37 c. the discrepancy between this

finding and the in vitro oxygen utilization rate at the same temperature was discussed.

.I 415

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948. cardiac activity in cranio-cerebral hypothermia

the onset of hypothermia rarely alters the heart

rate. as it deepens to 35-32, the

rate slows, and at the level of 30-29 it usually

amounts to only half its original va-

lue. at 28 or below, the development of

bradycardia is observed. after warming

to 32 the normal heart rate is restored.

during operations on the abdominal organs

the heart rate is only slightly modified.

the appearance of solitary extrasystoles is

rare and is usually associated with stimulation

of the diaphragm. the most marked

changes in the heart rate are observed during operations on the heart,

especially if

it is excluded from the circulation. an

idioventricular rhythm may develop before

the heart stops beating. after removal of the

ligatures from the venae cavae the nor-

mal rhythm is restored. as the temperature

falls, the excitability of the myocardium

increases. conduction is more resistant.

areflexia continues even during direct sti-

mulation of reflexogenic zones. in the surgical stage of cranio-cerebral hypothermia it is clear that no significant degree of energy or hemodynamic insufficiency develops, whether in experimental conditions or during operations on patients. at operation a well-marked stabilization of the contractile power of the myocardium may be observed.

.I 416

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946. respiration in hypothermia. i. respiratory pattern and acid-base balance in the blood mongrel dogs, under light pentobarbital anesthesia, were made hypothermic by immersing them in ice water and then normothermic in warm water. in the course of cooling, the respiratory rate and pulmonary ventilation, after an initial increase, were reduced as the rectal temperature fell, and spontaneous respiration was arrested at rectal temperatures of 21-25 c. alveolar p_{CO_2} was increased, after an initial slight lowering, with the progress of hypothermia. arterial pH and standard bicarbonate (jorgensen and astrup) decreased, and the alkalinity of the blood COH (winterstein) decreased markedly during hypothermia.

these findings suggest both respiratory and metabolic acidosis as the mechanisms concerned. in the course of rewarming all these changes disappeared rapidly and completely though the ventilatory stimulation observed as an initial transitory phenomenon during cooling failed to occur.

.I 417

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896. studies on blood viscosity and its significance in anesthesia the principles for measuring blood viscosity have been discussed. although blood does not behave in a newtonian manner, the data obtained in in vitro measurement are useful. a modified simple method for measuring blood viscosity relative to normal saline has been described. there is essentially no difference in viscosity between fresh blood and heparinized blood and between plasma and serum. viscosity varies with the quantity and nature of proteins in plasma and the cellular concentration. halothane and thiopental sodium reduce blood viscosity and seem to be indicated in conditions in which there is hemoconcentration and a tendency for red blood cells to aggregate. cyclopropane, hypothermia, and norepinephrine tend to raise

blood viscosity and would seem to be contraindicated
when the microcirculation is failing.

.I 418

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4612. flow considerations in regional cerebral hypothermia

it is suggested that low flows are dangerous
and may cause anoxia either directly
or by interfering with cooling. sixty dogs
have been subjected to local cerebral
hypothermia by the method of femoral to
carotid cooling of arterial blood with per-
fusion at a predetermined pressure rather
than predetermined flow rate. the cir-
cuit is described and its advantages for
clinical use mentioned together with its in-
accuracies as a method of scientific investigation.
these are chiefly concerned
with maintenance of systemic blood pressure
which may require the injection of
pressor agents. evidence for reduction in flow
at low temperatures is discussed
and evidence presented that this is not only due
to increase in viscosity but that
there is an active spasm, manifested by
'rewarming humps' which occur in the
cooling graphs. mean carotid flow rates
were determined by a revolution counter

attached to a pump of fixed stroke volume,
the output of which was linked to the per-
fusion pressure and thus determined by the resistance.
the place of added CO_2
is discussed particularly in relation to the fall
in partial pressure which accompa-
nies the cooling of the blood. the addition of 5% CO_2
did not increase total carotid
flows. halothane had been used as an anesthetic
because of its sympatholytic ac-
tion. it has increased flows by 37% and
abolished 'rewarming humps'. rheomacro-
dex used as a priming fluid instead of blood
produced increased flow averaging 75%
but did not abolish spasm. it is suggested that
cooling faster than 1 c. per minute
is not intrinsically dangerous if spasm is prevented
and high flow maintained by the methods described.

.I 419

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4613. selective brain cooling produced by cerebral ventricular perfusion
hypothermic cerebral ventricular perfusion
was applied to dogs. shivering appear-
ed to be directly related to the CNS temperature
rather than the peripheral body
temperature. selective heating of the brain-stem
produced panting. rewarming

of the body was retarded by the initiation of heat loss mechanisms controlled centrally when hyperthermic perfusion was used. shivering disappeared but panting was unaffected by pentobarbital anesthesia. cooling of one or both frontal areas and the anterior part of the third ventricle did not significantly affect the respiratory or circulatory systems but brain-stem hypothermia produced distinct respiratory and circulatory reactions. it is suggested that cooling of the 3rd and 4th ventricular areas may be utilized for anesthetic purposes.

.I 420

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1139. optimal coronary flow in the bypassed normothermic and hypothermic heart
a series of experiments were conducted in dogs in which bypass flow, temperature, and direct coronary perfusion pressure were varied. coronary flow, coronary venous saturation, myocardial oxygen consumption (mvo_2), and coronary vascular resistance were assayed. coronary flow as a percentage of total bypass flow did not vary appreciably at varying levels of bypass flow. induction of hypothermia, when total bypass flow is constant, results in decreasing

coronary flow. induction of hypothermia when maintaining a constant bypass pressure results in an increasing coronary flow with temperatures down to 22 c. further cooling causes a reduction in flow. using isolated coronary perfusion at 100 mm. hg, coronary flow fell and resistance rose during the first 15 min. of bypass. using isolated coronary perfusion at 100 mm. hg, induction of moderate hypothermia (25 c.) caused an increase in coronary flow and venous saturation and a decrease in cardiovascular resistance and mvo₂. under the same conditions, induction of hypothermia to 18 c. produced similar changes but caused myocardial hemorrhage and ventricular fibrillation. profound hypothermia probably leads to excessive fragility of the capillary bed. reduction of perfusion pressure to 50 mm. hg at near normothermia reduced coronary flow and slightly reduced venous saturation and mvo₂. the same reduction of perfusion pressure at 18 c. produced similar but less marked changes. reduction to 25 mm. hg at 18 c. markedly reduced coronary flow, venous saturation, and mvo₂

initially, but with partial recovery later. from this
data of acute experiments in
dogs, coronary perfusion using moderate hypothermia
(about 31 c.) and 50
mm. hg, slightly pulsatile mean pressure appears optimal.

.I 421

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974. extracorporeal hypothermia without thoracotomy. an ex-
perimental study in the use of cold for neurosurgery and
cancericidal perfusions
this paper includes minor clinical notes
on open heart surgery and cancer perfusion
but contains no experimental information
on neurosurgery or cancer perfusions. a
method of closed-chest hypothermic perfusion
in 30 dogs is reported. the authors
utilize drainage of superior and inferior cavae
by gravity. the volume of venous
drainage sometimes enhanced by transfusions
or 12.5% low molecular weight dex-
tran determined the flow rate. cooling was
maintained for quite variable periods
apparently generally to an unspecified
esophageal temperature. perfusion time va-
ried from 30 min. to 4 hr. animals with
low flows were perfused longer, had a high-
er incidence of ventricular fibrillation,

and a very low survival rate. eleven animals survived. all had pre-cooling flow rates above 40 ml./kg./min., good flow rates during the perfusion, and only 3 had ventricular fibrillation. flow rates and survival were increased in animals receiving low molecular weight dextran. fourteen of 15 animals with ventricular fibrillation were defibrillated electrically, 8 regained 'adequate' cardiac function, but only 3 survived. some interesting data on regional cooling of the lower half of the body is presented. the authors conclude without sufficient evidence that the most important factor in the mortality in hypothermic perfusion is the ability to maintain 'a flow rate approaching the estimated normothermic cardiac output of the animal'

.I 422

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2406. profound hypothermia

the aim of hypothermia is protection of vital cerebral structures from hypoxia

during aneurysm repair; profound hypothermia is also valuable in operating on certain cardiac defects which cannot be repaired even with whole body perfusion.

since the time needed for aneurysm repair often exceeded the safe limit of 8 to 12 minutes without circulation afforded by surface hypothermia of 29 to 30 c., the authors have investigated the drew (open-chest) technic, the closed-chest method, and isolated cerebral perfusion. the drew technic consists of substituting two pumps for the heart while the patient's lungs act as the oxygenator. because of its disadvantages (the large amounts of blood needed and the morbidity due to intra-cardiac cannulation and median sternotomy), a closed-chest method was developed, using a mayo-gibbons vertical-sheet pump-oxygenator to provide the perfusion and extracorporeal cooling without requiring thoracotomy. in cerebral perfusion, blood is taken from one artery, pumped through a heat exchanger, and returned to another artery. the authors describe anesthetic technics, offer comparisons of the three methods, give instructions pertaining to the production of hypothermia, and list the problems encountered in the management of these cases.

.I 423

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3194. systemic hypothermia via gastric cooling

eight dogs underwent gastric cooling for

systemic hypothermia. each dog was cooled

with the balloon filled with a 'safe' volume

based on weight (20 ml/kg) and subjected

to cooling with the balloon filled maximally,

but safely to a pressure of 10 mm

hg. consistently, the latter procedure was far

more efficient, averaging 2.6 times as

rapid for all degrees of hypothermia. a

decrease in core temperature by 7 c re-

quired an average of only 28.4 minutes.

on comparison with clinical reports of hy-

pothemia induced by the usual gastric

cooling, an improved efficiency of two-fold

to three-fold is still noted.

.I 424

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3820. the dubious haemopoietic

stem cell function of the lym-

phoid cells of the blood.

autoradiographic studies on

dogs

the migration, fate and turnover of

lymphoid cells in blood and bone marrow of

irradiated and non-irradiated dogs were

studied by serial autoradiography with co-

ping of the hind legs during the plasma clearance time of h3-thymidine injected into an anterior vein. in irradiated dogs, the h3-thymidine injection procedure was carried out during the early recovery phase following 250 r whole body x-irradiation. conclusive evidence of transformation of hematogenous bone marrow lymphoid cells into hemopoietic precursors was not found. however, in the light of the individual grain counts transformation of a few lymphoid cells into hemopoietic cells cannot be ruled out. the data obtained from a dog in the very early recovery phase following whole body irradiation strongly indicate such a transformation.

.I 425

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3927. studies on growth and cytomorphosis in the thymo-lymphatic systems - with special reference to the influence of the thymus and the thyroid in guinea-pigs migratory streams of lymphocytes between different parts of the thymo-lymphatic system were evaluated by comparisons between

lymphocyte populations in thoracic-
duct lymph and arterial and venous blood,
especially thymic venous blood. by re-
cording organ weights in sham-operated and
thymectomized guinea-pigs, treated
with thyroxin or untreated, the importance
of the thymus and the thyroid for growth
and regeneration in the thymo-lymphatic
system was studied. the main results are
as follows. there is a considerable venous
output of lymphocytes with low mito-
chondrial content (small lymphocytes) from
the thymus in normal young guinea-pigs.
this explains the much higher incidence of
small lymphocytes in blood than in tho-
racic-duct lymph. neonatal thymectomy
causes lymphatic hypotrophy with defi-
ciency of lymphocytes and pyroninophilic
cells in relation to reticular ones. body
growth and survival of the animals are not
affected. in the thymus, exogenous
thyroxin most probably promotes differentiation
of large basophilic cells to small
lymphocytes, resulting in an increased output of
small lymphocytes. in the lymph
nodes, thyroxin promotes differentiation of large
pyroninophilic cells ('transitional

cells') into immature and mature plasma cells.

the effects of thyroxin on differentiation are followed by an increased growth of the thymo-lymphatic organs, characterized by an increased incidence of large basophilic cells and increased weight of the lymphatic organs. growth of the thymus and lymph nodes precedes that of the red splenic pulp. this delayed splenic response is not due to a transformation of an increased number of immigrated thymic lymphocytes, as neonatal thymectomy does not prevent the thyroxin-stimulated occurrence of large basophilic cells in the red splenic pulp. the thyroxin-stimulated growth of the lymphatic system is accompanied by an increased output of larger lymphocytes through the thoracic duct, resulting in an increased number of larger lymphocytes in the blood. in postnatally thymectomized animals, having a normal (or above normal) amount of circulating small lymphocytes, thyroxin produces a drastic decrease in the number of small blood lymphocytes, indicating a decreased delivery and/or increased disappearance of these cells to and from the blood, respectively.

this decrease in number of small lymphocytes is not seen in sham-operated animals. as judged by studies of organ weights, the thyroxin-stimulated growth and regeneration of the lymphatic tissue are influenced antagonistically by thymectomy and synergistically by local factors in involuted tissue.

.I 426

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815. the origin of macrophages from bone marrow in the rat skin windows' and subcutaneous coverslips were applied to rats in a study designed to identify the tissues in which the precursors of macrophages proliferate. lymphocyte-depletion by either chronic drainage from the thoracic duct or 400 rads of x-irradiation failed to suppress the emigration of macrophages or to reduce the proportion of them which became labelled after an injection of tritiated thymidine. x-irradiation with 750 rads suppressed the emigration and the labelling of the exudate macrophages. both were restored to normal when the tibial marrow was shielded during irradiation. radioactively-labelled

cell suspensions obtained from thoracic duct lymph, lymph nodes, thymus, spleen and bone marrow were transfused into syngeneic recipients. the emigration of labelled macrophages on to coverslips could be demonstrated only in recipients of labelled bone marrow and spleen cells. labelled monocytes were found in the blood of rats which had received injections of labelled bone marrow. it was concluded that in the rat, bone marrow, and to a lesser extent spleen, are major sources of the macrophages which emigrate into foci of acute, non-bacterial inflammation.

.I 427

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1786. studies of the leucocyte compartment in guinea-pig bone marrow after acute haemorrhage and severe hypoxia evidence for a common stem-cell after a large acute hemorrhage, the absolute levels of neutrophils, eosinophils, and basophils in guinea

pig bone marrow are considerably reduced. all stages of differentiation are involved, the decline in myeloblasts and promyelocytes being particularly marked. exposure to severe hypoxia also temporarily depresses the number of marrow granulocytes. bone marrow lymphocytes are only slightly reduced after a single hemorrhage but in the later stages of severe hypoxia their numbers are greatly reduced. assuming the supply of stem cells in the bone marrow is not unlimited, the decrease in marrow granulocytes and lymphocytes following marked erythropoietic stimulation appears to favor a monophyletic theory of hemopoiesis; a heavy demand for stem cells to differentiate into the erythron may temporarily restrict the

number entering the leukon. the hypoxic animals showed a considerable loss of body weight and the notable reduction of marrow lymphocytes in the later stages of hypoxia may be specifically related to a generalized atrophy of lymphoid tissue. using h³-thymidine there is evidence of active dna synthesis in guinea pig metamyelocytes. although dna-synthesis was found in metamyelocytes of normal marrow, after hemorrhage these cells form a much larger proportion of the total synthesizing cells in the granulocyte compartment and also the ratio of labeled metamyelocytes to myelocytes is considerably increased. microspectrophotometric measurements of the feulgen dna-content of metamyelocytes after hemorrhage show that there are 2 populations

of these cells. one group has values typical of resting or nonsynthesizing cells but a 2nd group shows a complete range of dna-values up to levels characteristic of those found in dividing cells. certain small mononuclear cells with minimal but deeply basophilic cytoplasm are a distinctive group of dna-synthesizing cells in marrow after hemorrhage. morphologically, there appears to be a complete sequence between these cells and procrythroblasts.

.I 428

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3831. relative ability of parental marrow to repopulate lethally irradiated f1 hybrids

lethally irradiate (c57bl x 101)f1 mice injected with a mixture of 10 million c57bl and 10 million 101 bone-marrow cells were repopulated only by the 101 bone-marrow cells. experiments with other

cell mixtures indicated that the 101 marrow was relatively nine times as efficient as c57bl marrow in repopulating lethally irradiated (c57bl x 101)f1 mice. results from additional strain combinations suggested that the behavior of the donor marrows was not determined solely by h-2 factors. c57bl marrow, which frequently regresses in irradiated f1 mice, has shown to be relatively less capable of repopulating the recipient than regularly retained parental marrow. the differences in the relative abilities of parental marrows to repopulate f1 mice cannot as yet be fully explained. they might be correlated with physiological differences between the parental marrows or with a micro-environmental advantage of one hematopoietic cell type over another in the irradiated recipient. immunological and physiological factors that might favor this selective growth are discussed.

.I 429

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3832. pluripotent stem cell function of the mouse marrow
'lymphocyte'

bone marrow from normal and polycythemic mice was filtered through glass wool columns to remove cells other than 'lymphocytes'. for a given number of nucleated cells, filtered marrow was more efficient than the original marrow in repopulating the spleen of an isogenic recipient previously exposed to lethal irradiation. the proliferative capacity of both the filtered and unfiltered marrow suspensions appeared to be a constant function of the number of small and medium 'lymphocytes' present and not of any other cell type.

.I 430

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2045. the effect of unilateral limb shielding on the haemopoietic response of the guinea-pig to gamma irradiation
guineapigs were exposed to 150 r -irradiation whilst approx. 1/5 of the total bone marrow was protected by shielding 2 limbs. quantitative cell counts of both

the shielded and irradiated marrow were combined with observations on the thymus, spleen and blood during the recovery period, and compared with the effects of whole-body irradiation. following whole-body irradiation (150 r) the thymus shows a delayed secondary cellular depletion coinciding with a marked splenic hyperplasia. both phenomena were eliminated by limb shielding. the lymphocytes in the irradiated marrow of partially shielded animals continued to show both the overshoot and the secondary fall in numbers which characterize recovery from whole-body irradiation (150 r). after an initial fall in numbers of erythroid and granulocytic precursors, the shielded marrow showed a temporary increase in granulocytopoiesis coinciding

with an abortive phase of granulocytopoiesis in the irradiated marrow. there was no evidence of any effective colonization of irradiated marrow by cells from the shielded marrow. the significance of these findings is discussed.

.I 431

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4311. studies on intravenous transfusion of thymus cells and lymphnode cells. iii. influence of transfused thymus cells and lymphnode cells on the bone marrow in rabbits transfused with thymus cells and lymphnode cells the peripheral blood and bone marrow were studied. the transfusion of thymus cells caused a peripheral lymphocytosis and a diminution of lymphoid cells in the bone marrow of both young and adult rabbits. the transfusion of lymphnode cells resulted in a peripheral lymphopenia, and an initial increase and a subsequent diminution of lymphoid cells in the bone marrow. it is suggested that lymphoid cells

in the bone marrow may be lymphocytes which are stored or discharged according to a variety of conditions. furthermore, thymus cells are thought to mobilize lymphocytes from the bone marrow to the peripheral blood.

.I 432

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5041. studies on hypoxia. iii. the differential response of the bone marrow to primary and secondary hypoxia

twenty-five adult male guinea pigs were placed in a decompression chamber, at a simulated altitude of 14,000 feet for 5 days, then kept in ordinary air for 5 days, and finally returned to the decompression chamber to be subjected to hypoxia a second time, for periods ranging from 1 to 5 days. during this period of secondary hypoxia quantitative studies were made of the changes in the blood and bone marrow.

in secondary as in primary hypoxia there is a significant increase in the nucleated red cells of the marrow. in secondary hypoxia, however, there is a very marked increase in the marrow lymphocytes,

whereas in primary hypoxia the lymphocytes fall. the marrow reticulocytes remain at a fairly constant level despite marked fluctuations in erythropoiesis.

.I 433

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1044. an investigation of lymphocyte production in guinea-pig bone marrow evidence from a variety of experiments indicates that lymphocytes are produced in guinea-pig bone marrow. under certain conditions the numbers produced appear to be considerable. during recovery from irradiation there are numerous telophases in marrow smears which appear to be forming small lymphocytes. moreover, many lymphocytes are still found in shielded bone marrow after the rest of the body, including the conventional lymphoid tissues, has received lethal or supra-lethal irradiation. almost 50% of these cells are formed after the irradiation. finally, when bone marrow is cultured in the peritoneal cavity of a host whose own lymphocyte production has been suppressed by irradiation, small percentages of newly-formed

small lymphocytes are found in this marrow.

.I 434

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103. repopulation of bone marrow

in mice number and type of

cells required for

post-x-irradiation protection

fractionation of cells from mouse bone

marrow and autologous mouse spleen indi-

cates that the cell responsible for bone

marrow repopulation and x-irradiation

protection resembles the small lymphocyte.

experiments with injection of different

numbers of bone marrow and spleen cells

and observations on survival obtained by

fractional irradiation of the entire body and

of extirpation of the shielded spleen

after irradiation indicate that approximately

3×10^4 cells of this type are required

to provide 50% survival, and that approximately

this number migrates from the

shielded extremity or spleen of a mouse per hour

(slightly faster for spleen and slower for bone marrow).

.I 435

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104. hyperbasophilic cells as an

indication of proliferation of

bone marrow transplanted to irradiated dogs

a study was made of hyperbasophilic cells which appeared following transplantation of bone marrow to 20 irradiated mongrel dogs of both sexes. in the main series of experiments the animals were irradiated with a dosage of 600 r., using a four-tube rum-3 x-ray machine voltage 200 kv, current 10 ma, filters 0.5 cu mm + 1.0 mm.al, target distance 60 cm., rate 18-22 r./min. at 1-2 days after irradiation, a suspension of bone marrow cells in a dosage of $10^9 - 5 \times 10^9$ nuclear cells was administered i.v. the marrow was obtained by aspiration from various skeletal bones or by compression from the sternum, ribs and other bones. a study was made of the morphological composition of the blood and bone marrow before irradiation and at 1-5, 10, 15, 20, 25 and 30 days after irradiation and transfusion of bone marrow, and thereafter at 10-15 days intervals. smears of blood and marrow were stained with azure-ii-eosin. it was found that distinctive cells with basophilic protoplasm and frequent incidence of an

immature nucleus were present in the blood of dogs following irradiation with 600 r. and transplantation of bone marrow. hyperbasophilic cells appeared in the blood at 2 - 4 days after transplantation and attained a maximum 14 - 21 days later; thereafter their number diminished rapidly. the trend of number of hyperbasophilic cells coincided with that of other donor elements (leukocytes, erythrocytes). hyperbasophilic cells were not found during acute radiation sickness in dogs which were not given injections of bone marrow. they were found 3 mth. after transplantation of bone marrow to nonirradiated puppies at 2-3 days of age. when the irradiation dosage was increased to 800-1,000 r., the number of hyperbasophilic cells increased and attained a peak sooner than after the 600 r. dosage. such cells were formed from the donor cells.

.I 436

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172. autoradiographic studies of lymphoid cells in blood and bone marrow of nor-

mal and irradiated
dogs
the migration, fate, and
turnover of lymphoid
cells in blood and bone marrow
of 4 irradiated and 4 non-
irradiated dogs were studied
by serial autoradiography
with clamping of the hind legs
during the plasma clear-
ance time of h3-thymidine
injected into an anterior
vein. in irradiated dogs, the
h3-thymidine injection pro-
cedure was carried out during
the early recovery phase
after 250 r of whole-body
x-irradiation. the results on
2 irradiated and 2 normal
dogs were described in de-
tail. migration of lymphoid
cells from blood to marrow
parenchyma was confirmed
in the irradiated dogs. con-
clusive evidence of transformation
of these cells into
hemopoietic precursors was not

found. the relative
number of large lymphoid cells,
the labeling index of
the whole population of lymphoid
cells, and that of small
lymphoid cells were increased
in irradiated marrow;
few initially labeled small
lymphoid cells could also be
observed. these data indicate
that the pattern of pro-
liferation of lymphoid cells is
changed in irradiated re-
generating bone marrow.

.I 437

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175. lysozyme in bone
marrow and periph-
eral blood cells
by means of an indirect
histochemical technique,
the intracellular lysozyme of
the formed elements of the
peripheral blood and bone marrow
was estimated. evi-
dence is presented that monocytes,
as well as mature

neutrophils and their precursors
extending back to the
progranulocyte, contain significant
amounts of this enzyme. a rare mature eosinophil
demonstrated a trace
of lysozyme activity. there was
no evidence of lyso-
zyme activity in basophils,
erythrocytes, megakaryo-
cytes, platelets, plasma
cells, tissue mast cells or
bone marrow
reticuloendothelial cells.

.I 438

.W

1770. proliferative activity of the
lymphatic tissues of rats as
studied with tritium-labelled
thymidine
cytokinetic data are presented, employing
quantitation of ^3H -DNA in the lymphatic
tissues of normal rats serially sacrificed
after ^3H -thymidine administration. a marked
difference in the patterns of initial labeling
and label loss was observed between the
thymus and peripheral lymphatic tissue.

the data are compatible with other indications of rapid cell renewal in the thymus. there is suppression of initial uptake of ^3H -thymidine into the dna of each large lymphocytic progenitor cell in the thymus, apparently because of a feedback of thymidine containing material from small lymphocytes in the thymus. depletion of the thymus of small cells, as by operative stress or whole body x-ray, leads to a marked increase in the uptake of ^3H -thymidine into the dna of large thymocytes. this finding, which is in agreement with the previous findings of Sugino et al. suggesting transfer of thymine nucleotides from small thymus lymphocytes to precursor cells, may or may not be related to the apparent transfer of dna label between thymic cells. the evidence for the latter consists of the curvilinear dilution of the dna label in the thymus proliferating cell population and the relationship between the rate of dna label dilution in large cells and the dna in the small cells in the thymus. after the dna label in progenitor cells in the thymus and lymph nodes has entered the small cell population, the subsequent

dilution of grains in these dividing cells follows the same slope as the loss of radioactivity from the entire lymph node. there is a long retention of some h3dna label in the dividing lymph node cell population. this suggests that the loss of radioactivity from the dividing cells and from the small cell population as a whole occurs equally. this pattern prevails regardless of whether the percentage of large and small cells is altered experimentally. these findings can be explained by an interchange of the dna nuclear label between small lymphocytes and large lymphocytes. this could occur by some process such as phagocytosis or pinocytosis, or by transformation of the small lymphocyte into a large, dividing cell. the data fit best with the latter possibility. all or any of these mechanisms would lead to an equilibration of the dna label between large and small cells. this finding prevents the assignment of a finite life span to lymphocytes on the basis of dna labeling kinetics. nevertheless, there appear to be at least two different types of lymphocytes. one, the 'thymus-type' lymphocyte, is found in the

thymus cortex, bone marrow and germinal centers of lymphoid follicles. the other type, found abundantly in the widespread peripheral lymphatic tissue, shows a very prolonged retention of dna label and is believed to be recirculating, 'immunologically committed' cells described by others. these cells do not appear to enter the thymus cortex.

.I 439

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6674. the free and glucuronic acid-bound 17-hydroxy-corticosteroids in the plasma of patients with cancer of the breast on i.v. infusion of acth
seventeen patients with advanced mammary cancer were given an infusion with 3 u. of acth in 5 hr. and 6 others an infusion of 25 u. determinations were made of the plasma 17-hydroxy-corticosteroids, free and bound to glucuronic acid both before and after the infusion. in rapidly growing carcinomas, high initial values were found for the free corticosteroids (more than 20 ug./100 ml. of plasma). the ratio of free to bound corticosteroids is for stage iv patients 1.8 on the average,

and approximately 1 for the mixed forms stage iv + m. these ratios are not altered by acth. shifts in the ratio of free to bound corticosteroids with acth treatment can be seen, depending on the initial value of the free corticosteroids. the administration of 3 u. is enough and the 5 hr. value is some 70%, related to a maximal stimulation with 25 u.

.I 440

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4179. reduced estriol excretion in patients with breast cancer prior to endocrine therapy

the urinary quotient of estriol/estrone + estradiol-17b(eq) was measured chemically in women with and without breast cancer, as an index of the ratio of noncarcinogenic impeded estrogens to mammary carcinogenic estrogens. in 34 controls, the median eq was 1.3 before and 1.2 after menopause, with only 21% of the patients subnormal. in 26 breast cancer patients without endocrine treatment or recent surgery, the median eq was 0.5 and 0.8 respectively, with 62% of the patients subnormal. after major surgery or hormonal therapy, only 23% of 53 patients were subnormal, no remissions being observed unless the eq

rose toward normal. matching of 24 controls and patients in pairs by age and ovarian status in the wilcoxon test indicated that the decreased eq excreted in untreated cancer was significant at the 0.2% confidence level. the marked increase in eq induced by castration and androgen, estrogen, and corticosteroid therapy suggests that normalization of a precancerous metabolic imbalance between impeded and active estrogens derived from ovarian and adrenocortical sources contributed to arrested growth of estradiol-dependent metastases.

.I 441

.W

1107. urinary excretion of estrone, estradiol and estriol by patients with breast cancer and benign breast disease premenopausal patients with breast cancer and benign breast disease appear to excrete a significantly lower percentage of the total estrogen as estrone and a significantly higher percentage as estriol than women in the premenopausal control group. there was no significant difference in the excretion of total estrogen between cancer groups and controls in good health. postmenopausal patients with cancer excreted

higher levels of estriol than postmenopausal control groups. the increase in estriol excretion cannot be explained by debilitation.

.I 442

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5323. systemic effects of androgenic and estrogenic hormones in advanced breast cancer
the systemic effects of diethylstilbestrol (45 patients), testosterone propionate (48 patients), and both hormones (22 patients) were studied during the treatment (six weeks to over three months) of advanced breast cancer in postmenopausal women. serious complications included induced hypercalcemia and fluid retention. physiologic effects such as urinary incontinence (diethylstilbestrol), virilization (testosterone), or nausea and vomiting did not necessitate discontinuance of treatment. androgenic therapy stimulated erythropoiesis. observations on the systemic reactions to these hormonal agents definitely contribute to the evaluation of sex steroid therapy.

.I 443

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3478. the effect of dehydroepiandrosterone on the 17-hydroxycorticosteroids in the plasma in various stages of cancer and other diseases of the breast

the reducing effect of dehydroepiandrosterone on the plasma corticosteroids is on the average shortened in advanced (stage iv) cases of breast cancer. in 3 groups of patients, the lowest corticosteroid levels were found up to 6 hr. after infusion of dehydroepiandrosterone-phosphate. in patients with mastopathy the effect was still detectable 12 hr. later; in patients with breast cancer in stage iv the initial levels were reached at that time. in cases with stages i and ii lesions, the findings were intermediate. the shortening is attributed to a more intensive transformation of dehydroepiandrosterone in advanced cases of breast cancer.

.I 444

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5274. urinary excretion of estrone, estradiol and estriol by patients with prostatic cancer and benign prostatic hypertrophy

and hopkins c.e.

urinary estrone, estradiol, and estriol fractions excreted by 21 patients with prostatic cancer, 17 patients with benign hypertrophy, and 59 clinically well subjects were assayed to determine whether differences exist. absolute levels of estrone, estradiol, and estriol fractions were not significantly different. the excretion of relatively lower levels of estrone and estradiol, and relatively higher levels of estriol by patients with prostatic cancer compared to clinically well subjects resulted in significantly lower proportions of the total estrogen being excreted as estrone and estradiol. differences in the proportions of estrogen fractions between patients with benign hypertrophy and clinically well subjects were not significant. with the exception of a significantly higher percentage of the total estrogen being excreted as estrone by the patients with benign hypertrophy, differences between that group and the cancer group were also not significant.

clinical variations between the 3 groups, and within the cancer and hypertrophy

groups, preclude assignment of significant differences to prostatic dystrophies alone. cancer patients experiencing inanition due to a loss of appetite excreted significantly lower levels of estrone than patients who reported no loss of appetite. significantly lower levels of estrone were excreted by patients with benign hypertrophy hospitalized 6 days or more compared to patients hospitalized 5 days or less. a significantly higher urinary estrone-androsterone ratio was present in the cancer group than in the clinically well group. it is not believed, however, that an arbitrary ratio can be used to suggest an internal estrogen-androgen imbalance.

.I 445

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28029 enzymic synthesis of steroid sulfates. ii. presence of steroid sulfokinase in human mammary carcinoma extracts
extracts of human primary and secondary mammary carcinomas were shown to contain steroid sulfokinase(s) in every case examined. examination of normal breast tissue surrounding the tumors revealed

very weak steroid sulfokinase activity in some instances. this was thought to be due to the fibrous nature and poor cellularity of the normal breast tissue. normal ovarian tissue specimens, obtained from cancer patients undergoing oophorectomy, did not generally contain the enzyme, but trace levels were detected in 1 of 5 specimens examined. steroids, without necessarily showing conversion to steroid sulfate, were observed to increase the incorporation of s35-sulfate into one of the products formed enzymically on incubating breast tissue extracts with s35-adenosine-3'-phosphate-5'-phosphosulfate.

.I 446

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3752. steroid excretion in early breast cancer patients with advanced breast cancer who subsequently fail to respond to adrenalectomy or hypophysectomy have been found to excrete abnormal amounts of the urinary metabolites of androgen and cortisol. when similar measurements are carried out on patients with early breast cancer, it is found that approximately half

the cases presenting for mastectomy are also excreting abnormal amounts of these steroids. subsequent follow-up shows that these cases tend to have a poor prognosis, and a trial had therefore been started in which the abnormality is being corrected. in addition, it seems possible that the deficiency in androgen excretion may precede the onset of the disease. this problem is being investigated in a trial involving urinary steroid estimations in 5000 normal women. the measurements are being compared with the subsequent development of breast cancer.

.I 447

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2365. the excretion of oestrone, pregnanediol and pregnanetriol in breast cancer patients. i. excretion after spontaneous menopause
the urinary excretion of oestrone, pregnanediol and pregnanetriol was determined in a series of postmenopausal breast cancer patients receiving no endocrine treatment. the steroid excretion was studied both in relation to the age of the patients as well as in relation to the time elapsed

since the last menstrual cycle. the results indicate that after an initial slow decrease from the age of the menopause onward, the excretion of oestrone and pregnanediol increases again. a new maximum was found in the group 10-15 yr. after the menopause. the excretion of pregnanetriol however, remains relatively constant after a more rapid fall during the first few years after the menopause.

.I 448

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2366. the excretion of oestrone, pregnanediol and pregnanetriol in breast cancer patients. ii. effect of ovariectomy, ovarian irradiation and corticosteroids.

the urinary excretion of oestrone, pregnanediol and pregnanetriol was determined in breast cancer patients at different stages of their endocrine treatment. the results demonstrate that corticosteroids in substitution doses (cortisone 50 mg. daily or prednisone 10 mg. daily, divided in 4 daily doses) are very effective in depressing the excretion of all 3 steroids in postmenopausal patients. this is in agreement with

the clinical impression that these easily tolerated small doses of corticosteroids have the same therapeutic effect as adrenalectomy in patients with breast cancer. the results indicate that the ovaries may contribute to the production of oestrogens for many years after the menopause, and that this production is depressed by ovarian irradiation. this is in agreement with the clinical observation that ovarian irradiation has a therapeutic value in postmenopausal women with breast cancer.

.I 449

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414. estimation of the urinary 17-ketosteroids in the diagnosis of carcinoma of the prostate in 33 patients with histologically confirmed carcinoma and in 37 patients with confirmed benign hyperplasia of the prostate the amount of neutral 17-ketosteroids was estimated in 24-hr. samples of urine. the results revealed that, contrary to reports in the literature, this diagnostic method is quite unreliable. raised 17-ketosteroid levels were found also in a high percentage of control subjects.

moreover, the estimation of 17-ketosteroids is a very laborious biochemical method and involves a relatively great experimental error.

.I 450

.W

2820. influence of small doses of corticosteroids on the excretion of pregnanetriol and oestrone in a series of patients with breast cancer excretion of oestrone and pregnanetriol was determined. with administration of corticosteroids oestrone excretion in postmenopausal women diminished 67%. a decrease of pregnanetriol excretion values was observed as well. evidently a low oestrone excretion in patients subjected to corticosteroid therapy is due to a depression of the adrenal function.

.I 451

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5062. urinary 11-deoxy-17-oxosteroids in british and japanese women with reference to the incidence of breast cancer japanese women excrete more andosterone (5a) relative to aetiocholanone (5b) than do british women living in tokyo. the mean 5a/5b ratio in the former is 1.3

and in the latter 1.0, and these means differ significantly. the ratio is markedly affected by thyroid function, and thyroid disease has been reported to affect the incidence of breast cancer which in japan is only one eighth of that in white women in north america or great britain.

.I 452

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5318. the plasma 17-ketosteroids and 17-hydrocorticosteroids in women with breast cancer in 100 women in the menopause with breast cancer the mean level of plasma 17-ketosteroids (17-ks) and 17-hydroxycorticosteroids (17-ohcs) was significantly higher than in normal women of equivalent age. in 67 young women only the level of the plasma 17-ohcs was significantly higher than normal. in menopausal women with breast cancer whether treated or not there is no correlation between the level of the plasma 17-ks and that of 17-ohcs.

.I 453

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5319. urinary porter-silber chromogens following intravenous metho-

pyrapone and acth in patients with breast cancer urinary porter-silber chromogens have been measured in 2 groups of patients with breast cancer before, during and after intravenous methopyrapone and acth administration. the control group consisted of females free of disease 5 years or more following mastectomy while the study group had documented metastatic disease. no significant difference in the urinary porter-silber chromogens was found between the 2 groups on any day during the course of the study and were within the range of normal as measured in this laboratory. it is concluded that the functional reserve capacity for both pituitary acth secretion and adreno-cortical steroidogenesis in patients with advanced metastatic breast cancer is relatively normal.

.I 454

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2349. amyloidosis in the autopsy material of the pathology department of tuberculosis institute, warsaw, in 1945-1962 the autopsy material of the pathology department of the tuberculosis institute, in 1945-1962, included 1218 postmortem

examinations of patients who died from tuberculo-
sis. in 111 cases tuberculosis was
complicated by amyloidosis. in 1945-1957 amy-
loidosis accounted for 8.7% of the cases;
in 1958-1962 this percentage was 10.8.
there was no difference in the incidence
between men and women, the only difference
between the two sexes was that the peak
tuberculosis fatality curve in men was in
the 40-60 years age group, and that of
amyloidosis at the 20-30 age group, while in
women the greatest number of death from
tuberculosis was in the 20-30 age group,
and from amyloidosis in the 30-40 age group.

.I 455

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766. certain features of the haemogram in patients with pulmonary tuberculosis
complicated by amyloidosis (russian)
regression of amyloidosis in the early stages
seems possible and for this reason
russian clinicians are exploring the possibilities
of finding means of early diagnosis
of this complication. the author studied 300
complete clinical blood analyses made
in 60 patients, viz. 30 with chronic fibrocavernous
and cirrhotic forms of tb com-
plicated by amyloidosis and 30 with the same forms

of tb without amyloidosis. from
detailed serial study of the haemogram in patients
with pulmonary tb it is possible
to diagnose associated amyloidosis of the internal
organs in its initial stage. the
presence of amyloidosis of the internal organs can
be inferred from the following
changes in the blood picture (a) the appearance of
normochromic and hypochromic
anaemia in patients with various forms of tb (with
the exception of tb of the kidneys,
intestinal tract or larynx, and of caseous lymph
nodes), (b) progressive increase
in the leucocyte count with a neutrophil shift to
the left not corresponding with a
phase of quiescence of the main disease, (c) consistently
high esr in the absence
of an active process, (d) thrombocytosis in the phase of
subsidence of a flare-up,
and also changes in the thrombocytic formula tending
towards the appearance of de-
generative forms and old and mature thrombocytes.

.I 456

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1319. diffuse tracheo-bronchial amyloidosis a rare variant of a protean disease
a patient with diffuse tracheo-bronchial
amyloidosis is described; brief clinical

details supplement those published in a previous report (prowse,1958) and are followed by an account of the necropsy findings and the histological appearances at the site of amyloid deposition. the literature is reviewed and arguments are advanced in favour of a common aetiology for amyloidosis in all its forms. if this acts through the immunity mechanism, it is suggested that variations in the site, strength, duration, and frequency of the antigen stimulus and the antibody response may determine the nature and distribution of the amyloid deposits.

.I 457

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2091. modern methods of treatment of visceral amyloidosis in patients with pulmonary tuberculosis (russian)
the immediate and long-term results of treatment during 1945-1962 of 414 patients with pulmonary tuberculosis complicated by amyloidosis were studied. hormonal (corticosteroid) therapy is the pathogenetic treatment for visceral amyloidosis and is indicated in the proteinuric and early edema-hypotonic phase of amyloidosis when the functional capacity of the kidneys and

the liver is still adequate. in the azotemic phase of amyloidosis, hormonal (corticosteroid) therapy is not indicated, since it leads to rapid deterioration in the patient's condition. since hypoxemia is one of the main factors in the pathogenesis of amyloidosis, oxygen therapy is rational patho- genetic therapy for patients with pulmonary tuberculosis complicated by hypoxemia and with symptoms of the proteinuric or edema-hypotonic phase of amyloidosis (without ascites), in the form of subcutaneous introduction of oxygen or oxygeno-peritoneum. in patients with pulmonary tuberculosis surgical intervention on account of the main process is indicated only in the early stages of amyloidosis when pronounced functional disorders of the kidneys and liver are absent. co- joint therapy using protein vitamins (particularly ascorbic acid), hormonal (corticosteroid) preparations, oxygen and desensitizing agents and elimination of all foci of infection is indicated in treatment of pulmonary tuberculosis with even the earliest signs of amyloidosis.

.W

2317. the use of needle biopsy of the liver in the diagnosis of visceral amyloidosis in patients with pulmonary tuberculosis (russian)

the results of 86 puncture biopsies of the liver in 84 patients with pulmonary tuberculosis (55 men and 31 women aged from 18 to 73 yr.) for the purpose of diagnosing amyloidosis are reported. puncture was performed when amyloidosis was suspected on the basis of the case history (destructive process of more than 2-3 years' duration), clinical signs in the form of enlargement of the liver and spleen, edema, changes in the blood picture and blood protein formula, and changes in the urine (proteinuria, cylindruria, isohyposthenuria). amyloidosis was diagnosed or its presence surmised before puncture in 23 patients; the puncture biopsy confirmed the diagnosis in 14 and refuted it in 9 of them. in 8 patients without clinical symptoms, amyloidosis was diagnosed on the basis of the puncture biopsy alone. in 9 cases with fatal outcome, the post-mortem findings coincided with the results of the bioptic puncture. of the 62 patients in whom amyloidosis was not detected by biopsy, 31 had moderate

dystrophic changes and 9 had marked dystrophic changes while in 22 cases no pathological changes were found; 6 of these patients later developed amyloidosis. these findings supported the contention that liver amyloidosis is linked with dystrophic changes in the epithelial cells. marked dystrophic changes can precede amyloidosis or may occur simultaneously with it. moderate dystrophic changes are quite common in patients with an exacerbating tuberculous process in the lungs. the wide application of bioptic puncture of the liver in indicated cases can increase our knowledge of the morphological changes taking place in the liver in tb.

.I 459

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2701. the role of certain additional factors in the development of amyloidosis, and its prophylaxis in patients with pulmonary tuberculosis (russian) in patients with chronic fibrocavernous tuberculosis of the lungs, any toxic-allergic side reactions to antibacterial therapy, chronic foci of infection and diseases with an allergic component can contribute to the development of amyloidosis. the early detection and clearing of chronic

foci of infection and effective measures against even mildly pronounced toxic-allergic side reactions are of prime importance in the prevention of amyloidosis. the unsystematic and prolonged administration of antibacterial preparations, along with their toxic side effects, tends to increase the incidence of amyloidosis in patients with chronic fibrocavernous pulmonary tb. individual constitutional factors are of great importance in the development of side effects. side reactions to chemopreparations, in cases of hypofunction of the liver and kidneys and autonomic dysfunction promote the development of dystrophic processes, as is confirmed by the high frequency of toxic-allergic reactions in patients with fibrocavernous pulmonary tb who later develop amyloidosis. the administration of desensitizing drugs to patients showing side reactions therefore helps to prevent amyloidosis in cases of chronic fibrocavernous tb, and chemotherapy should be automatically combined with the administration of desensitizing and stimulatory drugs in this class of case.

.W

1835. the decrease of the steroids in the urine in the course of lung tb.

(the therapeutic value of their increase after calciferol)

quantitative determination of the urinary

steroids in 38 patients with extensive ul-

cero-caseous pulmonary tb confirmed

that the 17-ketosteroids are always decreased

in these cases. calciferol, in the form

of one ampoule of vit. d2 of 600,000

u. every 10 days, in combination with active

tuberculostatic drugs, in the majority of

the cases leads to an increase of the

urinary 17-ketosteroids from 50 to 100% in 2

moth. it appears that the calciferol

exerts its action through proteolysis; it stimulates

the liquefaction and evacuation of the

caseous material. this proteolytic effect is

related to that of the mineralocorticoids,

which are phlogistic and proteolytic sub-

stances. calciferol offers the advantage

over these substances that it does not affect

the electrolytes and is well tolerated by

the organism. for this reason, good results

may be expected from its administration

in cases of extensive pulmonary tb, in

which the myc. tuberculosis has remained

sensitive to the administered tuberculostic

drugs but nevertheless does not proceed towards recovery because of the marked caseous lesions. in such cases calciferol treatment leads to a rapid and pronounced decrease of the radiological shadows, improves the general condition and also modifies the steroid metabolism rendered abnormal by the disease.

.I 461

.W

1837. development of amylosis in less than 2 months in the course of a primary tb infection
the case is reported of a previously healthy young north-african male, in whom a post-primary ulcero-infiltrative tb in less than 2 mth. led to the development of visceral amyloidosis, which could be confirmed by biopsies of the kidney and liver.
during treatment with antibiotics, the hepatic amyloidosis regressed parallel with the improvement of the tb, and the biological signs of the renal amyloidosis disappeared with the exception of a pronounced proteinuria, the persistence of which renders the long-term prognosis highly doubtful.

.I 462

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2216. the relations between lupus erythematosus and diseases of the

lympho-reticular system

a case report of a patient with led
(aged 48 years), who developed secondarily
a lymphoblastic sarcoma. when the
sarcomatous degeneration of the lympho-
reticular system became apparent,
the serological and immuno-hematological tests,
typical for led, were negative. to
interpret the observation, 62 further patients
with lymphogranuloma, lymphosarcoma,
leukemias, other malignant tumors, sar-
coidosis, and tuberculosis were investigated
serologically and immuno-hematolo-
gically. antinuclear factors were found in
serum of 4 patients with lymphogranulo-
ma, one patient with anaplastic carcinoma,
and one patient with metastasizing
mixed parotid-tumor. the identity of the
antinuclear antibodies with those found in
led could not be proved by different methods.

the importance of certain diseases
of the lympho-reticular system for the production
of antinuclear factors was dis-
cussed.

.I 463

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4417. value and significance of the prednisolone test in diseases of the kidney

twelve normal subjects, 18 cases of tubulo-interstitial nephropathy, 12 cases of glomerular nephropathy and 17 cases of other renal disorders were investigated. all patients were given a prednisolone test, with urine culture before and after the test, and in many instances determination of the urinary osmolarity; the urinary sediment was examined with the sternheimer and malbin staining technique and with the peroxydase stain to investigate the urinary cytology. with the criteria adopted, the test was negative in the normals and was positive in 61.1% of the cases of chronic pyelonephritis and in 12.1% of the remaining cases of unequivocally non-infectious renal disease. the increase of the urinary bacterial count after corticosteroid administration, and investigation of the various components of the urinary sediment also supplied useful diagnostic information. on the contrary, the sternheimer-malbin stain for the urinary sediment proved of little use.

.I 464

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564. tumoral amyloidosis of the lung

an incidental finding at necropsy on a woman aged 95 was a tumor-like mass, 8.5 x 6.5 x 6 cm., in the lower lobe of the left lung. the detailed structure of this may suggested angioma of hamartoma; the stroma and some vessels contained amyloid. amyloid is not uncommon in the stroma of tumors. a summary of 17 tumoral amyloid cases reported by others is included.

.I 465

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7364. experimental amyloidosis in immunity much of interest in the mechanism of experimental amyloidosis as a result of the parenteral introduction of foreign protein has been centered around the nature of the links leading to cytological and biochemical changes in tissues and body fluids. some of the authors suggested that such links may be of immunological nature. there is however, no clear-cut proof either in favor of or against the theory of an immunological origin of amyloid. since injection of proteins during the perinatal period prevents an immune response when the animal is subsequently challenged with the same antigen, the authors studied

amyloidosis caused by casein in mice treated after birth with this protein. mice exposed soon after birth to casein acquire an immune tolerance to this antigen. this was demonstrated by the absence of circulating antibodies as measured by the disappearance of i-labeled casein from the circulation and by means of passive hemagglutination tests with ascitic fluids. both tolerant and control animals developed amyloidosis to the same extent. the results imply that the pathogenesis of amyloidosis does not rest upon a classic immunological basis; they do not exclude the possibility, that the disease may be due to some auto-immune process.

.I 466

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3535. electron microscopic study of six cases of human renal amyloidosis this study is particularly concerned with (a) the basal membrane in the different stages; and (b) the intercapillary spaces in the early stages. the conclusions may be put as follows (1) the amyloid substance seems to have a fibrillar structure from the start. (2) when the walls of the peripheral capillary loops are thickened

by voluminous amyloid deposits, the hyaline aspect of the primitive basal membrane persists, but its structure is altered by the presence of multiple amyloid fibrils. (3) on the other hand, in the initial stages, amyloid fibrils cannot be seen in the 'lamina densa' of the basal membrane; they only appear on the epithelial and endothelial surfaces of the membrane. this suggests that amyloidosis represents an abnormal precipitate of extrinsic origin, rather than a transformation 'in situ' of the basal membrane. (4) in the very early stages of amyloid infiltration into the glomeruli the fibrillar substance is found first in the intercapillary spaces, only later does it reach the peripheral capillary walls.

.I 467

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3544. morphology and development of infectious-toxic affections of the kidneys in pulmonary tuberculosis (russian)
the kidneys of 75 patients dead from tb of the lungs and of 30 rabbits with pulmonary tb were examined. the first lesions develop in the glomeruli, followed by changes in the stroma and tubules. infectious-toxic affection of the kidneys is a complex and

prolonged process involving organic immune reactions, lymphostasis, venous stasis and finally nephrosclerosis. infectious-toxic lesions were found in one third of the patients who died of pulmonary tb. these changes had produced clinical manifestations, on the basis of which the following affections had been diagnosed nephritis, nephrosis, amyloidosis. antibacterial therapy of the pulmonary process reduced the renal lesions. however, severe infectious-toxic affection of the kidneys may develop after recovery from pulmonary tb.

.I 468

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3553. diffuse nodular amyloidosis of the lungs in a 59-year-old man, who 12 yr. previously had ceased working in an aluminium factory and who had died from respiratory insufficiency, the postmortem examination revealed disseminated nodules in the lungs. the nodules were sharply defined, of a greyish color and of a doughy consistency and could easily be removed from their capsules. the diagnosis of amyloidosis was made on the basis of the histological findings, the staining qualities of the material,

its intraseptal and periarteriolar localization, and the existence of plasmocytic infiltrates and foreign-body giant-cell granulomas. amyloid deposits were also found in the spleen, kidney and some coronary branches. in regard to the pathogenesis, it is suggested that the exposure to aluminium products for more than 10 yr. might have constituted a predisposing factor.

.I 469

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3724. the bacterial induction of homograft sensitivity. ii. effects of sensitization with staphylococci and other microorganisms heat-killed strains of staph. aureus and staph. albus can induce in guinea pigs a state of altered reactivity to skin homografts which is indistinguishable from that which results from sensitization with homologous tissues or group a streptococci. challenge of suitably prepared recipients with 1st-set skin homografts obtained from unrelated randomly selected donors elicits white graft reactions or accelerated rejections of such grafts. other bacteria tested included lancefield streptococcal groups b, c, d, e, g, h, l, and o,

pneumococcus types ii, iii, xiv and a rough strain, c. xerosis, b. subtilis, e. coli, a. aerogenes, s. typhimurium, pr. vulgaris, n. catarrhalis, h. influenzae, and 2 human virulent strains of myc. tuberculosis. none of these microorganisms was active in the induction of homograft sensitivity in the guinea pig. pretreatment of recipients with gram-negative bacterial suspensions was associated with a slight increase in the mean survival time of 1st-set skin homografts. results of this study suggest the presence in staphylococci, as well as in group a streptococci, of antigens related in their biologic effects to tissue transplantation antigens.

.I 470

.W

6590. structure and function of cross-linked dna. i. reversible denaturation and bacillus subtilis transformation
reaction of nitrous acid with dna
results in covalent linkage of complementary polynucleotide strands. the resulting material denatures reversibly and retains biological activity in bacterial transformation.

.I 471

.W

4958. the mechanism of messenger-rna replication in bacteria

the transformation of bacillus subtilis

sb25 his-tryp-by two linked genetic mar-

kers under the action of hybrid molecules

of dna was investigated. the molecular

hybrids were obtained by thermal denaturation

and annealing of a mixture of two

dna's, each one extracted from a single

auxotrophic strain (h25 his-and 168 tryp-).

the formation of the heterozygous dna

double helices was proved by special experi-

ments. the transformation procedure

excluded dna synthesis by recipient cells

prior to the formation of enzymes for

histidine and tryptophane synthesis. it was

found that heterozygous molecules of

dna are able to transform in these conditions

the double auxotrophic cells to prototrophic

ones. this means that both strands of

the dna double helix can serve as templates

for the m-rna synthesis. the possi-

bility of a secondary replication of m-rna

outside the chromosome under the action

of rna-polymerases, using rna as a primer,

is discussed.

.I 472

.W

2567. the molecular basis of histidase induction in bacillus subtilis

bacillus subtilis growing at 37 °C on

glutamate, as only carbon source, is induced

to form histidase by L-histidine. this

enzyme, converting histidine to urocanic

acid, was isolated in a purified form.

a highly sensitive and convenient assay for

the induced enzyme is described and

applied to show that histidase appears in the

cell 5 min. after addition of the inducer.

histidase-synthesizing capacity appears

after 2 min. and decays exponentially after

addition of actinomycin (an inhibitor

of dna-dependent rna synthesis). the

half-time value of histidase-synthesizing

capacity of 2.4 is high, compared with the

half-time value of messenger

rna. the histidase formation after addition of

actinomycin was not only due to protein

synthesis directed by accumulated m-rna

but also by conversion of an enzymatical-

ly inactive protein, present on the moment

of actinomycin addition and product of

the specific m-rna, to the active enzyme.

the existence of this enzyme pre-

cursor was shown by means of experiments

performed in the presence of chlor-

amphenicof. finally, numerical values for the steady state of histidase synthesis, reached 9 min. after addition of the inducer, are calculated, on the basis of kinetics of histidase synthetic capacity, precursor and enzyme formation the cell contains sufficient precursor to form approximately 100 molecules of histidase. the cell produces approximately 50 molecules histidase per min. the cell acquires and loses, every minute, the capacity to make 15 molecules of histidase per minute. the maximal enzyme level is 15,000 molecules per cell.

.I 473

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2542. symposium on the fine structure and replication of bacteria and their parts. ii. bacterial cytoplasm comparison of the fine structure of the cytoplasm of the bacterial cell with that of the 'cell in general' reveals important differences leading to the conclusion that, in the bacterial cytoplasm, there is little differentiation into separate functional entities. there is no nuclear membrane, and fine fibrils appear to extend from the nucleoplasm into the cytoplasm where they may

expand in all directions. the cytoplasm is not necessarily intersected by membranous profiles of special configuration, as is borne out by *e. coli* b and other gram-negative organisms. when membranous profiles of special configuration are present, as in the gram-positive *b. subtilis*, these do not appear differentiated into clearly definable endoplasmic reticulum, golgi substance, microbodies, etc., and mitochondria. as for kinetosomes, the presence of centrioles is perhaps not very likely. the experiments in which tellurite is reduced in the cells suggest that there are structures at the base of the flagella with reductive capacity. however, upon application of the tetranitro-blue tetrazolium technic to *b. subtilis*, these are not stained. they are presumably identical with basal granules. the membranous structures in *b. subtilis* are called chondrioids by the author because probably one of their functions is that they are the sites of the respiratory enzyme chain. in the gram-negative *p. vulgaris*, the probable site of the respiratory chain has a structure very different from that in the bacillus; it

is not clear whether membranes are involved in their structure. morphologically, even in *b. subtilis* chondrioids differ fundamentally from the mitochondria in that they are not built up from composite membranes, they are extensions of the plasma membrane, and they may not be completely closed systems. regarding this last point, it was observed that chondrioids may possibly stand in open connection with the cell's environment, since its lumen is not separated from the cell wall by a plasma membrane. although as yet nothing is known about this, it does not seem to be precluded that these membranous organelles may function also as intracellular transport systems. contrary to porter's ideas about er, the chondrioids are not extensions of a nuclear envelope, but of the plasma membrane. on the other hand, they are in the nuclear area, in direct contact with the nucleoplasm, and therefore, perhaps, they need not carry in their interior some dna, as is now becoming known for ordinary mitochondria. the chromatophore vesicle is of a simple structure and in connection with the plasma membrane. it is

covered by a single membrane and thus resembles the granum disc, but it is much smaller. In tissue cells, an important function of the ER is the support of protein synthesis by ribosomes bound to their surfaces. Evidence is now accumulating that the active complexes for polypeptide synthesis in bacteria are also membrane-bound and are series of 70S ribosomes using the same messenger RNA molecule. It remains a contradictory situation that the particles obtained here through release of cytoplasm from protoplasts in diluted, rather crude fixing media, and identified as ribosomes, could not be recognized as such in thin sections of the Ryter-Kellenberger fixed protoplasts. This point is much in need of clarification. But even if the cytoplasm in the thin sections of the protoplasts is in a state of dispersion brought about artificially, it is still apparent from the various micrographs that basically the cytoplasm is a network of presumably linear arrays, with many interconnections due to fibrillar systems. Fibrils from the nucleoplasm penetrate deeply into the cytoplasm. The

presence of fine fibrils of various thicknesses,
electron densities, and orientations
makes high-resolution study of the cytoplasmic
details an intriguing prospect from
which much fundamental information can be
gained. the organizational pattern on
the ultrastructural level in bacteria reveals
fundamental similarities and divergen-
cies from that in the 'cell in general'.

.I 474

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906. molecular mechanism of genetic recombination in bacterial transformation
the mechanism of dna incorporation into
the recipient cell chromosome was in-
vestigated in a b. subtilis transformation
system. the recipient cells were auxo-
trophic for 2 linked markers. hybrid dna
used for transformation was heterozy-
gous for one of these markers. no differences
in transformation activity were found
when the effect of native and hybrid dna was
compared. according to the authors
this observation is easily explained if we accept
that each of both complementary
strands of the donor dna can be incorporated
into the recipient chromosome with
equal probability. the results on the segregation

of genetic characters in the progeny of transformed cells are also consistent with the model of independent incorporation of both dna strands. some calculations were done on the probability of the integration of a single dna strand carrying a particular genetic marker, and on the probability of recombination leading to double transformants.

.I 475

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1520. multiplication of bacteriophages
the reproduction of bacteriophages requires the participation of bacterial metabolism. synthesis of the viral protein components is accomplished by the same mechanism as ordinarily produces bacterial proteins; however, for the synthesis of nucleic acids (dna or rna) enzymes may be required which are not present in non-infected bacteria; their formation is then induced by the virus itself. the fundamental biological processes of replication, transcription and translation are discussed in this context.

.I 476

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1361. the mechanism of histidase induction and formation in bacillus subtilis

the role of the inducer, l-histidine, in the synthesis of histidase (l-histidine ammonia lyase) in *b. subtilis* was investigated. it was found that induced cells poisoned with actinomycin, an inhibitor of rna synthesis, lose their capacity for the formation of a protein precursor of histidase at a rate which is independent of the presence or absence of the inducer. these results show that the inducer does not increase the intracellular level of histidase-specific messenger rna by preventing the destruction of the major portion of this material, the fraction that is engaged in protein synthesis. the possibility has not been excluded that the inducer exerts its effect by bringing about the stabilization of the messenger rna that is still attached to dna or has not yet become attached to ribosomes. alternatively, the inducer may actually stimulate the synthesis of histidase-specific messenger rna. the conversion of the precursor to active enzyme appears to involve polymerization of monomers, rather than the release of ribosome-bound inactive enzyme.

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1362. the synthesis of phage and host dna in the establishment of lysogeny

a method of extraction is described which

prevents excessive fragmentation of bac-

terial dna. the larger bacterial dna can

then be separated from the phage dna

on sucrose gradients. the relative amounts

of phage and host dna made at various

times during infection of *s. typhimurium*

with phage p22 leading to lysogeny have

been determined. phage-specific dna

synthesis begins at about 4 min, continues

to increase for 2-4 min, and then decreases

until complete repression is attained

at 16 min. autonomous phage dna synthesis

remains repressed from then on. bac-

teria-specific synthesis proceeds at a

decreasing rate until about 16 min, when

almost complete inhibition is reached.

when dna synthesis recovers in the in-

fected cells, only host-specific material

is made. a new species of dna, which is

made only when phage dna is synthesized,

has been detected. the possible implica-

tions of these findings in the understanding

of the lysogenic interaction is discussed.

.I 478

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438. lag period characterizing the entry of transforming deoxyribonucleic acid into *Bacillus subtilis*

the kinetics of appearance of transformants

as a function of time of exposure to

DNA has been studied. a short lag period

of approximately 1 min at 37 °C is evi-

dent when the transformation is terminated

with deoxyribonuclease. the length of

this lag is independent of the genetic trait

transferred. moreover, the lag is unaf-

fected by transforming DNA concentration,

by the presence of homologous unmarked

DNA, and by shearing and cross-linking of

the transforming DNA. the lag shows

a strong inverse temperature dependence.

the energy of activation is 13.9

kcal. the lag is abolished when the transformation

is terminated by washing instead of

by addition of deoxyribonuclease. these results

are taken to indicate an immediate

adsorption of DNA to cells, followed by a

deoxyribonuclease-sensitive period of

1 min, during which time the genetic trait

is entering the cell. these results make

feasible an investigation of the configuration

assumed by the DNA molecule during

entry into the cell.

.I 479

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439. configuration of transforming deoxyribonucleic acid during entry into
bacillus subtilis

a correlation was obtained between map
distance and the length of the lag period
preceding the appearance of pairs of genetic
traits after the addition of dna to a
competent culture of b. subtilis. the results
are taken to indicate that dna enters
competent cells in lengthwise fashion.

the smallest length of transforming dna
which can participate in a recombination
event, and the number of nucleotide pairs
which enter the cell per unit time, have
been estimated. the evidence indicates
that only part of the lag period is devoted
to the transport of dna into the cell.

the significance of these results with
respect to the mechanism of entry of dna
into the cell is discussed.

.I 480

.W

2564. chemical inactivation and reactivation of transforming dna (russian)
the kinetics of the inactivation of linked
and unlinked genetic markers by means

of hno₂ or uv light was studied. closely linked markers are inactivated simultaneously, unlinked markers are inactivated independently. it seems that the chemical attack on dna impairs a large part of macromolecule, including many cistrons. it was shown by genetic experiments that chemical inactivation practically does not influence the process of dna inclusion into competent cells. by means of viscosity measurements it was shown that the molecular weight and macromolecular properties of dna do not significantly change during chemical inactivation by means of hno₂. two explanations for the inactivation of transforming activity of dna are discussed (1) structural deteriorations, preventing integration of dna molecule into the genome of recipient cell, or (2) deletion of a chain unit out of dna chain resulting in wrong reading of code triplets. it was previously described in the literature that extensive inactivation leads to a state of dna, apparently more resistant than the initial one. inactivation does not conform to exponential kinetics. the authors discuss the

coding mistake hypothesis

as an explanation for this remarkable fact. extensive

hno₂ or uv light action re-

sults in multiple lesions in the dna molecule and

leads to reactivation because

the deletions restore correct reading of the code

in a large part of dna molecule.

on the basis of this explanation reactivation of

chemically injured dna by means

of fusion and annealing with homologous but

genetically inactive dna, or by slight

fragmentation of dna by means of ultrasonic

vibrations may be expected. attempts

to achieve reactivation by both methods gave

positive results.

.l 481

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2565. separation of the transforming and viral deoxyribonucleic acids of a

transducing bacteriophage of bacillus subtilis

the authors used the transducing b. subtilis

phage ps 10 and present the fol-

lowing experimental data dna isolated from

ps 10 is effective for transformation

of competent b. subtilis cells. ps 10 dna is

distinguishable from b. subtilis dna

by its higher density in a cs₂so₄ gradient and

its lower thermal denaturation

temperature. the transforming activity present in dna from ps 10 denatures at a temperature characteristic of b. subtilis dna rather than of viral dna. the transforming activity of ps 10 dna bands in a Cs_2SO_4 gradient with bacterial dna. this data indicated that bacterial dna is incorporated into phage ps 10 without being integrated in the viral dna. this incorporated bacterial dna is involved in transduction.

.I 482

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2529. repair of damage induced by a monofunctional alkylating agent in a transformable, ultraviolet-sensitive strain of bacillus subtilis
a uv sensitive, transformable strain of b. subtilis (uvr-) was unable to carry out host cell reactivation of the virulent bacteriophage spo1. the ratio of the slopes (kuvr-/kuvr+) of the uv inactivation curves was 6-8 for cells or for whole phage, and 2 for indole+ transforming dna or for spo1 phage dna measured in a transforming system. whole phage inactivated with nitrogen mustard showed greater survival on uvr+ cells than on uvr-; there was no such difference for whole phage inactivated with

methyl methanesulfonate. whole uvr+ cells recovered from uv induced damage, as determined by an increase in extractable transforming activity during a period of incubation in which net dna synthesis did not occur. uvr- cells were unable to recover from uv induced damage but they did recover from methyl methanesulfonate induced damage in similar experiments. density labeled (h²n¹⁵) methyl methanesulfonate treated uvr+ cells incubated in (h¹n¹⁴) medium containing (h³) thymidine showed a 3-fold increase in extractable transforming activity, with no formation of new dna molecules as determined by pyknometric analysis. the repair of damage induced by uv irradiation differs by at least one step from the repair of damage induced by methyl methanesulfonate.

.I 483

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1451. the biosynthesis of 5-hydroxymethyldeoxyuridylic acid in bacteriophage-infected bacillus subtilis when phage ϕ , which contains 5-hydroxymethyluracil in its dna in place of thymine, infects b. subtilis, enzyme changes occur in the host organism which can account

for the synthesis of the abnormal base.
deoxycytidylate deaminase increases at
least 90-fold and the product of its action,
deoxyuridylic acid, is converted directly
into the deoxynucleotide of 5-hydroxymethyluracil
by a hydroxymethylase enzyme.
the activity of thymidylate synthetase, which also
uses deoxyuridylic acid as
substrate, decreases rapidly after phage infection.

.I 484

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5574. death anxiety in children with a fatal illness
the author reports studies of a series
of 50 children hospitalized because of fatal
illness due to leukemia or some other
form of cancer. it was postulated that the
younger children would experience
separation anxiety while the older children
would be more likely to experience
death anxiety. in general the hypothesis
was supported by the results of the study.
there was some evidence to indicate that
the younger children perceive death
anxiety but deal with it in more symbolic form.
in older children, it was felt that boys
tended to react to death anxiety by acting out
behavior while girls tended to become depressed.

.I 485

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1209. the theory and practice of the family diagnostic. ii. theoretical aspects and resident education

family intervention and observation have proved useful in 3 areas. the 1st of these is observation of the psychosocial context in the patient. on admission to a mental hospital the phenomenon of extrusion and separation from the family is evident, and the need for study of the interaction between the patient and his family milieu is vital. the 2nd area where the family interview has a major role is resident education. the traditional medical education of the ill prepares the student for consideration of the multifactorial problems of emotional disorder in which balances between members of a group may be the issue rather than external pathogenes. the family interview offers a unique point of observation of factually evident and emotionally convincing group data. in addition to the observation of family phenomena, mutual understanding of others' problems is created. finally, the family interview serves as an instrument for data collection and hypothesis seeking in relating individual psychopathology to family adaptations. the patient and his family at the time of admission are dealing with a crisis. sometimes this is traumatic, such as the unexpected loss of a young marital partner, an unexpected illness, or

a financial reverse. more commonly, however, it is developmental being a natural part of the life cycle. characteristically, the developmental task involved in dealing with the crises has been postponed so that one does not see the family at the age specific and appropriate time for this task. the crisis emerges disruptively because of inevitable biological maturation, personal decision, or social expectation. a primary concern of the leader is to determine what life task is being faced. families have a mentally ill member not merely because they are dealing with the vicissitudes of life. they are unable to cope with the crisis, because of the feelings which are aroused. each life crisis leads to a particular constellation of effects in any given family. these include primarily, sadness, anger, and guilt, but there may well be specific affective constellations appropriate to different developmental tasks. the patient's inability to cope with a life crisis is due to his particular adaptation of a style of dealing with feelings that is employed by other members of the family.

.I 486

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265. studies in personality. ii. a bio-psychological and experimental approach to problems of human adaptation in modern society
experimentally determined fixation-ambivalence
measures are related to some anxiety estimates obtained from a projective test in a group of male adolescents.

it is shown that (1) fixation increases with increase in corporal injury anxiety when ambivalence is kept constant, (2) ambivalence increases with increase in separation anxiety when fixation is kept constant, (3) extremely hetero-fixated subjects show presence of intense guilt and absence of aggression towards the mother; one effect of this system of organizers seems to be suicidal

tendencies, (4) extremely ambivalent subjects have intense separation anxiety; one effect seems to be suicidal tendencies combined with high ambition and impaired cognitive capacity.

.I 487

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2837. early indicators of outcome in schizophrenia

the case material of 50 persons who

were seen at a child guidance center in child-

hood or adolescence and were later

hospitalized with schizophrenia were examined

intensively. the study concentrated

especially on the differences associated with

chronicity vs. hospital release. the

following 12 factors were significantly related

to chronicity (1) psychotic or schizoid

pathology in the mothering person, (2) no se-

paration of any kind from the pathogenic

families, (3) pre-illness history of poor so-

cial and sexual adjustment, (4) failure to continue in treatment (during childhood) for at least 3 mth., (5) less acting out in the community, (6) neither disorientation nor confusion on admission, (7) no symptoms of depressive psychosis, (8) premorbid schizoid personality, (9) no clear precipitating events, (10) no concern with dying during the acute phase of the illness, (11) length of onset over 6 mth., and (12) schizophrenic reaction in patients' heredity.

items 1, 2, and 5 were derived from early life history data and are thought to be new to the literature of prognosis in schizophrenia. the remaining 8 factors can be scored from hospital data alone, and have been cited in previous prognostic studies.

.I 488

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4854. on the formation of object-relations and identifications of the kibbutz child

some of the issues relevant to the early stages of object relation formation and identification of kibbutz children are discussed. for this purpose the child rearing milieu of the kibbutz child is described and some clinical illustrations are given.

the relationship to the mother is seen as the main object-relation and those to the educators as transient-interchangeable need-satisfying relationships. on the basis of retrospective analytical material it appears that in the course of development the two relations as well as the two respective, originally distinct, object representations are synthetised into one. the conditions of communal education, characterised by double object-relation formation from birth on, are seen as factors that intensify the 'normative crisis of infancy', especially the transition from the symbiotic to the separation-individuation stage of object-relation development.

.I 489

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4846. the meaning of crying
the multiple meanings of crying are reviewed and, in particular, stress is laid on tears as a response to some type of separation loss.

.I 490

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2953. the death of a parent
in the case of depressive illnesses the death of either parent prior to the child reach-

ing the age of 15 seemed to be correlated as a significant contributory factor. with this exception, statistical studies suggest that it is the death of a mother in the first 7 yr. of a child's life, as opposed to that of a father, that is potentially an etiological factor for the future development of psychoses, delinquency and psychoneuroses.

the case histories of 6 boys who had lost their fathers were given. in each instance there was distinct evidence that the psychological symptoms and behavioral disturbances were to be attributed in large measure to the effect of the death upon the child, and that in some cases the symptom choice was to be correlated with specific circumstances surrounding the death of the father.

in some cases it was the unresolved grief reaction in the mother which helped to perpetuate the disorder in the child. resolution of this in the mother during therapy led to improvement in the child's functioning. in other instances improvement occurred especially when the child ceased to be preoccupied with a close identification with the dead father. those boys who were involved most closely in their mother's

grief reactions were the ones who were most disturbed. the brief treatment given these boys and their mothers appeared to be responsible for the considerable amelioration of symptoms that resulted. therapeutic intervention is worthwhile, especially in those instances where there is an unresolved grief reaction in the mother.

.I 491

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1848. the child's concept of death in this translation of a paper, which first appeared in 1912, it is shown, according to freud, how far a child's appreciation of being dead differs from its true significance. death means a reversible decrease in life functions, that can be interrupted at any time, like sleep. at other times it may mean a temporary separation; but always it is in man's power to change it. in this concept, the child's unconscious finds license for his sadism. cruelty to animals and death wishes against persons close to him appear, in overcompensation, as exaggerated pity for dead creatures and the belief in man's power over life and death.

.I 492

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1849. mother child interaction during separation individuation

after a stage of normal autism during the

1st weeks of extrauterine life, the infant

passes into a symbiotic phase, gradually

emerging from this stage of dual unity at

the end of the 5th mth and during the 6th

mth. just before this, the next phase

separation individuation begins. four

characteristic subphases of this separation

individuation process are described

differentiation, the practicing period, association

and a stage, characterized by unfolding

of complex cognitive functions. the relation

of mother and child throughout these

subphases are studied and illustrated by clinical

material. a poor relation between mother

and child in 1 subphase does not necessarily

or usually preclude impressive changes

for the better in the next subphase.

.I 493

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2736. the emotional needs of children in hospital

hospitalization of a child for physical

reasons brings with it separation from pa-

rents, siblings and familiar surroundings,

as well as the probability of subjection

to frightening and painful procedures.
unless steps are taken to prevent or modify
the resultant stress, behavioral
disturbances may arise and may result in per-
manent damage to the developing personality.

.I 494

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2906. early childhood separations

every child in this long-term study of child
rearing showed significant reactions to
ordinary separations by about 1 yr. of age.
the similar pattern of response in this
group of children suggests a biologically
determined cause. the clinging reaction
appeared when the child became mobile and
able to move away from his mother re-
gardless of the frequency or duration of his
separations. the majority of the mothers
did not understand this natural phenomenon
and regarded the clinging and crying of
the 1-year-old as evidence of spoiled or
regressed behavior. the pediatrician can
be helpful to a mother by anticipating and
explaining separation responses, by indi-
cating their universality, and by giving
specific recommendations for gradual changes
to modify these reactions.

.I 495

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9787. changes in developmental quotient under two conditions of maternal separation.

developmental scales were

administered to 2 groups of infants during and subsequent to a temporary period of institutionalization.

although both groups experienced maternal separation,

only 1 group was subjected to deprivation, in

that it received very much less stimulation than the

other. results from a longitudinal testing program

show that the scores of the deprived group during

the period of separation were significantly lower than

those of the nondeprived group, no progressive deterioration

of scores took place in the course of

institutionalization, immediately following return

home, while the scores of the nondeprived group remained

constant, those of the deprived infants jumped

to the level of the other group. 3 theories regarding

the mechanism underlying the association between

deprivation and developmental retardation are examined

and it is suggested that an explanation in motivational

terms best fits the results obtained.

.I 496

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1808. separation anxiety a factor in the object relations of schizophrenic patients.

the thesis is advanced that special vulnerability to separation anxiety is a crucial factor in the schizophrenic's difficulty in establishing and maintaining satisfactory interpersonal relationships. 2 major reasons for this are lack of autonomy and lack of object constancy. without a stable autonomous capacity for self-regulation and adaptation, he is inordinately dependent upon others for help, protection, and direction. without object constancy, he is unable to maintain a stable representation of the needed person in the latter's absence. evidence is presented from the intensive psychotherapy of schizophrenic patients. many of the vicissitudes of the doctor-patient relationship center about the patient's separation anxiety and his attempted defenses against it. these include clinging, perceptual and cognitive distortions designed to deny separation, and recourse to substitute objects. prominent in many of these efforts is the attempt to reverse passive victimization into active mastery. the practical implications of this thesis for the treatment of schizophrenic patients are discussed.

.I 497

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9101. separation experiences and health records in a group of normal adults. about 25% of 455 ostensibly normal ss reported a recent "separation experience" as defined in this study. the frequency of visits to the dis-

pensary for symptomatic complaints was not significantly higher among those who reported separation than among those who did not. the data suggest that an apparent association between relatively high cornell medical index score and history of separation experience may be understandable in terms of a cause-effect relationship between separation experience and illness.

.I 498

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11306. separation and attempted suicide.
of 3 groups of psychiatric patients-attempted suicides, those with suicidal urges, and non-suicides-there were significantly more attempted suicides among patients with a history of childhood and antecedent separation than controls. in childhood the significant difference was found primarily in the period from birth to 7 yr. there was no significant interaction between childhood and antecedent separation and suicide attempt or suicide urge.

.I 499

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1463. investigations of lens protein and microelectrophoresis of hydrosoluble protein in senile cataract
the investigations on lens protein and on agar-microelectrophoresis of hydrosoluble protein in normal lenses and in those affected with senile cataract revealed the following facts (1) in opaque

lenses, a diminution of the total protein and the soluble protein takes place, as well as an increase in the amount of insoluble protein. the decrease in the quantity of soluble protein is higher than the increase of insoluble protein which does not only point to a transformation of the soluble protein into the insoluble variety, but also to the disappearance of a protein fraction from the lens. changes in the quantity of soluble protein are accompanied by the decrease of protein in slow fractions of the electropherogram and even by the disappearance of these fractions and the increase of the amount of protein in fractions of medium velocity. with the development of cataract and the mature phase of cataract, all these processes become more and more distinct. in this respect, a strong parallelism exists between the protein changes and the clinical picture of senile cataract. (2) qualitative and quantitative changes which occur in the protein of normal lenses with advancing age show a character similar to those in senile cataract, however, they are less pronounced. in this instance, the de-

crease in the quantity of soluble protein is likewise closely associated with the diminution of the protein content in the slow fractions of the electropherogram. (3) the changes in the soluble protein content of the lens and the alterations of the protein amounts in the slow fractions which always accompany the former, play the principal role in the aging process of the lens and in the development of senile cataract. (4) the investigations seem to indicate that the aging processes, of lenses as well as the development of senile cataract are of a similar character, but of different intensity. (5) undoubtedly, the processes of transition from slow fractions of soluble protein into faster ones and the transformation of part of the soluble protein into insoluble protein which is likely to be associated with these processes as well as the partial disappearance of total protein from the lens seem to play a very important part in the mechanisms pertaining to the development of cataract.

.I 500

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1949. studies on the soluble proteins of bovine lens. immuno-chemical analyses of protein fractions
the lyophilized soluble lens proteins
were dissolved in 0.005 m phosphate buffer
at ph 6.8 and the solution was subjected to
column chromatography on deae (diethylamino ethyl) cellulose. elution was
accomplished by changing the ph and ionic
strength of the eluting buffer. the components
were fractionated by stepwise elution. the lens proteins were separated into
17 fractions by column chromatography. these fractions were compared with
a, b and γ crystallines for electrophoretic mobility, and the antigenic purity of each
fraction was examined immunochemically. the results showed that while the
fractions were not completely pure they
were purer than the a, b and γ crystalline
fractions, and that f-1-a, b, c and d
corresponded to γ crystalline, while
f-2-a, b, c, d, e and f corresponded to b
crystalline and f-3, 4, 5, 6, 7, 8 and
9 to a crystalline.

.I 501

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3107. studies on γ -crystallin from calf lens. ii. purification and

some properties of the main protein components
four proteins belonging to the γ -crystallin group
were purified by chromatography
on sulphoethyl-sephadex and phosphate-cellulose
columns. the proteins were homo-
geneous in gel and immunoelectrophoresis
experiments and could be crystallized.
their molecular weights, n-terminal amino
acid sequences and antigenic structures
were all similar, but their amino acid
compositions and the sulphydryl groups con-
tained showed certain dissimilarities. it
is probable that the 4 proteins possess
small differences in their primary structure,
which are not associated with the
antigenic sites and which may have arisen
from mutations during evolution.

.I 502

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3105. studies on the subunits of α -crystallin and their recombination

earlier investigations have shown that, in
the presence of high concentrations of
urea, α -crystallin from bovine lens is split
into a number of subunits with apparently
different electrophoretic mobilities but
similar molecular weights. the recom-

ination of these subunits after removal of the urea has been studied by ultracentrifugation and immunoprecipitation techniques. it was found that maximal recombination was obtained when the ionic strength during the removal of the urea was high (>0.2), whereas at low ionic strengths a molecule with only half the molecular weight of native α -crystallin and a much lower sedimentation coefficient was obtained. a complete recovery of the structure of native α -crystallin was never obtained, even at high ionic strengths, as was evident from electrophoretic and quantitative precipitation analyses. the subunits were fractionated by chromatography on deae-cellulose in the presence of 7 M urea. the purification was followed by polyacrylamide-gel electrophoresis. after removal of the urea at high ionic strength, 2 of the fractions obtained showed reactions of only partial identity with native α -crystallin in immunodiffusion tests, but all other fractions showed complete identity. the differences in the electrophoretic mobilities of the fractions in the presence of urea persisted after removal of the urea.

all fractions had much higher sedimentation coefficients in the absence of urea than in its presence, although the values for urea-treated unfractionated α -crystallin obtained after removal of the urea were not reached even at high ionic strengths. the amino acid composition of the fractions was found to differ. these observations suggest that α -crystallin is composed of a number of chemically different, but related, subunits of approximately the same size, which are bound together by nonspecific, noncovalent bonds, possibly hydrophobic bonds. moreover, when isolated, these subunits have the ability to associate and form molecules of high molecular weight.

.I 503

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3106. fractionation of β -crystallin from calf lens by gel filtration

β -crystallin was isolated from calf lenses by a combination of gel filtration on sephadex g-75 and vertical-column zone electrophoresis. it was subdivided into 4 fractions by subsequent gel filtration on dextran gels with low cross-linkage.

each fraction showed only 1 major peak in the ultracentrifuge, the sedimentation coefficients of which were 13.6, 9.6, 4.9 and 4.2 s for fractions i-iv, respectively. however, all 4 fractions contained some additional minor components, as revealed by sedimentation and immunoelectrophoretic analyses. the fractionation procedure may be of value as a first step in the isolation of individual proteins of the b-crystallin group.

.I 504

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195. properties of a cold-precipitable protein fraction in the lens
a soluble protein fraction which precipitates in aqueous solutions at temperatures below 10 °C has been isolated from the rat lens. this fraction appears to be responsible for the reversible 'cold cataract' which has been seen to develop when young mammals are exposed to temperatures below 10 °C. as the rat ages, the concentration of this protein fraction decreases, but the fraction does not completely disappear, even from the lenses of 3-year-old rats. although the molecular

species comprising this fraction appear to be homogeneous in the ultracentrifuge, disc electrophoresis and immunodiffusion have shown that they are a heterogeneous mixture of α -, β - and γ -crystallin subunits. the ability of the cold-precipitable protein (ccp) fraction to precipitate in the cold depends upon its concentration and the ionic strength and pH of the solvent. in solutions of pH 4.0, some aggregation of the 4 s ccp occurs to form a 17 s component, which no longer precipitates in the cold. the ability of this protein fraction to precipitate in the cold may depend on hydrophobic bonding and its influence on the conformation of the protein.

.I 505

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773. the effect of radiation on lenticular epithelial enzymes in young rabbits

the mitochondrial fraction and the soluble fraction of the epithelial cells of the lens from 6-week-old new zealand white male rabbits, exposed to 800 r of whole-head x-irradiation, were evaluated for glucose 6-phosphate dehydrogenase, isocitrate dehydrogenase, malate dehydrogenase,

glutathione reductase, glyceraldehydephosphate dehydrogenase, purine nucleoside phosphorylase, nadph2 diaphorase, and nadh2 cytochrome c reductase activities. increased enzyme activities were noted in the irradiated lenticular tissues for purine nucleoside phosphorylase, nadph2 diaphorase and nadh2 cytochrome c reductase. decreased activities for glucose 6-phosphate dehydrogenase, malate dehydrogenase, glutathione reductase and glyceraldehydephosphate dehydrogenase were observed in the lenticular tissues of irradiated animals. the activity of isocitrate dehydrogenase was the same in the irradiated and in the control animals.

.I 506

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465. conversion of α -crystallin of bovine lens into insoluble protein in vitro

α -crystallin can be converted into an insoluble form by treatment with alloxan and to a very small extent with iodoacetate. other reagents such as hcl, naoh, reduced glutathione, hydrogen peroxide, mercaptoethanol, were not able to convert α -crystallin into an insoluble form. the

alloxan treated insoluble α -crystallin could be made soluble by treatment with 7 M urea. the product thus made soluble had the same electrophoretic mobility as α -crystallin, but showed cross reaction with α -crystallin in Ouchterlony plate and did not have proteolytic activity. alloxan was effective in producing cataract of rabbit lens when very small amounts were injected into the aqueous.

.I 507

.W

1972. structural studies of α -crystallin
 α -crystallin has been isolated from the cortex of ox lens by isoelectric precipitation followed by chromatography on DEAE-cellulose. the amino acid composition is in agreement with that reported for α -crystallin prepared by a different method. there is one thiol group/20,000g. of protein (20,000 is the order of magnitude of the sub-unit molecular weight), and disulphide bonds are absent. the thiol group has been alkylated with radioactive iodoacetate in the presence of urea. partial acid hydrolysis of the alkylated protein gives, according to the conditions, mainly 3 radioactive

peptides or nearly exclusively one radioactive dipeptide. the dipeptide is n-seryl-(s-carboxymethyl) cysteine, ser-cmcys. the 2 other peptides are probably the tri-peptides related to ser-cmcys. the simplest interpretation of these results is that the sequence around the cysteine residue is a common structural feature of the sub-units of α -crystallin.

.I 508

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1751. on the subunits of α -crystallin
 α -crystallin was isolated from total water-soluble lens extract by preparative zone electrophoresis on starch or pevikon c870 blocks and purified by density gradient centrifugation and sephadex chromatography. these preparations were treated with urea or sodium dodecyl sulphate and submitted to electrophoresis on polyacrylamide gels containing either urea or sodium dodecyl sulphate. whereas in 7 m urea a large number of zones was detected, only three bands were observed in 1% sodium dodecyl sulphate. on the other hand, the sedimentation coefficient had the same value in both media. the authors re-investigated the

n-terminal amino acid content in the starch block preparations and compared the result with that obtained from the preparations isolated according to their new procedure. the concentration of dinitrophenyl-glutamic acid was lower in the purified samples. urea-treated samples had the same concentration of n-terminal glutamic acid whereas the concentration of the 'trace' end-groups did not change. sedimentation-diffusion equilibrium in the analytical ultracentrifuge revealed a slight heterogeneity in the purified samples. electron micrographs of electrophoretic and of further purified samples were very similar. at neutral or slightly alkaline ph they showed almost uniform spherical aggregates in which a substructure was observed. at acid ph, coiled filaments rather than small globules could be demonstrated.

.I 509

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1752. separation of the soluble proteins of bovine lenses on polyacrylamide gels
the soluble proteins of bovine lenses were separated by gel filtration on polyacrylamide gels. the presence of ethylenediaminetetra-

acetate in the buffer was found to be essential for achieving a good separation of the lens homogenate into four fractions - a, b, c and d. ultracentrifugal, electrophoretic and immunochemical analyses were used to compare these fractions with the soluble crystallin fractions of the lens. fraction a was compared with α -crystallin, fractions b and c with β -crystallin and fraction d with γ -crystallin. the distribution of these four protein fractions in the nuclear and cortical parts of calf and cow lenses was determined. the oxidation-sensitive protein fraction of the calf lenses was separated from fraction b on an se-sephadex column.

.I 510

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1745. the deaggregation of bovine lens α -crystallin sedimentation equilibrium studies of lens α -crystallin at neutral ph indicate that this material is composed of a number of different sized species. a study of the effect of alkali upon α -crystallin indicates a progressive deaggregation of the material with increasing ph. sedimentation equilibrium studies were performed at ph

12.8 as well as in guanidine hydrochloride, 7 m urea, and with succinylated material. under all of these conditions a molecular heterogeneity was observed. the data indicate that independent species coexisted under most dissociating conditions. the weight average molecular weights of the succinylated, and of the alkali-, urea-, and guanidine hydrochloride-treated material were found to have an integral relationship of 8 4 2 1, respectively. since a constant ratio of M_2/M_w was found, it was concluded that the same spread of distribution of molecular species occurred for each of the deaggregating conditions. the results in guanidine hydrochloride could not be evaluated in this manner because of a small concentration dependence. these conclusions imply that not only the weight average molecular weight in 7 m urea but the actual molecular weight of each individual species in urea was one-half of the value to be found in alkali and one-quarter that of the succinylated material.

.I 511

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1747. the problem of albuminoid

albuminoid is the main constituent of the insoluble fraction of the lens proteins.

albuminoid from the cortex of ox lens has been fractionated on deae-cellulose in 7 m urea; peptide maps of the fractions are very similar to those from the corresponding fractions from α -crystallin.

albuminoid can be regarded as an insoluble α -crystallin. an undiluted ground lens is clear but becomes turbid on dilution. if albuminoid is present in the normal lens, it does not cause turbidity even when the cellular structure is disrupted. it is perhaps more likely that the albuminoid is formed on dilution of the lens mush.

the high concentration of proteins in the lens, especially in the nucleus, entails a high degree of order, which will be destroyed on dilution this phenomenon may well be connected with the precipitation of the albuminoid.

.I 512

.W

787. further autoradiographic studies of the lens epithelium.

normal and x-irradiated rat eyes

cell proliferation and migration in

the lens epithelium of normal and x-irradiated

rat eyes were studied by means of autoradiography after labelling with tritiated thymidine. cells of the normal lens epithelium require 16 hr. to pass from the beginning of the synthesizing period to the completion of mitosis. this interval is partitioned as follows: G_1 period, approximately 10 hr.; G_2 , slightly less than 5 hr; and mitosis, 72 min. following division, labelled daughter cells migrate from the germinative zone to the postequatorial rows, and by 2 weeks after tracer injection many radioactive nuclei are found in the lens bow. epithelial cells irradiated while in the dna synthesis phase undergo degeneration beginning approximately 8 hr. after exposure. the onset of cell death corresponds to the time at which these cells would normally be preparing for mitosis indicating that they die in abortive divisions. a small percentage of the originally labelled cells survived until 3 days after irradiation, but by 2 weeks this number fell almost to zero. the loss of radioactive cells occurred most rapidly in the equatorial zone.

.I 513

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2627. chicken lens development epithelial cell production and migration

in the earliest stages of chicken lens

development, cell division occurred over the

entire lens. cell division first stopped

in the posterior side of the lens vesicle, as

the cells differentiated into primary lens

fibers. after the annular pad developed,

cell division occurred, for the most part,

in the anterior surface epithelial cells.

shortly after hatching and thereafter, a

germinative zone, consisting of a narrow

band of epithelial cells adjacent to the

annular pad developed. the cells from the

germinative zone migrated slowly and

differentiated first into annular pad cells and

then into lens cortex fibers over an

estimated 2-year period. this slow migration

of cells in the lens is discussed in

relation to the failure of the adult chicken to de-

velop radiation cataracts.

.I 514

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1494. selenium content of fish flour in relation to kwashiorkor and dental

caries

the fact that fish flour was shown to be a rich source of

dietary selenium (169 p.p.m. may have important implications (i.e. deleterious

effect on teeth) in the treatment and prevention of protein malnutrition. it indicates that some disease syndromes in man may be a manifestation of selenium deficiency. it is recommended that the role played by selenium in protein malnutrition should be given serious consideration by research workers.

.I 515

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2192. selenium content of fresh eggs

during a study of effects of traces of se on dental caries the authors determined this element in eggs. whole egg contains appreciable amounts of se; this is found chiefly in the yolk (mean value 0.324 0.039 p.p.m.) with only 0.051 0.029 p.p.m. in the white.

.I 516

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1541. selenium content of human milk possible effect on dental caries selenium appears to be a factor capable of increasing susceptibility to dental caries in children and rats. in an area considered to be nonseleniferous, milk collected from 15 mothers (17-44 yr. old) of low socio-economic class had a mean selenium content of 0.021 p.p.m. (standard error 0.003).

.I 517

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1577. mode of action of selenium in relation to biological activity of tocopherols

dietary selenium at levels below 1 ppm has a partially beneficial effect upon nutritional muscular dystrophy but is ineffective or detrimental at higher levels. the role of selenium in improving the effectiveness of vitamin e is due at least in part to the fact that dietary selenium increases

the retention of the a-tocopherols, especially d-a-tocopherol. this has been shown by chemical determination of plasma tocopherols and also by tracing the activities of tritiated tocopherols and selenium⁷⁵ in serum and in various fractions of serum proteins in chicks receiving these nutrients alone and in combination. se⁷⁵ and h³-a-tocopherol activities followed each other very closely in the serum proteins. these studies indicated that vitamin e may be carried by a selenolipoprotein fraction associated with serum γ -globulin. thus, one biological role of selenium appears to lie in a selenium-containing compound which acts as a carrier of vitamin e and which may function in absorption, retention, prevention of destruction, and perhaps transfer across cell membranes of d-a-tocopherol, thereby enhancing its biological activity in the blood and perhaps in cells throughout the body.

.I 518

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3123. effect of sodium selenate on acute poisoning with thallium

experiments were performed on wistar rats weighing 150-200 g. thallium was administered s.c. in doses of 20 mg/kg and 30 mg/kg. sodium selenate was given per os in doses of 10 mg/kg 2 hr after poisoning and 5 mg/kg daily for the next 2 days. results indicate that sodium selenate protects the animals from death. it binds the thallium ions and increases their deposition in organs. comparison of the level of thallium in organs of treated rats shows that selenate increases in liver by 290.6%, in kidneys by 326.8% and in bones by 210.0%. no influence of selenate on excretion of thallium in the urine was found, but fecal excretion of thallium increased by an average of 45% of the treated animals.

.I 519

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2281. inhibition of active transport of sugars through rat intestine in vitro.

ii. action of mepacrine, atractyloside and selenite

it is shown that mepacrine, atractyloside and selenite, which had been regarded as inhibitors of intestinal absorption of glucose, are inhibitors of active transport of sugars in sacs of everted jejunum of rat (wilson and wiseman's method). mepacrine 5×10^{-3} m and 10^{-2} m inhibit, by 85% and 100% respectively, the active transport of galactose. with atractyloside 10^{-5} m and 10^{-3} m, the inhibitions were 77% and 100% and, with selenite 10^{-4} m and 10^{-3} m, about 70%. in general the inhibitors are effective within orders of magnitude which are similar in vivo and in vitro. atractyloside is rather more effective in vitro than in vivo, and mepacrine rather less. it is easier to achieve total inhibitions of the active transport of sugars in vitro than of intestinal absorption from isotonic solutions in vivo.

.I 520

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2284. analogs parasympathetic neuroeffectors. ii. comparative pharmacological studies of acetylcholine, its thio and seleno analogs, and their hydrolysis products

acetylthiocholine and acetylselenocholine exert acetylcholine-like effects on the guinea-pig ileum and frog rectus abdominis preparations. with the latter preparation, responses to acetylthiocholine and acetylselenocholine, in contrast to that to acetylcholine, are not enhanced by the addition of an anticholinesterase. this is attributable to the relatively high activity of the hydrolysis products, cholinethiol and cholineselenol; acetylthiocholine and acetylselenocholine undergo enzymatic hydrolysis at approximately the same rate as does acetylcholine. the hydrolysis products of acetylthiocholine and acetylselenocholine, which have effects on the guinea-pig ileum comparable

to those of the parent esters, are readily oxidized in air to the relatively inactive choline disulfide and choline diselenide, respectively. these observations are helpful in explaining many of the apparently contradictory statements in the literature regarding the actions of acetylthiocholine.

.I 521

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3604. cytotoxicity of organophosphorus compounds. comparative activities of trimethyl derivatives of thiophosphoric and selenophosphoric acids on vegetable (pisum root) and human (hela) cells

of the 4 compounds studied, the seleno compounds were more cytotoxic for hela cells than their thio analogues, whereas the activities on pisum root cells were equal. the parent phosphoric acid derivatives have a wider activity range on hela cells than the seleno and thio derivatives.

further studies are in progress.

.I 522

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3640. poisoning with sodium selenite

chronic poisoning with na selenite (in the drinking water) causes hepatic cirrhosis, usually of atrophic type, in rats. in rabbits there seems to be a definite diabetogenic action, while attempts to demonstrate such action in dogs have so far given inconclusive results. the difference between these 2 species is perhaps due to the technique used (different spacing of injections for practical reasons). the action of selenite on the pancreas is discussed and it is pointed out that se can replace s in sh groups, thus rendering the latter ineffective. both in effects on the liver and in those on the pancreas se seems to resemble alloxan.

.I 523

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2552. the tissue distribution of ^{75}Se -selenouracil and ^{75}Se -selenourea when selenium analogues of thiouracil and thiourea labelled with ^{75}Se were injected into rabbits, high radioactivity appeared in lung, liver and kidney. the animal's lungs could be visualised by photoscanning, but quality was poor, and neither compound is recommended for trial for lung or adrenal scanning in man.

.I 524

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1142. sodium selenate toxicosis pathology and pathogenesis of sodium selenate toxicosis in sheep
the pathogenesis of selenium toxicosis was studied in 30 ewes fed subtoxic to toxic levels of sodium selenate for 1 to 5 mth. seventeen of the 30 died of selenium toxicosis. the most severe and consistent pathologic changes were found in the myocardium and lungs. myocardial alterations were focal to diffuse degeneration, necrosis and early replacement fibrosis. pulmonary changes, consisting of edema and interstitial hemorrhages, were typical of the degenerative processes which characterize passive congestion of the lungs resulting from left ventricular insufficiency. atrophy of lymphoid centers in the spleen and lymph nodes was common. degenerative changes were occasionally found in liver, kidneys, and gastrointestinal tract.

.I 525

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1143. sodium selenate toxicosis the distribution of selenium within the body after prolonged feeding of toxic quantities of sodium selenate to sheep
the distribution of selenium in the body tissues of adult sheep fed subtoxic to toxic quantities of sodium selenate daily for 1 to 5 mth. varied with the

tissue

type and with the level and duration of selenium consumption. selenium concentration was highest in the liver, followed by (in descending order) the kidneys, lungs, spleen, myocardium, skeletal muscles, and brain.

.I 526

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1172. studies on selenium toxicity and chondroitin sulfate and taurine biosynthesis in the chick embryo

fourteen-day-old chick embryos were used in in vivo experiments. a toxic selenite treatment did not cause a reduction in the extent of sulfate-s incorporation into chondroitin sulfate or into taurine or a reduction in the observed tissue levels of these metabolites. rather, the taurine level was significantly greater with the embryos which received selenium. the extent of the incorporation of selenite-se into the metabolites was low or not significant.

.I 527

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843. reactions of seleno- and sulfoamino acids with hydroperoxides
reactions of methionine, cystine and their selenium analogues with hydrogen peroxide and organic peroxides have been studied. methionine reacts most rapidly with hydrogen peroxide but selenocystine causes the most decomposition; both react much more slowly with organic peroxides. the results suggest that selenocystine may act as a biological antioxidant.

.I 528

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2127. selenium toxicity in domestic animals

the article, with an extensive bibliography, is a compendium of available

information on selenium toxicity in domestic animals. literature reveals evidence of organically bound se being more biologically active, when given orally to domestic animals, than inorganic se salts. there is also variation in toxicity of organic se analogs. when exposed to ruminal digestion, there is considerable reduction of se salts to the relatively biologically inactive elemental se; which may result in fecal excretion of se, as such, to as much as 40% of a single oral dose. fluorine, molybdenum, chromium, vanadium, cadmium, zinc, cobalt, nickel and uranium increase se toxicity. arsenic and tungsten give some protection against it. bromobenzene, benzene, and naphthalene mobilize tissue se and stimulate its excretion. since se preparations designed for topical application in treatment of skin disease have been available for use in both man and dogs, the literature has reported cases of poisoning from misuse of such preparations. selenium, properly used, can be a valuable therapeutic agent, though certain salts of se must be regarded as potentially toxic. however, there is considerable latitude between therapeutic and/or nutritional and toxic doses of these salts.

.I 529

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1845. further studies on specific transplantation antigens in rous sarcoma of mice mice allografted with different sarcomas, induced by the schmidt-ruppin variant of rous sarcoma virus (rsv-sr), showed a resistance against subsequent isografting of 9 different rous sarcomas. transplantation resistance could also be induced by

rous mouse tumor cells x-irradiated with 8000 r
or with cell-free tumor extracts,
containing no demonstrable virus. no
transplantation resistance could be demon-
strated after allograft pretreatment with
various polyoma tumors or non-viral tu-
mors. allograft pretreatment with rous
tumors induced no demonstrable resistance
against isografting of polyoma tumors.
inoculation of rsv-sr or rous chicken sar-
coma suspension into adult mice gave
no clear cut resistance against isograft-
ing of mouse sarcomas. neither after
allografting of rous tumors nor after virus
or chicken sarcoma inoculation into adult
mice could virus-neutralizing activity be
demonstrated in the sera. the results
demonstrate the presence of common, speci-
fic transplantation antigen(s) in different
rous sarcomas in mice and speak against
an identity between the transplantation
antigen(s) and viral antigen(s).

.I 530

.W

1846. anaphylactic tests in model tumour antigen investigations
the efficacy of anaphylactic tests in detecting
'tumor' antigen in serum was investi-

gated. a simple model of a tumor-antigen study was carried out using rat tissue and rat serum, with bovine γ -globulin (byg) acting as a mock cancer antigen. it was found that if byg (absolute dosage 100 ug.) had formed $1/6$ of the antigen mixture used for sensitization it was readily detected when present in a concentration of 10^{-3} in the serum used for challenge, but not invariably detected in a concentration of 10^{-4} . if byg (absolute dosage 50 ug.) had formed approximately $1/50$ of the sensitizing mixture, it was infrequently detected even when present in the challenging serum in a concentration of 10^{-2} . it is concluded that anaphylactic tests used in this context do not have a very high sensitivity or discriminatory capacity.

.I 531

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1066. the effect of lymphoid cells from the lymph of specifically immunised sheep on the growth of primary sarcomata in rats
the growth of primary fibrosarcomata induced in rats with 3:4-benzpyrene was retarded by the injection of lymphocytes obtained from the efferent duct of a

lymph node in a sheep immunized with a piece of the tumor to be treated. the action of the heterologous lymphocytes was specific to the particular tumor used for immunization suggesting that reaction against tumor-specific antigens is involved. the cells responsible are believed to be medium-sized pyroninophilic lymphocytes which may stimulate the immune system of the host to react against the autochthonous tumor.

.I 532

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2570. treatment of canine neoplasms with autogenous vaccinal preparations
inbred mice with transplantable sarcoma
and carcinoma were treated with implants of their tumours which had been grown in strains of mice normally resistant to the tumours. complete regression of transplantable tumours was noted in 22% of the treated mice and 78% had life spans double that of untreated controls.
one dog with spontaneous scirrhus mammary carcinoma and another with lymphosarcoma were treated with implants of their own tumours after growth in cortisone-treated mice. regression of the spontaneous neoplasms followed in both cases. it is suggested that growth of a neoplasm in a foreign host alters the mole-

cular structure of the neoplasm, making it antigenic when returned to the original host. antigens produced are also effective against the original lesions.

.I 533

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744. studies on protein and nucleic acid metabolism in virus-infected mammalian cells. the formation of a virus-specific antigen in krebs ii ascites-tumour cells infected with encephalomyocarditis virus

krebs ii mouse ascites-tumor cells infected with encephalomyocarditis virus were found to contain, in addition to mature virus, a virus-specific protein antigen. an assay, based on the ability of this antigen to block the neutralization of purified virus by its specific antiserum, was developed. this antigen was present both in the culture fluid 17 hr. after the infection of cells with virus and intracellularly, where its titer increased at a time when viral capsid protein was being synthesized. within the cell, it was mostly localized in the soluble cell sap. in contrast with virus, the antigen did not agglutinate sheep erythrocytes, and its immunological properties were destroyed by digestion with trypsin. ribonucleic

acid was not detected in concentrated preparations of the antigen, nor was the titer of antigen affected by ribonuclease. the antigen had a sedimentation coefficient (20) of approx. 14s, and its diffusion coefficient, determined by the method of allison and humphrey (1960), was 3.2×10^{-7} sq. cm. sec.⁻¹. the particle weight of the antigen was hence 420,000 40,000. the capsid protein from purified encephalomyocarditis virus could be degraded by treatment with ethanolamine into a protein of sedimentation coefficient (20) of approx. 4s. the 14s antigen, when similarly treated, yielded a protein of similar size. however, no such smaller antigen was detected in virus-infected cells. it is concluded that the non-hemagglutinating antigen represents a polymeric form of the basic viral capsid-protein molecule and that it is synthesized in the cytoplasm of infected cells. it may be either an intermediate or a by-product in the process of viral capsid-protein synthesis.

.I 534

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1368. immunologic competence and induction of neoplasms by

polyoma virus

thymectomy at 3 days of age in several inbred strains of mice and in an f1 hybrid resulted in a strikingly increased frequency of neoplasms following infection with polyoma virus. age susceptibility was extended to at least 30 days of age in highly resistant c57bl mice. the usual stigmata associated with thymectomy at birth were not found in the 3-day thymectomized mice. nonetheless the methods used to restore immunologically deficient thymectomized neonates were also effective in restoring the capacity to resist polyoma virus tumor induction: adult syngeneic spleen cells, thymus tissue in millipore diffusion chambers and syngeneic thymus grafts. growth curves of polyoma virus in kidney, salivary glands and liver were quite similar in thymectomized and intact litter mates. hemagglutination-inhibition antibodies determined periodically up to 30 days after infection were also similar in both groups. these results are discussed in terms of a concept involving virus-specific 'tumor' antigens and the immunologic status of the animal.

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1848. antigen analysis of sera from patients with malignant tumors by immunodiffusion methods immunoelectrophoresis and ouchterlony's method were used for the antigen analysis of sera from 320 cancer patients; 250 normal or non-tumorous cases served as controls. immunoelectrophoresis showed abnormal precipitin lines which could not be demonstrated in normal sera. most of the abnormal antigens were demonstrated in the α_2 - and β_1 -globulin fractions. the distribution of these antigens differed in individual cases and was not related to the histopathological classification and site of the tumors. however, these antigens increased in parallel with growth of the tumors and disappeared or markedly decreased after surgical removal of the tumor tissue. almost all sera of patients with myeloma, leukemia, and malignant lymphoma formed one characteristic line in the β_2 -globulin region and they could be differentiated from the patterns in cases of carcinoma.

.I 536

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2354. isoantigenic properties of tumors transgressing histocompatibility

barriers of the h-2 system

sublines capable of transgressing h-2 histocompatibility

barriers have been derived

from strictly strain-specific tumors by 1) passage

through newborn hosts of a

foreign genotype; 2) passage through adult h-2

incompatible recipients pretreated

with isoantisera directed against the tumor cells.

the nonspecific character induced

by these procedures was usually expressed in a

number of different h-2 incompati-

ble recipients. the changes responsible for

the conversion to nonspecific growth

appeared to proceed in a stepwise fashion.

expression of the nonspecific character

required exposure to the foreign host environment

for more than 30 days. at this

stage and during the subsequent 3 transfer

generations, reversion to strain-specific

growth occurred on back-transfer to the

strain of origin; after 4 passages in the

foreign hosts the nonspecific character was

permanently established, however, and

could not be reverted by prolonged passage

in the original host genotype. the

growth rate of strain-specific tumors and

their nonspecific sublines was compared

in the strain of origin. no difference was found with one tumor, while the strain-specific line grew better than the nonspecific sublines with another. this difference was detected in the homozygous strain of origin and in different semi-isologous f1 hybrids. all lines grew better in the homozygous strain than in the f1 hybrids, however. a comparison was made between the concentration of h-2 isoantigenic surface determinants in strain-specific tumors and their nonspecific sublines by a quantitative absorption technique in vitro. all nonspecific sublines had a lower concentration of h-2 isoantigens than the strain-specific tumors. this suggests that nonspecific tumors develop as a result of immunoselection of variants resistant to the homograft reaction and are characterized by a lowered concentration of h-2 antigens.

.I 537

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2371. participation of 7s and 19s antibodies in enhancement and resistance to methylcholanthrene-induced tumours
serum factors responsible for enhancement
and resistance to methylcholanthrene-

induced tumors in a syngeneic system in mice were studied. they were found to be part of the serum immunoglobulin system. the active components of specific anti-tumor serum were always contained in the 7s (γ-2) and 19s (γ-1m) fraction, while no activity was detected in the 4s fraction. in sera which in the given dose enhanced growth of the tumor graft, enhancing activity was present in both the 7s and 19s fraction of the serum and was higher in the former. in sera which in the given dose influenced the interaction of the organism with the tumor by producing resistance to the tumor graft, both fractions were again active, the activity of fraction 19s being higher than that of fraction 7s.

.I 538

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2372. the effect of immunity against sex-antigen on a tumour graft containing sex-antigen
the tumor bp 1 induced by benzpyrene in c57bl male mice contains sex-antigen.
sex-antigen is not lost during growth of tumor
against immunity directed against
this antigen. the tumor, however, becomes
more resistant to immunity and the

content of sex-antigen is decreased.

.I 539

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2373. factors influencing the induction of enhancement and resistance to methylcholanthrene-induced tumours in a syngeneic system

active immunological enhancement of the growth of methylcholanthrene-induced tumors was demonstrated in a syngeneic system in mice. enhancement was detected 3-5 wk. after preimmunization with irradiated tumor suspension and was succeeded after the 6th wk. by the development of resistance to the tumor. analysis by means of adoptive and passive transfer showed these to be true immunological phenomena. enhancement and resistance were transferred by serum and by the lymph node cells of preimmunized mice. threshold doses of tumor cells were found to be the most satisfactory for the detection of resistance and enhancement in this system.

.I 540

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5512. antigenic properties of human tumours
preliminary studies on the antigenic properties of human tumours have been

carried out using heterologous antisera, prepared in rabbits, against a number of different cancerous and normal tissues. after repeated absorptions, antisera were obtained which reacted only with tissue antigens. some antisera, after absorption with normal tissues, reacted only with tumours. seventy-two tumour and 31 normal tissue extracts were studied by means of the ouchterlony agar gel double diffusion technique. the results showed the presence of an antigen or antigens in some human malignant tumours which were not detectable in normal tissues, in foetal tissues, or in hela cells. in addition, there was some loss of normal tissue antigens from tumours. attempts are being made to isolate and characterize these tumour and normal tissue antigens.

.I 541

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5514. the incorporation of sv40 genetic material into adenovirus 7 as measured by intranuclear synthesis of sv40 tumor antigen the I.I. strain of adenovirus 7, free of detectable infectious sv40 virus, induced sv40 tumour antigen, demonstrable by

fluorescent antibody staining, in green monkey kidney, rabbit kidney, hamster embryo and human embryo kidney cell cultures.

in green monkey and human cell cultures there was a cytopathic effect and more cells contained the sv40 tumour antigen than in the other types of culture.

adenovirus 7 viral antiserum neutralized the sv40 tumour antigen inducing ability of the I.I. strain virus but anti-sv40 monkey serum and serum from sv40 tumour bearing hamsters did not. an adenovirus 7 preparation propagated exclusively in human tissue did not induce the sv40 tumour antigen. the sv40 tumour antigen was entirely localised within the cell nuclei and appeared to be transmitted to daughter cells during mitosis.

.I 542

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264. fluorescent antibodies to human cancer-specific dna and nuclear proteins

specific antigens have been demonstrated in certain cancers. in this study they were obtained from an adenocarcinoma of the colon and an ewing's sarcoma. homogenates were prepared and male rabbits were

immunized. the animals were bled to death 10 days after the last injection. testing included fluorescent antibody methods and agar-gel horizontal double-diffusion precipitin test. the pattern of reaction of these antibodies against various cancers seems to be dependent upon the source of the cancerous dna-bound proteins and the salt concentration used in their isolation. human cancer-specific cross nuclear antigens seem to be cross reacting rather than identical in structure. the cancer-specific antibodies could be removed only with absorption of the immune globulins with cancerous tissues. salt-soluble human dna-bound proteins from an adenocarcinoma of the colon and an ewing's sarcoma induced the formation of cancer specific antibodies which showed positive fta reactions (to a maximum titer of 1/128) against 95% of the cancerous tissues studied. these cancer-specific antibodies gave similar fta reactions with cell nuclei of normal appearing liver parenchyma adjacent to metastatic carcinoma of colon, normal appearing colon near to metastatic carcinoma of the colon, normal appearing

colon near to carcinoma of the colon,
and a long-standing case of chronic ulcerative
colitis. evidence is shown that this finding
possibly may represent a serological
detection of an early or latent cancerous
change in morphologically normal cells.
these cancer-specific antigens have been
identified as rounded, intranuclear dna-
bodies and nuclear proteins which can be
specifically destroyed by dnase trypsin.

.I 543

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266. immunology of the cancer cell: tumour-specific antigens
after a broad historical survey of immunological
studies of cancer, a review is given
of the evidence showing that antigens present in
normal cells are missing from the
malignant cells that arise from the same tissue.
this evidence is considered in con-
junction with the deletion hypothesis of carcinogenesis,
and the author emphasizes,
that in his view, the key event in carcinogenesis
is enzymatic deletion. antigenic
gain and intensification in the course of spontaneous,
chemical, and viral carcino-
genesis is reviewed, together with experiments
demonstrating the existence of

tumour-specific antigens. the question is then posed: if tumours have specific antigens, why is evidence for their rejection so scanty? the occasional spontaneous regression points to host resistance but its rarity suggests that tolerance generally develops. consideration is given to the application of immunological methods to therapy and although current achievement in this field is limited, new immunological stratagems might yet transform the picture. finally a plea is made for the integration of the disciplines of immunology and cellular differentiation. the prospect is raised that through a synthetic and holistic approach we might discover the susceptibility of the cancer cell to re-differentiation and re-recognition.

.I 544

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effets de la carence potassique

chez le rat sur le squelette,

le cholestérol plasmatique

l'histologie des surrénales

r. habib, j. lefebvre et p. royer

potassium deficiency in the male rat at the time of weaning,

provokes an increase in the weight of the suprarenals, an

atrophy of the glomerular zone and a lipoid hypertrophy of the fasciculae.

it causes a rise in the level of the blood cholesterol. it reduces the phosphate level in the blood and increases the phosphate in the urine.

the blood calcium level is not altered but a hypocalciuria is noted.

it leads to a severe osteopathy which has been investigated by radiography, microradiography and histological and biochemical study of the skeleton. the following are the characteristics : arrest of osseous growth, delay of maturation, arrest of chondrogenesis, formation of dense metaphyseal lines or lines of arrest, osteoporosis.

these facts are discussed and compared to the analogous changes found in the syndrome of chronic idiopathic hypokalaemia with hyperkaluria in the infant.

.I 545

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vergleichende renale phosphateclearance-untersuchungen beim hyperparathyreoidismus und beim sog. phosphatdiabetes the analysis of the function of the kidneys give a contribution to the pathophysiology of two different diseases of general osteopathies whose pathogenesis or etiology are still not clear in some points. the phosphate clearance pre- and postoperative in one patient with hyperparathyroidism showed that after the removal of the adenoma of the parathyroid the renal reabsorption of phosphate improved only temporary as a secondary form of hyperparathyroidism was already present.

in a patient with a "phosphatdiabetes" the clearance examination showed that under a high dosage of vitamin d the reabsorption of phosphate did not increase. based on these results we have not continued therapy with vitamin d which is certainly not indifferent. comparative renal clearance examinations were carried out in 10 patients which did not show any disturbances of calcium/phosphate-metabolism.

.I 546

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the unreliability of the titan yellow method for the determination of magnesium in patients receiving intravenous calcium gluconate gluconate was found to interfere with the determination of magnesium by the titan yellow method. with this method, false low results were found in the serum and urine of patients receiving intravenous calcium gluconate. the interference can be prevented by ashing of the specimen.

.I 547

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absorption and excretion of toxogonin, an alkyl-phosphate antidote, after intramuscular injection in man tolerance, absorption and urinary excretion studies of toxogonin (bis-(4-hydroxyiminomethyl-pyridine-1-methyl) ether dichloride), a specific antidote in poisoning by esterase-blocking organic phosphates, were made on 11 men by intramuscular injection of 250 mg. (ca. 3 mg./kg.) of the drug, given by self-injection ampoules. injections made

with the automatic ampoule autule caused no local irritation. certain facial symptoms reported can for the time being be regarded as resorptive side-effects of toxogonin. maximum blood levels of 6 ug./ml. were recorded within 20 minutes. even after four hours the level was still 1-2 ug./ml., a concentration amply sufficient to ensure reactivation of blood esterases. of the injected dose, 52% was excreted in the urine after two hours, 87% after eight hours. toxogonin appears to pass through the body unchanged.

.I 548

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the study of osteoporosis and osteomalacia radiological evidence strongly suggests that osteoporosis (with the possible exception of acute immobilization osteoporosis) may be an irreversible condition. the changes therefore to be expected in calcium balance when an osteoporotic is treated are small compared with those often seen in osteomalacia. methods of obtaining more accurate calcium balances are needed to show these small changes, especially when a high calcium intake is used. the method of continuous marking of stools with chromium sesquioxide seems to provide just such a method. using this

method, it has so far proved impossible to obtain prolonged large positive calcium balances in osteoporosis on either high calcium intake, anabolic hormones, or sodium fluoride. two alternative therapies to vitamin d have been explored for use in vitamin d-resistant osteomalacia. atp has been found to be ineffective. intravenous phosphate alone has been ineffective in producing positive calcium balances, but is effective as a complement to vitamin d under certain conditions.

.I 549

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the aetiology and treatment of urinary calculus investigations in this laboratory have been based on the hypothesis that calculus formation is primarily a process of crystallization from super-saturated solutions rather than one of adsorption on a specific protein matrix, as has been postulated by boyce and his colleagues (boyce and king, 1963). that crystallization is the primary factor is strongly suggested by the recent studies of vermeulen, lyon and gill (1964). these authors produced artificial concretions which closely resembled urinary calculi by immersing a rotating wire loop in normal urine for several days and

slowly adding the appropriate stone-forming elements.

if the above hypothesis is correct then the factors of primary interest in urinary stone formation are those responsible for supersaturation, nucleation and crystal poisoning. much remains to be learnt about these various factors, their inter-relationships, and their relative importance.

the significance of the urinary colloids (proteins, muco-proteins and polysaccharides) in calculus formation is still not clear but it is probable that they play an important secondary role in binding crystalline precipitates to form a non-friable calculus. since time is an important factor in crystal growth such non-specific binding by proteins would increase the chances of stone growth and retention within the upper urinary tract.

.I 550

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control of idiopathic hypercalciuria

the paper discusses the causes of hypercalciuria and describes 15 cases of different origins all of which presented similarly with renal stones. the diagnosis of idiopathic hypercalciuria was made by exclusion. the effects of dietary restriction of calcium, sodium bicarbonate, cortisone, sodium phosphate, sodium phytate, and cellulose phosphate were demonstrated by

calcium and phosphorus balance techniques. all were shown to have some urinary-calcium-lowering effect. finally, a chlorothiazide derivative--namely, bendrofluazide--was also demonstrated to have a hypocalciuric effect, and the mode of action is discussed.

.I 551

.W

effects of parathyroid hormone and other proteins in vitro on mitochondrial metabolism

it is apparent that in addition to parathyroid hormone, several non-hormonal basic proteins stimulate mitochondrial respiration, ion transport, and atpase, but inhibit the 32pi -atp exchange reaction. thus these effects may not be so uniquely a measure of the biological actions of parathyroid hormone as the previous reports suggested. rasmussen et al. (1964) have also isolated from parathyroid extracts a protein that is inert in vivo but stimulates mitochondrial transport of phosphate in vitro. they postulated that this protein might be yet another biologically important factor produced by parathyroid glands. the latter speculation may not be warranted in view of the uncertain specificity of protein effects on mitochondria. all of our tests completed to date show that the non-hormonal parathyroid proteins c1 and c2 are unrelated either biologically, immunologically, or chemically (by amino-acid analysis) to the parathyroid hormone. further rigorous studies are necessary to precisely determine whether any effects of parathyroid hormone on mitochondria validly reflect the mechanism of action of the hormone and whether it is sound to use the in vitro tests as bioassay tools.

.I 552

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the treatment of phosphatic encrusted cystitis

(alkaline cystitis) with nalidixic acid.

phosphatic encrusted cystitis is caused by

persistent infection by *b. proteus* or *ps. pyocyaneus*

associated with an alkaline urine. its incidence

may be increasing and may follow megavoltage

therapy of a bladder tumour. its incidence in

post-radiation cases is 2 per cent.

mandelamine often fails to relieve this

condition. in this series of ten patients who had

failed to respond to mandelamine, eight

responded to treatment with nalidixic acid. no side

effect of treatment was noted in the series.

nalidixic acid is of value in the treatment of *b. proteus*

infections of the urinary tract, and is the drug

of choice in the treatment of phosphatic encrusted

cystitis.

.I 553

.W

role of the liver in the glycoprotein mobilizing property of

parathyroid extract

studies were carried out to de-

termine the action of hepatectomy on the

glycoprotein action of pte as well as on

pte-induced renal calcification and deposi-

tion of glycoprotein. our data showed that in hepatectomized rats, pte no longer caused an elevation in serum glycoproteins. however, hepatectomy did not alter the formation of glycoprotein tubular casts produced by pte administration. the data suggest that the liver is the major source of the elevated serum glycoproteins found in rats receiving pte. in addition, it is possible that pte may have a direct stimulating action on biosynthesis of glycoprotein by the kidney.

.I 554

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distribution and excretion of radioactivity after parenteral administration of radioactive polydiethylstilbestrol phosphate to rats and a cow.

polydiethylstilbestrol phosphate (psp), a water soluble polyester of phosphoric acid and diethylstilbestrol, was injected in rats and a cow and the distribution and excretion of radioactivity were followed in both species. after a subcutaneous or intramuscular injection the bulk of the radioactivity was accumulated at the site of injection. the disappearance of radioactivity from this depot was very slow. as late as 90 days after the injection into rats, 20% of the

administered radioactivity was still accumulated at the site of injection. the liver was very effective in removing labeled material from circulating blood. twenty-four hours after intravenous injection in rats, about 50% of the radioactivity was recovered from this organ. the distribution of radioactivity in the cow indicated that the polymer was preferably accumulated in organs containing reticuloendothelial cells.

.I 555

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study of phosphate excretion by the stop-flow technique

m. de myttenaere

the stop-flow technique has been applied to the dog in an attempt to rule out tubular secretion of phosphate and to locate the site of action of parathyroid hormone (p.t.h.) on the renal tubule. under the experimental conditions used, no significant inward transtubular movement of p32 could be demonstrated, ruling out tubular secretion of phosphate. stop-flow experiments performed in parathyroidectomized dogs before and after p.t.h. administration demonstrated inhibition of phosphorus reabsorption by the hormone. in addition, the stop-flow pattern indicated that this phenomenon took place mainly in the distal part of the proximal tubules.

.I 556

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stupor, hypercalcemia and carcinoma of the

renal pelvis

since albright suggested that some tumors

"might be producing parathyroid hormone," hy-

percalcemia associated with malignant tumors with-

out bony metastases has been recorded with increas-

ing frequency. transitional-cell carcinoma of the

renal pelvis is here added to the list of neoplasms

that hypercalcemia may accompany.

.I 557

.W

anodized aluminium grains labelled with radiophosphorus

for medical purposes

g. b. fasolo, r. malvano, u. rosa and e. zimmer

interstitial b-therapy, by implantation in tissues of

radioactive sources, is widely applied to the treatment

of certain forms of human malignancies. among the

radio-elements proposed for this therapeutic technique,

yttrium-90 and gold-198 are the most generally used.

radiophosphorus (^{32}P) shows some attractive features

because of its suitable half-life (14.3 days) and its rather

high-energy b-emission (maximum energy 1.71 mev);

but the use of this radionuclide is limited by the diffi-

culties found in the preparation of safe solid sources. the

only techniques we have found in the literature are those

reported by riechert and munding and by rames and

moravek, who used respectively small plastic capsules

filled with phosphomolybdic acid solution, and $\text{Ca}(\text{PO}_4)_2$,

grains, labelled with phosphorus-32. these methods require a delicate preparative work, and, moreover, a large b-self-absorption effect can be expected in both cases.

a new simple method for the preparation of grains labelled with phosphorus-32 basically consists in adsorbing labelled PO_4^{3-} ions on an active aluminium oxide film produced by anodic oxidation of aluminium wire. the adsorption capacity of the oxide film for PO_3^{3-} ions is quite high, but the process is reversible: the phosphorus-32 activity is partially desorbed, even after 'sealing' in boiling water, when the labelled wire is kept in isotonic sodium chloride solution.

.I 558

.W

effect of parathyroidectomy and ferric dextrin upon calciphyllactic sensitization by uremia experiments on the rat indicate that calciphyllactic sensitization can be achieved by bilateral nephrectomy. intravenous administration of a ferric dextrin preparation (fe-din) induces selective calcification in the buccal mucosa, esophagus, trachea and mediastinum of the nephrectomized rat although it produces no such changes in intact control animals. conversely, fe-din prevents the cardiovascular calcification normally elicited by nephrectomy. parathy-

roidectomy protects the nephrectomized rat against the fe-din-induced calciphylaxis. hence, it may be concluded that: 1) autologous parathyroid hormone, in amounts secreted by the glands, can act as a calciphylactic sensitizer and 2) fe-din is highly effective in protecting the cardiovascular system against uremic damage.

.I 559

.W

mediastinal parathyroid adenoma

a case of hyperparathyroidism with hypercalcemic crisis is presented. the tumor was a well differentiated and encapsulated parathyroid adenoma, unusually located in the anterior mediastinum, lying both within and without the pericardial sac. the surgical approach was directly through the sternum with a mediastinal exploration. the postoperative course was uneventful and gratifying, with complete correction of both symptoms and abnormal laboratory findings.

.I 560

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clinical experience with

primary hyperparathyroidism:

evaluation of treatment

forty-four patients with "operatively proven" hyperparathyroidism were evaluated to decide 1) whether or not the diagnosis could be substantiated by some postoperative observations other than the gross anatomic diagnosis of the operative specimen and 2) what the long term value of operative treatment would be. it was found that an immediate and significant fall

in urinary phosphorus excretion best documented the diagnosis of primary hyperparathyroidism. over intervals up to 10 years, follow-up of the patients suggested a favourable response of the disease to operative treatment.

.I 561

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the dilution test as a measure of renal function in niobium-poisoned rats control, female, albino rats given a water load of 50 ml/kg, excreted 50 per cent of this load as urine within 94 ± 11 minutes (teu50).

the administration of a single intraperitoneal dose ranging from 10 to 30 mg nb/kg resulted in 2- to 4-fold increases in the teu50 value 24 hours after the niobium was injected.

when niobium was complexed with ascorbic acid prior to injection the teu50 value was within control limits. however, rats given a single intraperitoneal dose of niobium and then given 3 doses of ascorbic acid at intervals of 1, 3, and 6 hours showed teu50 values that were not markedly different from those observed in rats given niobium only.

increased teu50 values were observed in rats given single intraperitoneal doses of uranyl nitrate (1.2-2.4 mg u/kg), mercuric chloride (2.0 mg hg/kg) and sodium tripolyphosphate (480 mg/kg).

.I 562

.W

influence of parathyroid activity on ion exchange in various tissues

1. balance data from three patients with hypoparathyroidism, who were given parathyroid extract, are presented. the metabolic response was complex. the data demonstrate losses of phosphate, magnesium, sodium

and potassium which were not accounted for by destruction of either bone or non-osseous tissues. preferential depletion of these minerals from bone, or loss from non-osseous tissues, must be presumed.

2. the exchange of ^{45}Ca , ^{28}Mg , and ^{32}P in a spectrum of rat tissues has been studied in sham operated, parathyroidectomized, and parathyroid extract treated rats. the effects of parathyroidectomy on the development of magnesium deficiency were determined.

3. four hours after parathyroidectomy, increased transport of calcium into bone, kidney, intestine, liver, brain, and muscle was found. six days after parathyroidectomy equilibrium had been reestablished and exchange rates were identical to those in sham operated animals.

4. the administration of parathyroid extract was associated with decreased transport of ^{45}Ca , ^{28}Mg , and ^{32}P into bone. ^{45}Ca exchange in kidney was reduced but in all other tissues exchange of ^{45}Ca and ^{28}Mg was increased. ^{32}P exchange in both intestine and kidney was markedly increased in animals receiving the extract.

5. parathyroidectomy greatly minimized the manifestations of magnesium deficiency in young rats on magnesium deficient diets.

6. the results suggest that parathyroid hormone may affect the transport and exchange of calcium, magnesium, and phosphate (and perhaps sodium and potassium) in tissues other than those usually considered to be target organs.

.I 563

.W

effects of alkalosis on plasma concentration and urinary excretion of inorganic phosphate in man
acute respiratory and metabolic alkalosis have

been shown to depress plasma phosphorus concentration in normal man. the fall in plasma phosphorus concentration is greater in respiratory than in comparable levels of extracellular metabolic alkalosis. this fall is not attributable to increased renal excretion or to migration into red blood cells. the evaluation of low serum phosphorus concentrations should always be carried out with a knowledge of the pH and total CO₂ content of the plasma.

.I 564

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the relationship between vitamin D and parathyroid hormone

marit von Stedingk

the effect of parathyroidectomy and parathyroid hormone administration upon the concentrations of plasma calcium and phosphate have been measured in vitamin D-deficient rats and the results compared to those observed in D-fed animals. also, the influence of dietary calcium and phosphate content upon these responses has been investigated. parathyroidectomy in the D-fed animal results in a rapid fall in plasma calcium and a biphasic plasma phosphate response with an initial fall followed by a striking rise. in contrast, parathyroidectomy in the D-deficient rat is fol-

lowed by no significant change in plasma calcium and an immediate rise in plasma phosphate that can be prevented by the administration of parathyroid hormone. dietary phosphate restriction abolished the effect of parathyroidectomy in both groups of animals.

administration of a dose of 500 u of hormone to the intact d-deficient rat had little influence upon plasma calcium; a dose of 2,000 u did increase plasma calcium. a dose of 25 u was sufficient to increase the plasma calcium of the d-fed animal. these results are discussed in relation to the effects of vitamin d and parathyroid hormone upon mitochondrial metabolism.

.I 565

.W

decrease in serum and urinary phosphorus in man in the course of pyrotherapy during the fever peak occurring a few hours after the injection, urinary phosphorus (up) disappears entirely. this fact cannot be accounted for by the parallel decrease in gfr, because serum phosphorus level (sp) does not increase (as it would be expected to, should retention occur) but on the contrary, it, too, declines to a

marked degree.

the possibility that changes in sp and up could have been brought about by an increased utilization of glucose was also considered. an intravenous glucose tolerance test (method of macho and licko (8)) was carried out in another group of patients on control days and on days of pyrotherapy five hours after the pyrogen administration. an increase in the rate of "glucose utilization" was observed (table 2). however a different opinion is found in the literature. in the course of glucose tolerance tests, conn (3) and comparini (9) observed a lowered rate of glucose utilization in febrile subjects. malizia (10) found an accentuated rate of decline of serum phosphorus during glucose tolerance tests in subjects with high temperatures, but the glycemic responses did not differ from those obtained when controls without fever were subjected to the same tests. whether it be for utilization purposes or not, the fact remains that a massive transfer of phosphorus from the serum into the tissues takes place in fever.

.I 566

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relationship of maximal tubular phosphate

reabsorption to filtration rate in the dog

a maximal renal tubular rate of reabsorption of phos-

phate (tmp) has been demonstrated in the normal dog. in

the dog, as in the man, considerable variability in the tmp

often occurs. while some of this variability remains unex-

plained, a direct relationship between glomerular filtration

rate (gfr) and tmp can be demonstrated when the gfr is

varied over a wide range. this relationship suggests that

glomerular intermittency may exist in the dog.

.I 567

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human growth hormone

clinical measurement, response to hypoglycemia and suppression by

corticosteroids

a standard test of growth-hormone secretory ca-

capacity, based on radioimmunoassay of plasma growth

hormone after insulin hypoglycemia, is described. in

normal subjects a standard insulin tolerance test, caus-

ing an average blood glucose drop to 34 per cent of

resting values, produced a mean rise in growth hor-

mone to 45.2 millimicrogm. per milliliter at one hour,

with a total range of 25 to 70 millimicrogm. per mil-

liliter. no response was observed in 5 hypopituitary

subjects.

under comparable hypoglycemic stimulation glucocorticoid-treated patients showed a marked inhibition of the growth-hormone response, which was related to dose. subjects receiving more than 60 mg. of cortisol equivalent per day showed a mean plasma rise to 6.7 millimicrogm. per milliliter (range, 1.5 to 13 millimicrogm.). subjects receiving 20 to 60 mg. of cortisol equivalent per day showed a mean rise to 16.6 millimicrogm. per milliliter (range, 13 to 20 millimicrogm.).

inhibition of human growth hormone was also affected by duration of glucocorticoid treatment, being greater with long-term than with short-term administration.

.I 568

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obesity and plasma levels of insulin and growth hormone

studies of serum levels of glucose, free fatty acids, insulin, and growth hormone during prolonged fasting suggest that insulin and growth hormone are not responsible for certain metabolic abnormalities accompanying obesity.

.I 569

.W

hypophysectomy, replacement therapy, and the tolerance of the euryhaline killifish, *Fundulus heteroclitus*, to hypotonic media hypophysectomized *Fundulus heteroclitus*, as previously reported, survive only a few days after transfer from salt to fresh water. survival time is the same

when fish are tested 2 weeks or 2 months after hypophysectomy. gradual dilution of the external medium produces failure at an average salinity of 0.26‰ (0.67-0.02‰). this salinity is comparable to that causing failure after abrupt transfer. although failure is associated with hypochloremia, daily injections of a balanced salt solution or 0.6% nacl shorten survival.

daily injections of teleostean neurohypophysial peptides, arginine vasotocin (2.25 and 0.0225 pressor μ g per gram) and isotocin (1.32 and 0.026 oxytocic μ g per gram) do not prolong survival. an extract of caudal neurosecretory tissue (urophysis) from male tilapia mossambica had no beneficial action at doses of 50 μ g per gram every other day. purified ovine prolactin. 105 μ g per gram on alternate days, maintained survival of 10 of 11 fish for the duration of the 28-day test period in fresh water, irrespective of the period of pretreatment in salt water. purified bovine prolactin prolonged survival and 2 of 6 fish were maintained for 28 days. purified bovine growth hormone was ineffective. monkey growth hormone containing 2 u per milligram of prolactin activity, administered at a dose of 20 μ g per gram (equivalent to 40 μ g per gram prolactin activity), prolonged survival. human growth hormone containing 4 u per milligram of prolactin activity, at a dose of 20 μ g per gram (equivalent to 80 μ g per gram prolactin activity) also prolonged survival and 4 of 6 fish were maintained for 28 days.

the ability of pituitary preparations to protect hypophysectomized f. heteroclitus from failure in fresh water appears to be related to their prolactin activity and not to their content of neurohypophysial peptides.

this suggests that an adenohypophysial hormone resembling mammalian prolactin is essential for survival of this fish in hypotonic external media. carp pituitary preparations do not protect hypophysectomized f. heteroclitus although f. heteroclitus pituitaries are known to be effective.

.I 570

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resistance to human growth hormone in pituitary dwarfism:

clinical and immunologic studies

thirteen pituitary dwarfs have

been treated with human growth hormone

(hgh), and growth acceleration with doses of

5-7 mg/week has been observed in all but one

patient. on therapy, this 7 1/2-year-old girl grew

at a rate of 1.05 cm/month for 7 months.

thereafter, despite larger doses of growth

hormone (15 mg/week), growth rate fell to

0.27 cm/month. this rate of growth persisted

after stopping hgh. on retreatment on 2

occasions, acceleration of growth did not

occur. antibodies to hgh, absent in her

serum before treatment, were repeatedly

demonstrated in her serum in high concentra-

tion (hgh binding capacity up to 100 mg/1)

during treatment. comparable titers of anti-

body have not been found in any of the 12

other patients receiving long-term hgh treat-

ment. the specificity of the human anti-hgh

serum differed from rabbit anti-hgh serum.

whereas both monkey growth hormone

(mgh) and hgh were effective inhibitors of

the binding of hgh-131i by rabbit antiserum,

only hgh was an effective inhibitor with human antiserum. in like manner, a crude placental extract which was an effective inhibitor for rabbit antiserum was ineffective with human anti-hgh serum.

.I 571

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influence of alloxan diabetes on growth hormone content of the rat hypophysis

homogenates of adenohypophyseal tissue obtained from alloxan-injected adult male rats varying in duration and severity of diabetes, as well as from diabetic rats maintained on an insulin replacement regimen, were assayed in immature hypophysectomized female rats. the ability of these crude hypophyseal extracts to encourage tibial cartilage width expansion gain in body weight, and to depress hematocrit and blood area levels was determined. significant decrements in ability to increase epiphyseal cartilage width and ability to depress hematocrits were noted 14 to 28 days following injection of alloxan. increasing the intensity of the diabetic state was associated with decreased growth-promoting potency of hypophyseal preparations as well as with decreased ability to influence the hematological indices. hypophyseal extracts taken from insulin-treated diabetic rats contained more growth hormone than equivalent amounts of tissue obtained from control rats. it is concluded that the adenohypophyses of

diabetic rats contain diminished amounts of growth hormone and the insulin repairs or encourages greater than normal accumulation of somatotrophin in these animals.

.I 572

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pheochromocytoma

without hypertension

the patient developed symptoms of pheochromocytoma about 15 years after the diagnosis of eosinophilic adenoma of the pituitary gland. the predominating symptoms were profuse sweating and tachycardia. hypertension, hyperglycemia, and glycosuria were absent. the relation of the quantity and the relative composition of catecholamines to the symptomatology is discussed. some speculation regarding the etiological importance of hypersecretion of growth hormone in pheochromocytoma seems to be in order.

.I 573

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hypoglycemia, growth retardation, and probable

isolated growth hormone deficiency in a

1-year-old child

a heretofore unreported association of defects, namely hypoglycemia, growth retardation, and deficiency of serum growth hormonelike activity in a 1-year-old child is described. human growth hormone (hgh), 3 mg. a day for 7 days, doubled the fasting blood sugar, prevented the postprandial hypoglycemia,

and reversed the sensitivity to tolbutamide and leucine. treatment with 1 mg. of hgh 3 times a week produced a growth of 7 inches in 3 months compared to a growth of 1 inch in the previous 13 months. since the protein-bound-iodine and the response to methopirapone were normal and the blood level of growth hormone was low, this case is presented as a probable isolated growth hormone deficiency.

.I 574

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production, secretion, and availability
of insulin

a more precise understanding of the metabolic phase of diabetes mellitus requires reliable information concerning the synthesis, manner of release and transport of insulin, as well as of the behavior of agents which interfere with the actions of the hormone by inhibition or destruction. we shall deal with a variety of these problems here and it might be helpful at the outset to outline first our present understanding of the chemical structure of insulin since many useful hints flow out of a consideration of the nature of the molecule.

.I 575

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growth and growth retardation

various attempts have been made over the years to define growth. from the standpoint of this review, growth is the physiological accretion of new tissue which is reflected in the acquisition of protein and water. this process in almost all instances leads to increase in size (length, weight, and volume) and actively progresses from the fertilization of the ovum to the period of sexual maturity where millions of cells are present in a state of advanced organization. with further time, growth is less and, indeed, may

become negative insofar as cells are lost.

.I 576

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long-term treatment of hypopituitary and of
achondroplastic dwarfism with human
growth hormone

we have treated an 8 year old hypopi-
tuitary dwarf intermittently with hgh
(wilhelmi) for 4 years. with 1 mg. 3
times a week the monthly growth rate
was 1/4 inch. as treatment continued he
became resistant. increasing the dosage
to 3 mg. 3 times a week at the age of 12
induced a monthly growth rate of 2/5
inch. this growth-promoting effect is at
least as great as that reported for the
li and raben preparations. we have
also treated a 15 year old severely de-
formed 'achondroplastic' dwarf for a
year. with 3 mg. 3 times a week he
grew 1/2 inch in the first month. the
spurt in growth subsided. with 5
mg. 3 times a week he grew another 1/2 inch
in a month, but growth was not main-
tained.

.I 577

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acromegaly

the effects of various steroid hormones on the

insulin-induced growth hormone response

and peter h. forsham

the availability of a sensitive assay for human growth hormone has made

it possible to directly measure the effects of various agents purported to

alter growth patterns. acromegalic patients present a special problem both in

early diagnosis and in therapy. being able to measure growth hormone in

these patients provides an accurate index of activity and a precise measure

of therapeutic effectiveness.

in an attempt to determine whether a pituitary block of growth hormone

secretion is feasible in this condition, a study was made of the effects of

estrogen, androgen and glucocorticoid administration on growth hormone

response to a standard insulin tolerance test in a patient with active acro-

megaly. in the dosage schedules used in this study, it was not possible to

suppress either basal growth hormone secretion or blunt its responsiveness

to the normal physiologic stimulus of hypoglycemia.

.I 578

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practical human growth hormone

preparation and clinical use

human growth hormone was prepared from

acetone-dried pituitary powder by hot glacial

acetic acid extraction and subsequent precipita-

tion by sodium chloride and cold acetone. the

yield was 13 per cent and the preparation was

called practical growth hormone in recognition

of its complement of corticotropin.

treatment of two dwarfs with practical growth hormone in aqueous solution, 1 or 2 mg intramuscularly on alternate days, accelerated the growth rate and there were no physical signs or laboratory indications of adrenal stimulation or other adverse effects. the preparation is recommended for its safety, simplicity and relatively good yield.

.I 579

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hypophysectomy and the lipolytic action of epinephrine in vitro

the response of normal adipose

tissue to epinephrine (0.05 ug/ml incubation

medium) is completely abolished by hypo-

physectomy of the donor rats. treatment of

hypophysectomized rats with crude, whole

rat pituitary extract restored the lipolytic ac-

tion of epinephrine to normal. posterior pi-

uitary extract and corticotropin replacement

was without effect. thyrotropin injections

produced a partial, and growth hormone

treatment a full restoration of the lipolytic

action of epinephrine. treatment of hypo-

physectomized rats with cortisol or cortico-

sterone reestablished the sensitivity of their

adipose tissue to epinephrine, but only when

relatively large doses of these hormones were given. physiological doses of triiodothyronine (1 ug/rat/day), however, restored the normal response to epinephrine. it is concluded that several endocrine factors can influence the lipolytic action of epinephrine but that their physiological importance cannot yet be quantitated.

.I 580

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c-acetyl bovine growth hormone
a procedure is described for labeling bovine growth hormone and human albumin with c-acetylation. the labeled molecule was biologically and antigenically similar to unlabeled bovine growth hormone. following administration of the labeled hormone to animals, the label appeared to remain attached to the growth hormone molecule for at least 4 hours. administration of the labeled hormone promoted growth in hypophysectomized rats and increased the free fatty acid concentration in rabbit serum to a degree comparable with that seen following administration of unlabeled growth hormone. rabbit anti-bovine growth hormone serum neutralized the rat growth response to the acetylated hormone, and immunized rabbits had altered isotope dilution and no increase in serum free fatty acids after intravenous injection of the labeled hormone.

.I 581

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growth hormone

growth hormone influences protein, fat, carbohydrate, and mineral metabolism. it promotes nitrogen retention, growth of cartilage, transportation of amino acids through the cell wall, and incorporation of amino acids into protein. this factor mobilizes free fatty acids from adipose tissue and increases the serum concentration of these substances; long-term administration of this hormone is followed by depletion of body fat stores and inhibition of fatty acid synthesis. in diabetic subjects growth hormone administration is followed by hyperglycemia, glycosuria, and ketosis; its effect on carbohydrate metabolism in normal subjects is more subtle. sodium, potassium, and inorganic phosphate are retained following the administration of growth hormone.

hypercalciuria also accompanies such treatment, an effect mediated through the parathyroid glands.

human growth hormone may be detected in the serum through the use of the radioimmunoassay. the hypothalamus is intimately involved with the control of the secretion and release of growth hormone

from the pituitary. there is a correlation between the availability of glucose for metabolism and the plasma concentration of growth hormone; when glucose is unavailable growth hormone is released in order to provide a substitute source of energy, fatty acids.

the administration of growth hormone to the patient with hypopituitarism is followed by growth in many instances, but it has not usually been effective in promoting growth in individuals with other abnormalities. acquired resistance to the effect of growth hormone is accompanied by the development of antibodies directed against this protein.

.I 582

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recent advances in physiology of bone: part i
our introductory textbook summarizes knowledge of the biochemistry and physiology of bone and calcium metabolism up through 1960. in this lecture, we will outline a few important advances appearing since that time. references to the original literature need not be repeated here. the object is to bring some of the subjects we are investigating up-to-date and to present new problems for laboratory research. the hypothetical new hormone, calcitonin, of copp and cameron will be discussed in detail in dr. mclean's lecture on the parathyroid glands and bone.

.I 583

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hyperplastic lesions of mouse mammary

glands after treatment with 3-methyl-

cholanthrene

hyperplastic lesions were present in the mammary glands of

mice treated with 3-methylcholanthrene and exogenous hormones. the

lesions were similar to those found in glands that were exposed to mammary

tumor virus. it is probable that the production of mammary gland hyper-

plastic lesions could serve as a measure of the effectiveness of a chemical

compound as a carcinogenic agent for the mammary gland.

.I 584

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bone growth and metabolic studies of premature

infants treated with human growth hormone

the influence of exogenous human

growth hormone on growth and metabo-

lism of premature infants was observed.

it was not possible to register any in-

crease of linear bone growth after hormone

administration; concomitantly urinary hy-

droxyproline excretion did not change

significantly.

nitrogen balance studies indicated a

sharp increase of nitrogen retention, due to

a reduced urinary excretion, in all infants.

calcium and phosphorus balances rose in

three out of four premature infants treated with growth hormone, but the characteristic sth calciuric action of sth was not observed. furthermore, sth failed to induce any significant increase in nefa serum concentration of premature infants. it may therefore be concluded that the metabolic response of premature infants to sth differs consistently from that normally observed in more mature subjects.

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growth hormone action on rat liver rna polymerase

the effect of growth hormone on the activity of the rna polymerase measured in this system is shown in table 2. it can be seen that hypophysectomy of the rat results in decreased activity of the rna polymerase and that the injection of 1 mg of human growth hormone into the rat 12 h before death increased the enzyme activity both in hypophysectomized rats and in normal rats.

however, the stimulating effect of growth hormone was only seen in the absence of high concentrations of ammonium sulphate; raising the ionic strength of the assay medium abolished the growth hormone effect. it should be mentioned that addition of growth hormone in vitro in the presence or absence of ammonium sulphate has had no

significant effect on the labelling of the rna by the nuclear preparations.

.I 586

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mammary growth in rats treated with somatotropin during pregnancy and/or lactation

groups of rats received daily

injections of 2 mg somatotropin (sth) from

either day 3-19 of pregnancy or day 1-13

of lactation. another group of rats received

graded increments (0.5-3.0 mg) of sth

every 6 days during both pregnancy and

lactation. other groups of rats served as

pregnancy and lactation controls. mammary

gland deoxyribonucleic acid (dna) content

was determined in all rats and milk yield

was determined in all rats carried to day

14 postpartum. significant increases in mam-

mary dna occurred in all rats treated with

sth irrespective of dose or schedule of in-

jections when compared to gestation controls.

a significant elevation in mammary dna

above the lactation control level was also

evident in rats receiving the hormone and

carried to day 14 of lactation. milk yield

of rats treated with graded increments of

sth was significantly greater than that of

control lactators but milk yield of rats receiving a constant daily dose of the hormone did not differ from that of controls.

.I 587

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growth retardation accompanying diabetes insipidus: an additional mechanism?

from the above considerations, we may divide patients with nephrogenic diabetes insipidus into at least two categories: (1) those who fail to respond to currently available therapeutic products as well as to their own presumably normal secretion of adh; (2) those with similar unresponsiveness to treatment but with presumably reduced secretion of adh. the adh-growth hormone theory may well account in part for growth retardation in the later group.

.I 588

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studies on growth hormone secretion

in rats with the hypophysis autotransplanted to the kidney capsule

the secretory capacity of the pituitary gland, autotransplanted to the kidney capsule, was studied with special regard to the secretion of growth hormone (gh). body weight, body length, tibial epiphyseal width and the mammary gland development after testosterone stimulation were studied.

body growth and tibial epiphyseal width were markedly reduced in the rats with transplanted hypophysis, but not as much as in the hypophysectomized controls. after injections of 0.25 mg testosterone propionate daily for 10 days, only a few groups of alveoli were seen in the mam-

mary glands of the transplanted rats. these observations show that there is a considerable deficiency of gh in rats with the pituitary gland autotransplanted to the kidney capsule. however, the development of a few alveoli in the mammary glands is in favour of the theory that a small amount of gh is secreted from the transplanted pituitary tissue. injections of a purified vasopressin preparation (pitressin) in the rats with autotransplanted hypophysis did not influence body growth, tibial epiphyseal width or mammary gland development. further, no effect of pitressin was seen on the tibial epiphyseal cartilage of rats with intact pituitary gland as has been reported by del vecchio et al. (1958) and hiroshige & itoh (1960). these experiments therefore do not support the view that vasopressin acts as a gh releasing factor.

.I 589

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the effect of human growth hormone in hypopituitary dwarfism

human growth hormone (hgh) raben has been used in a dosage of 2 mg./m.²/day or 5 mg./m.² twice weekly. this dosage is probably in or below, but certainly not above, the range of physiological replacement therapy.

in a standardized five-day metabolic hgh test hypopituitary dwarfs retain more n than children without gh deficiency. this test is valuable diagnostic help in hypopituitary dwarfism.

a prolonged treatment with hgh accelerates growth in hypopituitary dwarfs but not in children

without gh deficiency. growth rate, induced by this treatment, is first above average and later average or below average for age. this decreasing response to hgh is typical for the general phenomenon of catch-up growth and is not caused by the development of antibodies.

of 9 hypopituitary dwarfs, treated for at least 9 months, 3 were growth resistant from the beginning in spite of a high n retention in the preceding hgh test. this resistance is caused by the development of high titres of specific hgh antibodies in the very first few months of treatment. these antibodies suppress the effect of hgh both on metabolism and on growth. the unexpected occasional induction in man of antibodies against a homologous protein hormone is of great interest. the possibility that these antibodies might be active not only against the homogenous but also against the endogenous hormone could have a far-reaching biological importance.

.I 590

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effects of short term administration of physiological doses of human growth hormone in three patients with turner's syndrome

h. e. sjoberg

the effect of apparently physiological doses of human growth hormone was investigated in three patients with turner's syndrome in short term

metabolic balance studies. the subjects presented an abnormal sex chromosome constitution and an increased level of sulphation factor activity in serum.

two dose levels of hormone were used, and there appeared an anabolic response to both. no correlation with dose was obtained for any of the parameters used except for urinary magnesium, where the retention was greater with the higher dose. the sulphation factor activity of serum increased during hormone administration in the one case studied in this respect.

the urinary excretion of hydroxyproline was within the normal range in the two patients studied in this respect, and was not altered by growth hormone.

all patients had an increased urinary excretion of creatine which at present cannot be explained. the creatinuria diminished during growth hormone treatment.

the mechanism behind the retarded growth is discussed. it is suggested that a major factor might be a defect in the center for linear growth, i.e. the epiphyses that would make these less responsive to all the factors normally stimulating the growth processes in the epiphyseal zones.

.I 591

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the effect of growth hormone

on kidney transaminidase in the

hypophysectomized mouse

the role of growth hormone and certain other endocrine factors in regulating kidney transaminidase has been investigated in the mouse. the kidney transaminidase values are low following hypophysectomy. growth

hormone administration in doses of 0.5 to 5.0 ug/day (ovine nih) restore the enzyme activity towards normal. a bioassay for growth hormone is suggested based on the determination of the total kidney transaminidase. intact mice that had been given relatively large doses of triiodothyronin had low enzyme activities. enzyme values in alloxan-treated mice were normal.

.I 592

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influence of hormones on tumor growth and plasma prolactin levels in rats bearing a pituitary "mammatropic" tumor the effects of estradiol, cortisol acetate, thyroxine, or thiouracil on tumor growth, organ weights, and plasma prolactin levels were determined in rats bearing a furth pituitary "mammatropic" tumor (mtt.f4). this tumor is known to secrete large amounts of adrenocorticotropin, somatotropin, and prolactin, but no follicle-stimulating hormone, luteinizing hormone, or thyrotropin. at the dose levels used, estradiol significantly suppressed tumor growth without influencing body growth, and it partially inhibited enlargement of the adrenals and atrophy of the thymus. cortisol acetate significantly reduced both tumor and body growth. thyroxine had no significant effect on tumor growth but enhanced the somatotropic effect as indicated by increases in body growth and organ weights. thiouracil had no significant effect on tumor or body growth, although it significantly increased thyroid weight. estradiol, cortisol acetate, and thyroxine each increased the plasma prolactin levels of the tumor-bearing rats.

.I 593

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studies with human growth hormone

ten dwarfed patients whose short stature was of varying aetiology were studied by investigation of some of the metabolic effects of human growth hormone, 10 mg. being administered daily for a period of 5 to 9 days. the patients were maintained on a constant diet during a preliminary control period, while receiving hgh, and in 7 patients from 2 to 7 days in the post-hgh period. hgh produced a reduction in serum cholesterol, with a rebound on withdrawal, in 7; a delayed clearance of fat from the blood after a fat load in 9; and the appearance of pre- β lipoprotein in the fasting state, as measured by paper electrophoresis, in all of them.

the fall in serum cholesterol and the rebound on withdrawal of hgh has some relevance to the observation that hypercholesterolaemia occurs in some hypopituitary patients even in the absence of hypothyroidism.

no change was observed in tests of thyroid and adrenocortical function during the short-term high dosage administration of

hgh. hypopituitary patients show a considerable retention of nitrogen on hgh administration, and we have confirmed the work of prader and his colleagues that this provides a valuable diagnostic test for growth hormone deficiency. the measurement of urinary nitrogen excretion after the withdrawal

of hgh also promises to be a useful investigation in the differential diagnosis of short stature. nitrogen excretion in the withdrawal phase in hypopituitary children returns slowly to its pre-hgh levels; two non-hypopituitary dwarfed children excreted much more nitrogen in the withdrawal period than they retained in the hgh period. one primordial dwarf showed a negligible change in urinary nitrogen excretion both in the hgh and in the post-hgh periods.

.I 594

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hormonal modification of the distribution of 1-amino-cyclopentanecarboxylic acid-1-c¹⁴ in the rat four hormones have been examined for their ability to alter the distribution in the rat of the new model amino acid, 1-aminocyclopentanecarboxylic acid-1-c¹⁴. although the total tissue concentrations of this amino acid were considerably less than those found previously for α -aminoisobutyric acid, the changes produced by the hormones were much the same for both amino acids. hydrocortisone elevated the liver level of 1-aminocyclopentanecarboxylic acid within 2 hr. bovine growth hormone accelerated entry of the amino acid into both skeletal muscle and liver of hypophysectomized rats within 1

hr. testosterone propionate elevated its distribution ratio in the kidney but not in skeletal muscle, whereas b-estradiol significantly increased uptake of the model amino acid only by the immature uterus. only growth hormone produced a significant change in the serum level of 1-aminocyclopentanecarboxylic acid under the conditions used.

.I 595

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insulin and insulin antagonism as i said earlier, no simple answer has yet emerged from the large amount of research that has been directed toward determining the nature of the substance or substances responsible for the diabetes-inducing and insulin-antagonizing actions of the anterior lobe of the pituitary gland, and to ascertaining their mechanism of action. growth hormone and corticotropin certainly qualify, but so do any other factors that can increase the mobilization of fats as plasma albumin-bound free fatty acids. the idea that the yet incompletely characterized insulin antagonist in the pancreas may be liberated into the blood under the influence of growth hormone and may play a role in the process by which growth hormone diminishes

the activity of insulin in promoting
the utilization of glucose is attractive to me,
but still remains to be confirmed.

.I 596

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relationships of growth hormone, steroids and relaxin in the
transformation of pubic joint cartilage to ligament in
hypophysectomized mice
the histological changes occurring
in the pubic joint of hormonally
treated intact or hypophysectomized mice
have been studied. estrogen treatment resulted
in bone resorption and transformation
of the cartilage caps of the pubic bones to
fibrocartilage in intact mice but not in hypophysectomized
mice. furthermore, relaxin
failed to influence the appearance of the pubic
joint of estrogen-primed hypophysectomized
mice, whereas it induced the development of
long interpubic ligaments in intact mice.
when growth hormone (sth) was administered
to hypophysectomized mice, the pubic
joints responded to estrogen with bone resorption
and transformation of the cartilage caps
to fibrocartilage. sth treatment also restored
the ability of the pubic joint of hypophysectomized
mice to proliferate long interpubic ligaments

when estrogen and relaxin were administered.
progesterone specifically inhibited
ligament formation due to relaxin injection
without altering the histological changes
associated with estrogen treatment, both in
intact mice and in sth-maintained, hypophysectomized mice.

.I 597

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effect of testosterone propionate and growth hormone on
growth and chemical composition of muscle and other
tissues in hypophysectomized male rats
the effect of testosterone
propionate and growth hormone on the
growth of muscle, bone, pelt, viscera and
seminal vesicles was studied in hypophysectomized
male rats. testosterone (0.1 mg/day)
stimulated growth in the levator ani muscle
and seminal vesicles but had no effect on the
other tissues studied. growth hormone (0.1
mg/day) accelerated growth in all tissues
except the seminal vesicles. testosterone did
not enhance the growth-promoting effect of
growth hormone in any tissue except the
levator ani muscle. growth hormone stimulated
deposition of myosin, sarcoplasmic
proteins, collagen and alkali-soluble proteins
in the thigh muscle of hypophysectomized

rats. the composition of the muscle in treated and control hypophysectomized rats was the same as that in normal rats. growth hormone also increased the collagen, keratin-clastin and globular protein content of the pelt. the effect of growth hormone on the proteins of muscle and pelt was not enhanced by testosterone. testosterone given alone had no effect on the chemical composition or content of the muscle and pelt in hypophysectomized rats.

.I 598

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growth hormone and diabetes mellitus since the advent of insulin the vascular and neurological lesions have replaced ketoacidosis as the major problem in diabetes. although good control of hyperglycemia and glycosuria with diet and insulin may influence favorably the development of the ocular angiopathy, there remains a high incidence of these lesions with resulting blindness despite such good control.

growth hormone may be a major factor in the pathophysiology of diabetes mellitus and its effects may be a reflection of the genetic disturbance. its importance was first realized by the classical experiments of houssay and those of young which revealed its diabetogenic effects in experimental animals. the association

of acromegaly with diabetes has been for a long time the major argument in support of the hypothesis of the diabetogenic effect of growth hormone in man.

.I 599

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experiments on the contribution of somatotrophin to prenatal growth in the rat hypophyseoprivus in a fetal rat induced by decapitating the fetus in utero retards fetal growth. this effect can be prevented by injected somatotrophin. these observations substantially support the view that in the normal rat shortly before birth the fetal somatotrophin from the developing hypophysis governs in part the prenatal growth which occurs at that time. although complete hypophysectomy of a pregnant rat retards the growth of fetuses, the manner of its action is obscure. in an individual litter, combined hypophysectomy of the mother and hypophyseoprivus in a fetus retards fetal growth but not to any greater extent than hypophysectomy of the mother without hypophyseoprivus in the fetus. in the intact fetus injections of somatotrophin (armour) do not accelerate fetal growth, presumably because ample fetal somatotrophin from the developing hypophysis is present.

.I 600

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insulin and protein metabolism

the present status of protein synthesis within cells has been outlined. protein is formed in the absence of insulin; the net formation of protein is accelerated by insulin. the effects of insulin on protein metabolism take place independently

of the transport of glucose or amino acids into the cell; of glycogen synthesis; and of the stimulation of high energy phosphate formation. in the case of protein metabolism, as in certain studies on the pathways of glucose and fat metabolism, these observations reveal striking intracellular effects of insulin in many tissues. within most tissues the effect of insulin appears to find expression predominantly at the microsomal level. incidentally, other hormones which affect protein metabolism such as growth or sex hormones appear to act at the microsomes. the fact that insulin exerts effects on protein metabolism at other intracellular sites as well as the above independent effects leads one to agree that its action consists of a stimulation of multiple, seemingly unrelated, metabolic events.

the fact that an immediate effect of insulin on protein synthesis is independent of the immediate need for extracellular glucose or amino acids does not mean that the sustained functioning of cells is likewise independent. the biochemist is fully aware of metabolic defects in diabetes which are not altered by insulin in vitro, but which demand varying periods of pretreatment of the animal. it is also known that in diabetes some proteins (enzymes) may be deficient while others may be produced in excess in the absence of insulin.

it is suggested that the physician desires at least two kinds of relation between these fundamental studies and his patients. one is the possible relation of a deficiency of insulin

action to pathological processes in tissues which have not as yet been examined by the methods described. the other is the need for more accurate measurements of the metabolic disorder and its control than such things as urinary and blood glucose. in developing such future improvements, the place of insulin in protein biosynthesis must be kept in mind.

.I 601

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the influence of blood glucose on the plasma concentration of growth hormone

a. berson, m.d.

a sensitive and specific assay method has been used to demonstrate acute changes in plasma hgh in normal and diabetic subjects. hgh secretion is suppressed by glucose administration and markedly stimulated by hypoglycemia, by interference with intracellular glucose utilization. high levels of hgh were also observed during prolonged fasting, after exercise, and four to six hours following oral glucose administration. abnormalities in hgh secretion were found in association with acromegaly and obesity, and following section of the hypophyseal stalk.

the half time for disappearance of endogenous plasma hgh is twenty to thirty minutes.

.I 602

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failure to thrive: the diencephalic syndrome of infancy and childhood

we have presented a case of a patient with an astrocytoma of the optic chiasm who demonstrated the features of the "diencephalic" or "failure-to-thrive" syndrome. overactivity, overalertness and emaciation were significant symptoms in this patient. roentgenograms characteristically demonstrate normal bone growth, good muscular outline, and absent subcutaneous fat. increased growth hormone was found and may be a factor in the disturbed lipid metabolism.

.I 603

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increased stature

the fact that some patients respond to growth-hormone administration with linear growth does not indicate growth-hormone deficiency or hypopituitarism. yet this appears to be the main factor that led these authors to assume that their patients were suffering from hypopituitarism. the conclusion that children with growth retardation should be subjected to a short trial period of treatment with growth hormone to single out those who are deficient in growth hormone is therefore of questionable validity.

rather, because of the limited supply of human growth hormone, it appears that much more stringent criteria for administration of human growth hormone should be advocated. every effort should be made to uncover the patients who might benefit from growth hormone by utilizing reliable

tests of pituitary function and perfecting a suitable growth-hormone assay. those who have more than suggestive evidence of hypopituitarism and growth-hormone deficiency should then be treated and carefully evaluated for response after long-term treatment.

.I 604

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on language disorders in young children: a reorganization of thinking current questions and confusions about the use of the term aphasia with reference to young children seem often to reflect semantic problems accruing from professional habits of thinking in terms of etiologic and pathologic labels. it is argued that if the term aphasia is generalized simply to refer to inabilities or interferences in the development of language comprehension and use, then it is the task of an evaluating group to describe as well as possible, and in detail, the specific impairments of function in each child. this task commonly requires the use of an extensive period of "diagnostic teaching," wherein care is taken to explore which sensory and motor modalities are working and which are not, and whether integration

of various stimuli is taking place.

some current ideas are discussed with reference to descriptions of impairment, causal factors that are fairly unique in childhood, some thoughts about the neurophysiology of the human "language system," and some psychosocial factors important for language-learning. special attention is given to various relations, in terms of temporal resolving power, between sensation and sensory integration. a scheme, or model, is suggested which may prove fruitful for experimental design in attacking some of these problems at a prelanguage or premeaning level. it is argued that the proportion of "unknowns" can be reduced by careful study based on information about impaired functions within the sensory-integrative-motor complex, without particular regard for "site and extent of lesion."

.I 605

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therapy for hearing-impaired children in comparison with the u.s.a. and europe, canada is still in the early stages of developing rehabilitative services

for speech and hearing-impaired children and adults. they are available in some large canadian cities, but in the opinion of the authors, these services and more should be made available to the hearing impaired of every canadian community.

specialists in the rehabilitation of communication problems, along with members of other medical, paramedical and social services, recognize the vast variety of communication problems that can occur in persons of all ages, the tremendous handicap that such problems represent to the individual, the loss that such handicapped persons represent to our society and the pressing need for efficient and effective rehabilitation. more practically, it is hoped that this article has made its readers more aware of the vast variety of rehabilitative procedures available today for the hearing impaired. with a better understanding of the problems of defective hearing, it is hoped that all readers, professional and non-professional, will join in mutual support for the establishment of these vitally needed services

in their respective communities.

.I 606

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baby habits, genesis and ontogenesis

for adam may be looked upon

as the personification of paleolithic

man-100,000 generations of primitive

human animal-whose evolution

can be of vast importance to

the understanding of the ontogenesis

of the behavior of babies. not

for nothing did the deuteronomist

reiterate "remember the days of

old, consider the years of many generations"

.I 607

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speech therapy with selected patients with

congenital velopharyngeal inadequacy

this paper has described the clinical speech problems of three patients

without cleft palates but with velopharyngeal inadequacy. pharyngeal

flap surgery was performed on each patient after speech therapy was

found to be ineffective following systematic trial. therapy continued

following the surgery. the youngest child, a first grader, realized normal

speech following the surgery and therapy. the two other children continue

to have aberrant but improved speech.

.I 608

.W

stimulus overload, action cycles, and the completion gradient

systematic inquiries into the origin of certain emotional disturbances of infants show that consistent maternal care is vital for the child's normal physical, psychic, and social development, indeed, for his survival. the most elementary precondition for consistent maternal care is the physical presence of the mother or her substitute.

it has, however, become increasingly apparent that children's development can also be stunted, and that they suffer damage of varying extent by the attention of, and close contact with, a mother who dispenses what seems to be the "wrong kind of mothering".

a model of the mother-baby interaction is proposed to explicate the dynamics of the "wrong kind of mothering" and its consequences: my proposition is that the mutual exchanges between mother and baby consist in a give and take of action and reaction between the two partners, which requires from each of them both active and passive responses. these responses form series and chains, the single links of which consist in what i call "action cycles," each completed in itself and at the same time anticipating the next link. i designated these seriated response exchanges as the "precursor of dialogue," as a primal dialogue.

the dialogue acts as a vector of the baby's development, influencing its direction and stimulating it to adaptive efforts and psychic growth. it follows that inappropriate mothering (quantitatively as well as qualitatively) results in what is referred to at this time as the "derailment" of the primal dialogue.

controlled experiments with animals, findings of experimental psychology, and, lastly, clinical findings illustrate the

mechanics of the derailed dialogue and its sequelae.

in the cases under review a surfeit of stimulation, a psychic overloading, resulted in the derailment of dialogue. overloading prevents its subject from completing actions or responses initiated by him. long-lasting overload results in the cumulation of "incompleted action cycles". the sequelae of this cumulation are profound changes in the behavior of the individual. these changes are manifested in a departure from the norms of individual and social behavior patterns that are maladaptive for the individual and asyntonic with his society, that is, asocial.

the derailment of the dialogue is triggered, perhaps even caused,

by the nature of the social setting. one setting, over-population, is extensively discussed in connection with an animal experiment, and the implications for the human community are examined.

.I 609

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children at kelbourne

kelbourne school, glasgow, which educates both spastic and aphasic children, is the first school of its kind to be administered by a local education authority. its aphasic department, largely experimental in nature, contains children aged three to eight. in the spastics department there are 45 children with severe physical handicaps and their ages range from 3 to 16.

the school, which celebrated its golden jubilee last year,

has its origins in the Maryhill Hall public school for defective and epileptic children which opened in 1907 with 12 pupils in premises of which, as an H.M.I. reported four years later, 'it was impossible to speak favourably'. the report continued, 'a public hall, used frequently in the evenings for public entertainments, lacking proper cloakrooms, bare in appearance, and generally comfortless, should not be used for this purpose'. the inspector's words did not go unheeded and seven years later the children were transferred with others to the new buildings of Percy Street special school. in the 1950s the name was changed to Kelbourne school.

between and through two world wars the school provided education for physically and mentally handicapped children but in 1955 a new unit was added and spastic children were admitted for the first time. gradually the emphasis shifted from children with other physical and mental handicaps to the cerebrally palsied and finally the entire building became available for spastics. two years ago the aphasic children joined the school. Miss E.F. Hamilton is the headmistress.

.I 610

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deafness

methods of detection, diagnosis, and management of deafness in children depend so entirely on a knowledge of the processes involved in communication by speech and in the acquisition of

this skill that i propose to consider them first. it will be found that the practical steps to be taken in dealing with patients flow naturally from this knowledge.

.I 611

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pharyngoplasty in speech

where adequate palate repair is undertaken at 1 year there is no indication for pharyngoplasty as well at that age.

pharyngoplasty is indicated as a "supportive" operation only when the result of the palate repair can be assessed (5 years plus), and where the speech result proves disappointing.

the figure of 171 pharyngoplastics in 944 cases applies to the known speech results up to april 1963. it follows that with follow-up of the more recent primary cases pharyngoplasty may well be necessary in some.

the hynes pharyngoplasty has proved to be the most satisfactory.

.I 612

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verbal effects in the intermediate-size transportation problem

preschool children were given an intermediate-size discrimination problem, told before each response that the reward was under the "medium" stimulus: and 1- and 3-step transposition tests. during training, group i was group ii was told that it was "not under the big or little one"; and group iii was not told anything. the verbalizations were not given during the tests. groups i and ii learned the initial discrimination faster than group iii, and transposed more than group iii, but there was a distance effect in all three groups. these results, and other data, suggest that the deficiency in the verbal control over motor behavior in young children arises

from deficiencies in both the decoding and encoding processes.

.I 613

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the acquisition of formal features of language

children from different groups do not learn the same uses and functions for language. but every child must learn the formal features, or the "code" for his language, thus creating a constant in every language acquisition situation.

.I 614

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mongolism-some clinical aspects

this is a review of 86 mongoloids seen over 5 years at the nebraska psychiatric institute. one-half of the sample were evaluated before their second birthday. eighteen per cent of the cases for whom birth weight data were available weighed less than 5 1/2 lbs., double the national rate for prematurity. there was a bi-modal distribution of mother's age at the birth of the mongoloid child. pregnancy, labor and delivery complications were reported in almost one-half of the cases. seven per cent were breech deliveries. all cases were mr. the most frequent type was moderate. most frequently mentioned characteristics were: generalized hypotonia (all but 2 cases); psychiatric disorders, 11 cases; abnormal eeg, 8 cases; hearing loss, 5 cases.

.I 615

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learning problems in children: ii. emotional aspects

at the last meeting we tried to deal with a general over-all approach to the problem of learning, considering it not merely as a problem in reading, but learning in general which begins at birth.

we hope to deal with this problem at a relatively high level and we want to have the emotional problems dealt with in this manner rather than in terms of diagnostic criteria. the child with learning problems should not be compartmentalized in terms of "organicity" and "nonorganicity". the subject of this talk, then, is emotional issues in learning.

.I 616

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management of communication problems in infants and children
early detection and referral of a
child with a hearing or speech-language problem
is feasible and in most cases, very critical. further
consultation can then be obtained and the child
placed on a training program geared to his needs.

.I 617

.W

the formation of a cleft palate unit- a preliminary report
with cleft palates, as in other surgical fields, changing
techniques and better management of the patient as a whole
render inexcusable the operative procedures that merely
drag together the edges of the defect and then leave a
cosmetically and functionally crippled child, to adapt itself
as best it may to the harsh competition of the outside
world.

ironically the problem of congenital defects increases as
our competence to deal with them advances. in the past
these cases struggled to take their place on the marriage
market but the more skilled our rehabilitative procedures

become, the more likely are they to perpetuate their disability,
since a significant number show a hereditary tendency.

.I 618

.W

acquisition of language

although the work of bullowa, jones, and bever has some of its greatest
promise in the light it may shed on the development of functions of language
in children, the promise cannot be realized unless the authors give
a great deal of explicit attention to the framework of such analysis, for there
is not, as may be the case for phonological and grammatical development,
anything like a satisfactory body of linguistic theory and method as to the
terminal state. while a good deal may be learned without such a theory, and
necessarily must be so learned, since the work in progress cannot be suspended
until such an unpredictable millenium, it still would be a pity if the
chance were lost for the interaction of the acquisition of data and the
improvement of theoretical notions.

let me complete my discussion by developing my argument in two
ways: (a) by briefly stating the nature of the problem with regard to the
terminal state of verbal development, (b) and by indicating what present
and future contribution such fields as anthropology, sociology, and social
psychology may be able to make to the solution of the problem.

.I 619

.W

the speech production and spoken language of the deaf

the distinction was made between speech production and spoken language in
analysing the oral output of those with hearing impairment. a brief review of
studies in both areas was undertaken, including the report of a new electronic

visual monitoring device, the glossal transducer. it was postulated that the deaf utilise a unique visual-to-motor conversion within the brain when speaking and monitor consciously by tactile-kinaesthetic control. the more recent studies relate to the syntactical features of the speech of the deaf. these show that deafness creates telegraphic speech with reduced sentence length and omissions of essential words such as functors. the speech of the deaf seems to contain mostly nouns and verbs, with a limited number of words used to expand verb forms.

.I 620

.W

cognitive functioning in early infantile autism: an examination of four cases by means of the wechsler intelligence scale for children

the results are communicated which were obtained from an examination, by means of the wechsler intelligence scale for children, of four cases of early infantile autism. these cases had developed in such a way that a reliable investigation by means of a mental test had become possible.

according to their full scale iq's the four cases fell within the category of dull normal intelligence or less. all of them showed a considerable discrepancy between the verbal and the performance iq, the performance iq being of much higher value. the composition of the autistic test profiles was characterized by a large variability in the subtest scores, discriminating the autistic group significantly from non-autistic control groups. the subtest score divergencies, responsible for the large variability, showed a distinct pattern, being specific for the autistic group as a whole. this group could be considered as a distinct group particularly by a marked tendency to achieve poorly and far below the subject's average level in the subtests comprehension and vocabulary, and to achieve superiorly and far above that level in the

subtests block design and object assembly. by specifying the mental functions, conditional for success in these four subtests that occupy extreme positions within the autistic test profiles, it was concluded that the autistic patients apparently were able to achieve well, or even superiorly, only if the task could be performed on a purely perceptual level. but they failed as soon as an appeal was made to thinking proper. this was thought to be due to a disability in dealing with imaginary things and imaginary situations, or, in other words, to an incapability to objectify what is not actually present in the subject's concrete situation. it is proposed that this impairment could be reduced to a lack of symbolic means, being the correlate of a defective or insufficiently developed language in the patients. it is further proposed that children suffering from early infantile autism might not be able, or at a later stage only, to reach that level of language development in which words can be used as symbols, representing absent things and absent situations.

.I 621

.W

otologic care of cleft palate cases

the purpose of this study was to review the ear pathology in 480 patients whose cleft palates had previously been repaired.

despite concern over speech regression, tonsil and adenoid surgery was carried out on 66 of these patients. when carefully done, this was accomplished with considerable overall improvement, particularly for the benefit of the conductive hearing loss.

sixteen cases had exact documentation of these results by

virtue of speech recording and accurate audiometric records.

.I 622

.W

congenital heart disease, deaf-mutism and associated somatic malformations

occurring in several members of one family

m.d. and patrick h. lehan, m.d.

a unique family is described in which the

mother and four of her eight children have pulmonary

stenosis. two of the four affected children

are deaf-mutes; one of these has, in addition

to the pulmonary valvular stenosis, idiopathic

hypertrophic subaortic stenosis. all the affected

children had several associated somatic malformations.

genetic and nongenetic factors and

their role in the development of the malformations

are discussed. it is suggested that the cardiac

defect is transmitted by a single non-sex-linked

genetic factor (dominant autosomal

inheritance). in the presence of a normal karyotype

it appears that a single dose of either a

point mutation, or a small deletion or translocation

is the most likely cause.

.I 623

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histidinemia

a review of published reports of

histidinemia indicates that this condition

has a variability of clinical and biochemical expression. three children with histidinemia, born of a consanguineous marriage are reported here. they had blond hair, blue eyes, speech defects, mental retardation, and a peculiar eeg abnormality. they also exhibited characteristic biochemical findings of the disease: elevated blood and urine histidine, increased urine imidazolepyruvic acid, and a sustained high rise in plasma histidine following an oral histidine tolerance test. they did not, however, have the reduction of skin histidine α -deaminase activity which has been observed in some children with this condition. tests for determination of heterozygotes in the family were not successful.

parental consanguinity and normal skin α -deaminase activity set these children apart from other reported cases. the first lends support to the hypothesis that histidinemia is inherited as an autosomal recessive trait; the second supports the idea that the genic fault which results in reduced histidine α -deaminase activity can be expressed to a different degree in different tissues. these children seem to represent a variant of

histidinemia where liver histidase activity is reduced while skin histidase activity is present.

.I 624

.W

interpretation within the metaphor

analytic investigation of the use of the metaphor was first given impetus by ella freeman sharpe (1950), who explored the symbolic meaning of particular metaphoric phrases with reference to the body and libidinal needs. currently, interest has become focused upon the use of the metaphor as a self-conscious, rational therapeutic technique of communication, of particular value with those patients who have reached "the borderline of sanity". ekstein (1961) and ekstein and wallerstein (1957) have emphasized that the use of the metaphor should be regarded as an essential technique for gradually establishing communication and initial insight with borderline and schizophrenic patients but that it must not be regarded as a treatment technique in itself. it is but a preliminary approximation to the final therapeutic act, which ultimately will consist of a classical interpretation at the level of the secondary process. the use of the metaphor derives its primary value from maintaining contact with patients who are constantly in danger of being inundated by a break-through of primary-process material.

.I 625

.W

evolution of a characteristic speech disorder in juvenile cerebral lipidosis

juvenile cerebral lipidosis is being diagnosed with increasing frequency in this country, especially in schools for the visually handicapped. the manifestations of rapidly developing loss of vision, seizures, muscular rigidity, ataxia, retinitis pigmentosa and eeg abnormalities are well known in this disorder. a speech disorder described as a "lolling, stammering speech" was mentioned by sjogren (1931) in his comprehensive description of juvenile amaurotic idiocy, but this has not been emphasized in recent descriptions. this report, based upon an analysis of 5 cases, describes the evolution of a characteristic form of speech pathology that is invariably present in juvenile cerebral lipidosis.

the initial speech abnormality seen early in the disorder is a hesitancy of speech and occasional repetition of words. in time, dysarthria becomes evident with slurring, nasality and impairment of phonation similar to that seen in pseudobulbar palsy. in addition to the dysarthria, a highly characteristic perseverative speech appears which often has a close resemblance to true stuttering. this stuttering-like speech has been observed in 4 of the 5 cases at some time during the course of their illnesses. as the speech patterns deteriorate, the patient becomes less communicative and finally lapses into mutism. the speech disorder is often the most disabling aspect of this syndrome.

.I 626

.W

relation of crying activity in early infancy to speech and intellectual development at age three years

rosenfeld

cries of 38 infants, age 4 to 10 days, were measured for outburst frequency during the most active 20-sec. period of crying. crying

scores showed a significant correlation (.45) with stanford-binet iq at 3 years, a borderline correlation (.32) with cattell iq at 15 to 20 months, and a nonsignificant trend with speech ratings at 3 years. although no correlations were adequate for individual prediction, infant crying is deemed worthy of further investigation as a possible indicator of intellectual potential.

.I 627

.W

labial supportive appliance

the patient with a repaired cleft lip and palate and an associated displacement and deficiency of the premaxilla presents problems which may be of concern to the plastic surgeon, speech pathologist, orthodontist, and prosthodontist.

the upper lip may appear flat or retruded in relation to the lower lip.

when maxillary anterior teeth are missing, either congenitally, naturally (as in the mixed dentition period), or because of neglect, the upper lip may appear to be rolled under the premaxilla. the lower lip usually assumes a characteristic 'pouty' appearance.

this complex of tissue deformities also may be important in the articulation of speech sounds. fricatives and plosives are difficult to produce correctly because of the malposition of the lip. there may be interference with direction of air current, contact of tongue to alveolar ridge, and normal contact of lips.

corrective procedures are designed to improve the labial profile and to establish more normal relationships of intraoral structures. these procedures, employed individually or in combination, may include orthodontic movement of maxillary segments, dental prosthesis, and cheiloplasty.

another more recently developed adjunct involves autogenous
osseous implantation in the cleft areas.

.I 628

.W

heterogeneity of the 'cleft palate population' and research designs
the primary point made in this paper is that we must reject the notion
that there is some inherent, universal commonality among individuals
who are born with a cleft lip and/or cleft palate. we must recognize the
various pertinent subgroups within this population. this does not mean,
however, that one must always recognize the smallest subgroup in doing a
given study. on the contrary, we would defend the use of fewest possible
subgroups consistent with the specific research purpose. nevertheless, we
feel that time spent considering the purposes of a study and the subgroups
which need to be identified will tend to minimize the number of
contradictory results, and will assist us in the interpretation of the
observations that our insight and technology make possible.

.I 629

.W

cineradiographic comparison of normal to noncleft subjects with velopharyngeal
inadequacy

cineradiographic studies of the normal subjects were compared with
studies of noncleft subjects who demonstrated velopharyngeal inadequacy.
the following conclusions were made: a) there was a significant difference
between soft palate length in normals and the velopharyngeal inadequacy
group. b) there was not a significant difference between depth of nasopharynx
in normal and the velopharyngeal inadequacy group. c) the
difference of the means of the soft palate length and depth of nasopharynx

between the normals and velopharyngeal inadequacy group was significant.

d) the thickness of the soft palate was greater in the normal than the abnormal group. e) in 70% of the normal and velopharyngeal inadequacy groups the height of soft palate elevation was above the palatal plane. f) in 80% of the normal group the height of velopharyngeal closure took place below the palatal plane. none of the subjects in the velopharyngeal inadequacy group obtained velopharyngeal closure. g) there was no significant correlation between amount of gap and voice quality. h) there was no significant correlation between amount of gap and intelligibility of speech. i) there was a difference between vital capacity readings for the velopharyngeal inadequacy group with nose occluded and unoccluded. j) the correlation coefficient between quality judgment and intelligibility judgment was highly significant.

.I 630

.W

spontaneous verbal rehearsal in a memory task as a function of age
a distinction is made between 2 alternative hypotheses for explaining an often-reported deficiency in verbally mediated performance during early childhood: (1) the verbal response is made, but tends not to mediate performance ("mediational-deficiency hypothesis"); (2) the verbal response tends not to be made ("production-deficiency hypothesis"). a study is described which attempts to meet the ideal criteria for a test of the production-deficiency hypothesis. the method used was that of direct observation of s's spontaneous verbalizations, and the hypothesis was confirmed by the finding that kindergarteners are less likely than older children to rehearse stimulus names in a nonverbal serial recall task.

.I 631

.W

early experience and the socialization of cognitive modes in children
this paper deals with the question: what is cultural deprivation and how
does it act to shape and depress the resources of the human mind? the
arguments presented are: first, that the behavior which leads to social,
educational, and economic poverty is socialized in early childhood; second,
that the central quality involved in the effects of cultural deprivation is a
lack of cognitive meaning in the mother-child communication system; and, third,
that the growth of cognitive processes is fostered in family control systems
which offer and permit a wide range of alternatives of action and thought and
that such growth is constricted by systems of control which offer predetermined
solutions and few alternatives for consideration and choice.

the research group was composed of 160 negro mothers and their
4-year-old children selected from four different social status levels.
the data are presented to show social status differences among the
four groups with respect to cognitive functioning and linguistic codes and
to offer examples of relations between maternal and child behavior that are
congruent with the general lines of argument laid out.

.I 632

.W

recovery of mycoplasmas in the study of
human leukaemia and other malignancies
numerous reports have been published concerning the
necessity of testing for the presence of mycoplasmas before
the interpretation of experiments performed in cell
cultures. such tests are especially important when
the presence of viruses is suspected, since recent evidence

indicates that some mycoplasmas are capable of eliciting a transmissible cytopathic effect.

in addition, some mycoplasmas and viruses share properties, such as size, filterability, morphology in electron microscopy, sensitivity to ether, ability to haemagglutinate and cause haemadsorption, interference with virus replication in vitro, lack of inhibition by certain commonly used antibiotics and inhibition of growth by homologous antiserum. thus, the absence of ordinary bacteria and moulds in preparations eliciting a cytopathic effect in cell cultures is an unreliable criterion for viral identification. great caution should be exercised in classifying new agents as viruses, especially as myxoviruses, without adequate testing to exclude their identity as mycoplasmas.

.I 633

.W

pneumonia due to mycoplasma pneumoniae
its incidence in the membership of a co-operative medical group
ruth mcmahan, edmund r. clarke, william a. maccoll, and j. thomas grayston
a total of 1051 cases of pneumonia occurred in
72,992 persons who were members of a medical
co-operative in the period december 1, 1963, to
december 31, 1964. the annual rate of pneumonia
was 12.9 per 1000. isolation of mycoplasma pneumoniae
from throat swabs was attempted in over
half the cases reported, and paired blood specimens

were obtained in one third. on the basis of laboratory examination of these specimens, the incidence of clinically recognized pneumonia due to *m. pneumoniae* was between 1 and 1.5 persons per 1000 per year.

although peak rates of pneumonia occurred under five years of age (45 per 1000) pneumonia due to *m. pneumoniae* was uncommon in this age group. it was most common in children five to nine years old, and was frequently the cause of pneumonia in adolescents (ten to nineteen years of age). the rates in children in primary school was twice the average incidence. *m. pneumoniae* pneumonia also differed from the pneumonias of other etiology in that it occurred throughout the year, with no seasonal excess whereas total pneumonia showed a predominance in winter.

the typical clinical syndrome of the pneumonias in which *m. pneumoniae* was isolated was one of prominent systemic manifestations of headache and fever, but few respiratory symptoms occurred except cough. upper-respiratory-tract complaints and an elevated white-cell count were much more frequent in the other pneumonias. the patients with *m. pneumoniae* pneumonia were almost never hospitalized but suffered significant absenteeism. they came from larger families, usually with children of

school age. reporting physicians were usually correct
in diagnosing these pneumonias as "atypical" or "viral."

.I 634

.W

establishment of a turkey flock free of 'n' strain mycoplasma
mycoplasma of the 'n' strain are frequently isolated from
turkey poultts affected with airsacculitis but free of
mycoplasma gallisepticum. research on the 'n' strain has
been impeded by the presence of a high proportion of
turkey poultts with airsacculitis in all breeding flocks
examined, by the difficulty of culturing and identifying
the mycoplasma strains, and by the lack of a practical
serologic test. this communication describes the establishment
of a small nucleus of 'n'-free turkeys from a commercial
breeding flock known to carry 'n' mycoplasma.
hens and toms for the production of 'n'-free poultts were
selected from the parent flock by serology and culture.

.I 635

.W

septicemia due to mycoplasma hominis type 1
viola m. young, ph.d., and sheldon m. wolff, m.d.
a febrile illness that followed therapeutic abortion
and was accompanied by the presence of
mycoplasma hominis type 1 in the blood is described.
the patient upon recovery exhibited a specific
antibody response to the mycoplasma isolated
from the blood, as well as to another strain of the

same serotype. these findings are regarded as additional evidence for the pathogenicity of *m. hominis* type 1 organisms, particularly in situations favoring their dissemination from the female genital tract.

.I 636

.W

infectie door *mycoplasma hominis* bij een pasgeborene *mycoplasma hominis* infection in a newborn child. --in a baby born by a difficult forceps delivery, abscesses began to form in the neck a few days after birth. *mycoplasma hominis* was recovered from the pus.

.I 637

.W

some intraspecies differences in antigens on the surface of certain living human cells surface antigens of several types of living cells of human origin were partially characterized with hyperimmune antisera prepared in the rabbit against living hela cells and living, uncultured, full-term, human amnion cells. hemagglutination, mixed-agglutination, and direct and indirect immunofluorescence (fab) techniques were employed. with these techniques and fractional absorption procedures, common and specific cell antigens were detected on the surface of several human living cells: uncultured and primary amnion, two established human cell lines (rp am 1 and u amnion) of presumed normal origin and two (hela and hep-2) of presumed malignant origin, and human erythrocytes. none of the antigens were found on nctc 2555 mouse cells. the human cells possessed species-

related antigens demonstrable by hemagglutination. after removal of the hemagglutinins by absorption with human erythrocytes, antibody in high titer for the homologous cells was detected by fab methods. in addition, some changes in antigens on the surface of amnion cells during primary culture were observed. finally, an antigen was found on hela and hep-2 cells, by use of anti-hela serum absorbed with human erythrocytes and rp am 1 cells, that was not found on either human erythrocytes, uncultured amnion cells, or on the cells of the two established amnion cell lines. at the dilutions used in the tests, antibodies to the abo blood group isoantigens, forssman hapten, or adsorbed serum proteins could not account for the antigens detected. the possibility that mycoplasma sp. antigens were responsible for the reactions was inconsistent with the results. the specificity of the fab methods on living cells was confirmed.

.I 638

.W

coombs-positive hemolytic anemia and generalized amyloidosis in mice following transmission of subcellular leukemic material following transmission with cell-free supernatant fluid or with virus extract of leukemic tissue or plasma from various types of murine plasma cell leukemias a disease developed, characterized by hypergammaglobulinemia, weight loss, anemia, marked splenic, renal and hepatic amyloidosis and plasma cell infiltrations in the lungs. the disease was also transmissible through the placenta or with the milk of infected

mice. in dba/2 males the incidence of the disease was much higher (100%), the survival shorter and the anemia much more severe than was the case in dba/2 females and in (dba/2 x cba) f1 mice of both sexes. it is proposed that the development of the lesions is mediated through an auto-immune mechanism created by the antigenic effect of the virus-transformed host cells.

.I 639

.W

the ph 6 antigen in strains of *pasteurella pseudotuberculosis* and its relation to biological activities it may be concluded that only part of the *p. pseudotuberculosis* strains can synthesize the ph 6 antigen, whereas this property seems to be shared by all the strains of *p. pestis*. as in the case of *p. pestis*, three kinds of biological activities were related to the presence of the ph 6 antigen isolated from a strain of *p. pseudotuberculosis*.

.I 640

.W

serological relationships among human mycoplasmas as shown by complement-fixation and gel diffusion and robert m. chanock antigenic relationships among human

mycoplasmas were studied by complement-fixation and agar gel diffusion techniques. four recognized human species. mycoplasma hominis type 1, m. hominis type 2, m. salivarium, and m. fermentans were antigenically distinct in these tests. in addition, m. pneumoniae (eaton agent, the etiological agent of cold agglutinin-positive atypical pneumonia) was different from these four species. although these species were distinct, evidence of shared antigenic components was obtained in complement-fixation and agar gel diffusion tests. since rabbits were immunized with mycoplasmas grown in rabbit muscle infusion broth supplemented with rabbit serum or, in the case of m. pneumoniae, with infected chick embryo lung suspension, the possibility that the heterologous reactions resulted from antibody to growth medium components could be excluded. four recent mycoplasma isolates from the oropharynx were analyzed, and three were shown to be closely related to m. hominis type 1, and the fourth was closely related to m. salivarium. although the recent isolates could not be distinguished from the related "prototype" human species by complement-fixation, differences could be detected by the agar gel diffusion technique.

.W

mammalian cell cultures contaminated with

pleuropneumonia-like organisms

ii. effect of pplo on cell morphology in established

monolayer cultures

the occurrence of cytopathogenic changes in monolayer cultures of

pplo-contaminated mammalian cells has been shown to be related to

deficiency of arginine in the medium. the same effects were seen when the

cell culture medium was depleted by pplo prior to application to pplo-free

cell cultures even though viable pplo were no longer present. the fact that

the same picture resulted in the absence of pplo when either arginine or

glucose were omitted from the medium would indicate that, while the defi-

ciency created under the conditions described was specific, the cellular

changes could as well be the result of omission or depletion of other mam-

malian cell growth requirements. the importance of surveillance of cell

lines for the presence of pplo to avoid misinterpretation of cytopathogenic

effects was stressed.

.I 642

.W

suppression of rous sarcoma virus growth in tissue

cultures by mycoplasma orale

an agent

which produced cell destruction in human diploid and chick-embryo fibroblasts

was isolated from wi-26 strain of human diploid fibroblasts and shown to be a

mycoplasma. the multiplication of rous sarcoma virus (rsv) and rous associated

virus (rav) was inhibited in wi-26, wi-38, and chick-embryo fibroblasts

infected with this mycoplasma. the mycoplasma isolate, designated strain 941,

reacted strongly in the complement-fixation test with antiserum to mycoplasma orale ch19299, an isolate obtained from the human oral cavity. the cytopathic effect of mycoplasma strain 941 could be eliminated by growing the mycoplasma on an artificial agar medium before inoculation into chick-embryo fibroblasts. serial passage in chick-embryo fibroblasts restored the cytopathogenicity of the agar-grown mycoplasma. however, growth of rsv and rav was inhibited by both the tissue culture-grown and the agar-grown 941 strain, and also by the ch19299 strain which did not produce any cytopathic effect.

.I 643

.W

a method for direct demonstration of pleuropneumonia-like organisms in cultured cells.

direct microscopic observation

of pleuropneumonia-like organisms (pplo)

in cell cultures is easily accomplished follow-

ing hypotonic treatment, air-drying and

staining with orcein. a rapid technique using

fl human amnion cells, inoculated with su-

pernatant from suspected cultures, is de-

scribed. the demonstration of pplo con-

tamination of 30 cell lines by this rapid

method was in complete agreement with re-

sults of pplo-agar techniques.

.I 644

.W

a fatal septicemic disease of infant puppies caused by

cytopathogenic organisms with characteristics of mycoplasma.

pathogenic organisms were isolated from 2 outbreaks of a fatal septicemic disease of infant puppies and from dog kidney cells that degenerated spontaneously. the isolates were indistinguishable serologically and possessed characteristics of mycoplasma. the pathogenic organisms were cytopathogenic for dog kidney cell cultures, and in inoculated puppies, produced pathological changes that resembled those seen in natural cases. lesions consisted principally of necrosis and hemorrhage. the isolates were culturally and serologically distinct from recognized canine mycoplasma species.

.I 645

.W

chromosome changes in pplo-infected fl human amnion cells.

characteristic chromosome

changes were observed in pplo-infected fl human amnion cells. these changes included a gradual reduction in chromosome numbers, increase in chromosome aberrations, and the appearance of 3 new varieties. although some of the aberrations appeared early after infection, most changes developed slowly, over a period of several months.

.I 646

.W

studies on mycoplasma pneumoniae

infection in sweden

sera from 107 cases of pneumonia and 132 cases of milder respiratory infection were examined by the cf test against m. pneumoniae antigen. thirty-five patients with pneumonia and 2 patients with bronchitis had serologic evidence of m. pneumoniae infection. all cases which had a significant antibody rise with the cf test also showed a corresponding rise with the fluorescent antibody test. m. pneumoniae was isolated from 10 of 18 serologically positive cases. cold agglutinins were demonstrated in 17 of 37 cases (46 per cent) with m. pneumoniae infection. m. pneumoniae infections occurred during all seasons of the year and were most common in older children and young adults. the clinical features of the cases with m. pneumoniae infection in this study resemble those described in similar investigations in other countries.

.I 647

.W

spontane genetische veränderungen am zellstamm I (earle)

the chromosomal constitution of a clone of the cell strain „I“ was studied by repeated chromosomal analyses within 2 years. there resulted the stability of the cellular clone with regard to the tested feature for the duration of about one year.

the maximal number of chromosomes amounted to 60-64. in later tests a spontaneous doubling of the chromosomal number (maximum 120 chromosomes) was ascertained. the cause of this phenomenon could not yet be cleared up. this new chromosomal pattern remained unchanged in the subsequent examination period of 6 months.

as was proved by these observations, under the present cultivation-conditions cell populations can be retained stable in vitro for a certain period. the defined substances, however, still imply unknown factors which may have a mutagenous effect, so that sudden changes of cell populations may result. the respective physiological features are hardly known as yet.

.I 648

.W

chromosome changes in human diploid-cell cultures infected with mycoplasma

this communication shows that mycoplasma may also change cell chromosomes, and therefore emphasizes the need for caution in interpreting experimental results without adequately testing for the presence of mycoplasma. chromosome damage similar to that described here has been induced by viruses in cell cultures and in blood cultures. chromosomal abnormalities have also been reported in blood cultures and bone marrow from leukaemic patients.

.I 649

.W

evaluation of tylosin in preventing egg transmission of mycoplasma gallisepticum in chickens

the inoculation of mycoplasma gallisepticum infective yolk into the left posterior thoracic air sac of laying chickens

resulted in an infection which produced a rate of egg infection satisfactory for experimental purposes. culturing of all live embryonating eggs as well as all dead and infertile eggs was necessary to determine the rate of egg infection. tylosin, either injected subcutaneously, administered in the drinking water, or employed in an egg-dipping solution, greatly reduced but did not completely eliminate egg infection. in the 3 egg dipping trials, only 11 isolates of *m. gallisepticum* were obtained from 2329 tylosin-dipped eggs, compared to 400 isolates from 2984 control eggs.

.I 650

.W

epidemiology of *mycoplasma pneumoniae*

infection in families

and ruth mcmahan

the transmission and clinical manifestations of infection with *mycoplasma pneumoniae* were studied in 114 families in which there was a case of atypical pneumonia. *m. pneumoniae* was isolated from a throat culture of the index pneumonia patient in 36 of these families. transmission to other family members occurred in 23 of the 36 families. in these 23 families, 84% of the children and 41% of the adults were infected. the index cases are included. of the total 59 patients with family-contact infections, 42 had lower-respiratory-tract symptoms, 6 had pharyngitis alone, 9 (all children) were asymptomatic, and 2 had probably unrelated symptoms. the

time intervals between cases within a family suggested a median incubation period of 23 days. treatment with tetracycline seemed neither to cure the symptoms completely nor to abolish the carrier state that often lasted one to three months.

.I 651

.W

case of salpingitis due to pleuro-pneumonia-like organisms

a case of acute salpingitis following a diagnostic curettage and aspiration of the pouch of douglas is described. this case was resistant to penicillin and streptomycin therapy. a pure culture of pleuropneumonia like organisms (pplo) grew from pus removed from the secondary pyosalpinx by aspiration. these organisms were sensitive to tetracycline which cured the adnexal infection. no pplo were found in the vaginal discharge.

pplo have frequently been isolated from the vaginae of healthy and infected women. however, only 9 cases of pelvic inflammatory disease with a pure culture of pplo have been reported. the possibility that these growths of pplo in the internal genitalia followed the use of antibiotic therapy is discussed.

infection with pplo should be considered when pelvic inflammatory disease proves resistant to the common antibiotics.

.I 652

.W

the serological differentiation of mycoplasma strains (pleuropneumonia-like organisms) from various sources

a complement fixation test with rabbit antisera was used to differentiate 82 cultures of mycoplasma from man, mammalian cell cultures, laboratory rats and mice, cattle, goats, poultry, embryonated eggs and sewage.

seventeen serotypes were distinguished, 5 from man, 1 from mammalian cell cultures, 4 from rats and mice, 4 from cattle and goats, 2 from poultry and one saprophytic. most of these corresponded to recognized species of mycoplasma, but 1 of human origin (represented by 1 strain, navel), and 1 from tissue cultures (5 strains), may represent new species. r38, one of the serotypes from rats, could be distinguished from the species *m. arthritidis*, but is probably an antigenic variant rather than a distinct species. two species hitherto recognized as distinct *m. arthritidis* and *m. hominis* type 2, could not be distinguished and appear to constitute a single species. these findings illustrate the necessity, from the viewpoint of taxonomy, of comparing mycoplasma strains by serological methods.

the serotypes of human and animal origin were largely host-specific.

exceptions were the inclusion of *m. arthritidis* from rats and *m. hominis* type 2 from man in a single serotype, the finding of a bovine organism among the strains isolated from goats and of a saprophytic strain in a rat.

in relation to the aetiology of disease in man and animals, the isolation of an endogenous mycoplasma from embryonated eggs used to passage infective material illustrates the importance of identifying these organisms serologically. the demonstration of mixed mycoplasma infections in lesions in two rats shows the necessity of adequately purifying all cultures of mycoplasma before examination.

.I 653

.W

spiramycin in the treatment of experimental

mycoplasmosis in day-old chicks and turkey

poults

day-old chicks and turkey poults experimentally infected with *m. gallisepticum* have been treated at the time of infection, with spiramycin administered by subcutaneous injection or drinking water medication.

a dose of 100 mg/kg. bodyweight by subcutaneous injection or an 0.04 per cent. concentration in the drinking water continuously for three days eliminated the infection in most of the birds, which remained free of air-sac lesions and did not react to the slide agglutination or haemagglutination inhibition tests.

.I 654

.W

further studies of agents isolated from tissue cultures inoculated with human leukaemic bone-marrow

d. a. woods

mycoplasmas were isolated from tissue cultures inoculated with bone-marrow from leukaemic patients.

all cultures which showed a cytopathic effect contained mycoplasmas.

there was no evidence of mycoplasmas in control cultures.

the mycoplasmas isolated seemed biologically and serologically to be of one strain which was different from any previously reported as being isolated from human sources although there was some relationship to a rodent mycoplasma, *m. pulmonis*. mycoplasmas cannot readily be distinguished from viruses electron-microscopically.

the relationship of mycoplasmas to leukaemia is not yet clear.

.I 655

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microbiological studies of reiter's disease attempts were made to demonstrate viruses and pplo in body fluids and synovial tissues of patients with various rheumatic diseases. all attempts to demonstrate viruses were negative. pplo were looked for in 499 specimens from 114 patients with rheumatic and non-rheumatic diseases. whereas these organisms were readily isolated from genito-urinary specimens, they were found in none of 31 synovial fluid specimens. they could not be grown from synovial tissue biopsies of patients with rheumatoid arthritis, ankylosing spondylitis, gout, gonococcal arthritis, psoriatic arthritis, traumatic arthritis, or arthritis accompanying ulcerative colitis, but they were present in one and possibly in two of eight synovial tissue specimens from patients with reiter's disease. complement-fixation tests were negative in nine patients with reiter's disease, including the two from whose synovial tissues pplo were thought to have been isolated.

.I 656

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recovery of a pleuropneumonia-like organism

(p.p.l.o.) from the genitalia of the female

albino rat

the genital organs of seventy-seven nonproductive breeder female rats were examined grossly and histologically and bacteriological cultures of the uterus and ovaries were made. three of the seventy-seven animals showed a purulent salpingitis and oophoritis. a pleuropneumonia-like organism was isolated from the uterus and ovaries of 29% of the animals examined. the cultures obtained from the genitalia were compared with the p.p.l.o. isolated from the middle ears of some of these same animals and the two appeared to be identical. intraperitoneal injection of the p.p.l.o. cultures into young rats and mice produced oophoritis and salpingitis in the mice but not in the rats.

.I 657

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chronic respiratory disease in mice and rats

chronic respiratory disease (crd) in both mice and rats embraces two separate entities, namely: infectious catarrh caused by mycoplasmas (pleuropneumonia-like organisms) and enzootic bronchiectasis by a virus.

the two syndromes are discussed in regard to their etiology, pathologic manifestations, and transmission. particular attention is paid to the relation of mycoplasmas to infectious catarrh. the morphologic and cultural characteristics of the catarrhal types of these organisms are considered from the standpoint of differential diagnosis. the importance of crd in the maintenance of breeding colonies and in the use of animals for experimental purposes is stressed. methods for the establishment of specific pathogen-free colonies, as a means of control, are briefly outlined together with observations on a cesarean-derived line of swiss mice.

.I 658

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further observations of the lymphomas

of african children

during 1963, cytopathogenic, filtrable agents were frequently encountered in cultures of embryonic human kidney cells following their inoculation with supernatant fluids from primary human amnion cultures which had previously been exposed to extracts of tumors and other specimens from east african children with malignant lymphomas of the kind described by burkitt and others. the results seemed noteworthy because they suggested an intimate association between the agents and the disease, and also because of the nature of the isolations which involved two phenomena, an initial induction of a peculiar spindling and twisting of the amnion cells

(fig. 1) and subsequently destructive changes

in kidney cells inoculated with fluid from such altered amnion cultures. the direct inoculation of embryonic kidney cells with extracts of tumors or bone marrow never caused cytopathogenic effects nor did the isolated, transmissible agents have the capacity to induce the amnion lesions. nevertheless, the two effects were closely associated and clearly related to the specimens. the cytopathogenic agents were later cultivated on protein-rich media and found to have the characteristics of mycoplasma. they failed to induce tumors in a variety of animals, and serologic tests in which they served as antigen gave suggestive but inconclusive evidence of a relationship to the disease. the mycoplasma also failed to induce the amnion lesions caused by the specimens.

.I 659

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mycoplasma species of man

at present, six distinct species of mycoplasmas are known to infect man. certain biological and ecological properties of these agents have been defined. one species, *m. pneumoniae*, has been definitely shown to be an important respiratory-tract pathogen, and another species, *m. hominis* type 1, may play a role in respiratory-tract and genital-tract disease.

.I 660

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pleuropneumonia-like organisms

despite their small size, the pplo carry the full complement of the chemical compounds and enzymes contained in larger bacteria and in cells. they contain both dna and rna, and in their independent metabolism they are essentially like other free living cells in contrast to the viruses which have no independent metabolism outside the living host cell. several strains of pplo have been cultivated from the mucous membranes of apparently normal human subjects, especially from the respiratory and urinary tracts. until recently, however, definite evidence of the association between the pplo and clearly defined clinical disease in the human sub-

ject was lacking. in 1962 it became evident that the so-called eaton "virus," originally isolated by eaton and his associates in 1944 from patients with primary atypical pneumonia, was in reality a pleuropneumonia-like organism. typical pplo colonies are produced on a cell-free agar medium which is enriched by the addition of blood serum or yeast. a number of strains of pplo has now been identified, and in recognition of their unique characteristics, they have been classified in a separate order, the mycoplasmatales, genus mycoplasma.

.I 661

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problems of disease of

parathyroid glands

if biochemical tests indicate unequivocally that there is a functioning parathyroid tumour, usually an adenoma, its removal will relieve symptoms and prevent any further damage to organs such as the kidneys. in 80 per cent, of such cases the operation is not particularly difficult to anyone with experience of thyroid surgery. the tumour is seldom of great size, usually less than half an inch in diameter, but a careful search in the expected position, in

close apposition to the posterior surface of the thyroid lobes, will usually reveal it. such adenomata are usually more brown in colour than the normal yellow gland; but in some 20 per cent, of cases one or more of the glands may be aberrant, or possibly absent, and supernumerary glands may be present. it is usually one of the lower pair of glands which occupies an ectopic position and, as i explained in the outline of the embryological development, it may accompany the thymus into the mediastinum, rather a vast area in which to seek a small tumour. such an exploration cannot be lightly undertaken, but if the evidence is indisputable the burden must be shouldered. it is correct policy, i believe, first to carry out a thorough exploration of the neck, and if this proves unavailing, to inspect the mediastinum through a sternum-splitting incision some two weeks later, rather than completing this major undertaking at one session.

.I 662

.W

the age factor in experimental hypertension of the dca type in rats

rats aged 25 and 86 days were sensibilised by unilateral nephrectomy and a week later were given 1.1 mg/100 g dca every third day for 6 weeks and a 1% nacl

solution to drink. the younger rats reacted with a greater increase in blood pressure, more so male rats. hypertrophy of the heart and kidneys and mortality and suppression of growth were also all more evident in the younger age group. only male rats given the steroid hormone starting from day 25 showed permanent suppression of growth.

.I 663

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response of a serum glycoprotein to tissue injury
and necrosis

1. the response to necrosis, hyperplasia and tumour growth

a serum glycoprotein of the rat underwent a 20-fold increase during 15 days growth of the walker tumour and this increase was not affected when the rats were treated with terramycin. the protein increased at the same or a greater rate when rats were subjected to ischaemic necrosis of one kidney or of two-thirds of the liver. boiled kidney tissue, on the other hand, had little effect upon the protein response, and kidney hyperplasia had none. it is suggested that this protein increase is a response to substances liberated from damaged or necrotic cells.

.I 664

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the natural history of autoimmune
disease in nzb mice

a comparison with the pattern of human
autoimmune manifestations

all mice of the nzb/bl strain spontaneously develop serological and
pathological evidence of autoimmune dis-

ease during adult life. the nzb/bl strain was developed by dr. marianne bielschowsky in dunedin, new zealand, by inbreeding from an outbred colony of mixed coat color. several inbred strains--nzb, nzc, nzo, nzw, nzy, and others, have been evolved in dunedin from the original colony. evidence for autoimmune disease in the nzb strain was first reported by bielschowsky, helyer, and howie who found evidence of an autoimmune hemolytic anemia. the dunedin group used the presence of agglutinins for ficin-treated red cells as the index of the disease.

.I 665

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the remaining kidney in irradiated survivors of wilms's tumor the intravenous urograms of 10 patients who had survived 5 years after irradiation for wilms's tumor were studied for kidney size and configuration. the diseased kidney had been removed by nephrectomy. the remaining kidneys had been subjected to varying doses of ionizing radiation at the time the area of the diseased kidney was irradiated. in none was there

evidence of atrophy. all were within the range of expected normal size and most of them were enlarged.

.I 666

.W

cellular proliferation and deoxyribonucleic acid synthesis in compensating kidneys of mice and the effect of food and water restriction

compensatory enlargement of the kidney occurred after unilateral nephrectomy in mice. fourteen days after the removal of one kidney the surviving renal tissue

6

weighed 23 per cent more than single kidneys from sham-operated animals. the hyperplastic response of the cortex on the second postoperative day was 8 times greater than that seen in the same zone of kidneys from sham-operated animals. by 10 days after surgery the mitotic index of the cortex returned to control values. the outer medulla also underwent hyperplasia but only on the second day following unilateral nephrectomy was the increase significant. an increase in mitotic activity was found in the inner medulla of surviving kidneys, but it was not statistically signifi-

cant.

both starvation for 48 hours and water restriction for 60 hours prevented the hyperplastic responses in the remaining kidneys 2 days after unilateral nephrectomy. when water was given 48 hours after unilateral nephrectomy (after 60 hours of water restriction) significant increases in mitotic activity were noted in the cortex of remaining kidneys on the fourth and fifth post-operative days. however, even after free access to food was allowed (after 48 hours without food) no significant increase in mitotic frequency of the remaining kidney was found.

deoxyribonucleic acid synthesis in control kidneys of mice was highest in the cortex and lowest in the inner medulla as revealed by radioautographic studies following the injection of tritiated thymidine. two days following removal of one kidney the labeling index of the cortex of remaining kidneys increased 3-fold. no statistically significant increases of deoxyribonucleic acid synthesis were noted in either the outer or inner medullary regions of the remaining kidneys.

.I 667

.W

compensatory renal enlargement

hypertrophy versus hyperplasia

after unilateral nephrectomy in the mouse, the compensatory growth of the remaining kidney is characterized by an increase in rna and protein synthesis within the first hour. dna synthesis remains unchanged for about 18 hours and then rises to a maximum at 48 hours. by the end of the fifth day, when dna synthesis has passed its peak and is in decline, cellular hyperplasia has accounted for only one-fourth of the increase in kidney weight. thus it is shown that cell hypertrophy is both the primary and the predominant response in the early phase of compensatory renal enlargement.

.I 668

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cell proliferation

in experimental hydronephrosis

and compensatory renal hyperplasia

mitosis counts and autoradiographic counts of nuclei labeled with tritiated thymidine were made in the renal cortex of male rats in which the left ureter was ligated. these were compared with corresponding counts in the remaining kidney after left nephrectomy, and in sham-operated controls 24, 48 and 72 hours after operation. the cortex of the kidney on the obstructed side showed a greater number of tritium-labeled nuclei and mitotic figures than in the kidney undergoing compensatory hyperplasia. epithelial and interstitial cells responded simultaneously on the obstructed side, whereas in the remaining kidney after

nephrectomy, the epithelial response preceded a slight interstitial response by 48 hours. the contralateral kidney in rats subjected to ureteral ligation showed no response.

we concluded that the early response of increased dna synthesis and cell division in the obstructed kidney was not mediated by humoral factors; it was localized and probably had a different mechanism than the proliferative response occurring in compensatory renal hyperplasia.

.I 669

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renal factors in the pathogenesis of hypertension

renal arteriography and other modern diagnostic procedures have provided the means of establishing a close relationship between high blood pressure and renovascular disease. many of these cases are amenable to surgical cure. at the present time there is no single test for the definitive diagnosis of renal hypertension. careful and intensive studies are mandatory in the selection of cases suitable for surgery, since hypertension has many etiologic factors and involves many complex and sometimes obscure mechanisms. aortography, intravenous urography and split-function tests are among the most important methods for definitive diagnosis and for the planning of appropriate surgical procedures.

at operation, the most commonly observed cause of renal arterial constriction in the elderly is atherosclerosis, whereas in younger patients it is hyperplasia of the intimal and muscular coats of the renal artery and its branches. renovascular surgery may require a variety of technical procedures. in the successful cases there is a striking and permanent reduction in blood pressure.

the accuracy of blood pressure readings is emphasized, since hypertension

is usually discovered for the first time during the course of a routine physical examination.

.I 670

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cell proliferation in compensatory renal growth

rats with one kidney removed showed a progressive increase in weight of the remaining kidney over a six-week period.

autoradiographic and radiochemical studies with ³H-thymidine indicated that the increase in new kidney cell formation was maximal forty-eight to seventy-two hours after unilateral nephrectomy. this early response was chiefly due to the production of new cells by the renal cortical tubules. normal rates of tubule cell turnover were achieved two weeks after operation. the glomerular tufts contained fewer new cells and their peak production was delayed to the one-week period with a slow decline thereafter.

rats forty-eight hours after unilateral nephrectomy were chosen as a model to study the effect of various substances on the magnitude of new cell formation. the number of dna-synthesising cells in the stimulated kidney was reduced by treatment with hydrocortisone, acth, 9,10-dimethyl-1,2-benzanthracene, and 1,2-benzanthracene; the numbers were increased by the administration of deoxycorticosterone and aldosterone.

.I 671

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effects of adrenalectomy on

the parathyroids in nephrectomized rats

rat parathyroids were studied both after nephrectomy and after combined nephrectomy and adrenalectomy. as early as 24 hours after nephrectomy there were morphological indications of increased para-

thyroid activity in the form of increased glandular volume and enlarged cell nuclei. the corresponding changes after combined nephrectomy and adrenalectomy were less marked and the total serum calcium was higher than after nephrectomy only. these observations suggest that the adrenals could induce a change in calcium homeostasis opposite to that of the parathyroids.

.I 672

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pathogenesis of polycystic kidneys

microdissection confirms our previous description of an uncommon variety of polycystic kidney found only in the newborn periods. it is characterized by symmetrical enlargement caused by saccular or cylindrical increase in size of all collecting tubules. the number and relative length of different generations of collecting tubules are normal. nephrons are present in normal numbers, and their attachment to collecting tubules is normal. the pattern of the nephrons is normal except for minimal localized areas of dilatation. interstitial connective tissue is not increased. intrahepatic bile ducts are invariably cystic. siblings may be affected. we believe that in such kidneys the behavior of the ampullae of the branches of the ureteral bud is normal and that secondary

hyperplasia of the interstitial portions of the branches is responsible for the greatly increased renal size.

.I 673

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concurrence of hyperplasia and neoplasia of the parathyroid glands the concurrence of parathyroid hyperplasia and neoplasia in a group of six patients is reported. two patients had long-standing renal disease with azotemia and hyperphosphatemia. in both hypercalcemia developed while they were under observation and they were found to have parathyroid adenomas as well as hyperplasia of the other glands. a third patient followed an apparently similar course. one patient with primary hyperparathyroidism due to a large mediastinal adenoma displayed hyperplasia of other glands in association with moderate renal insufficiency. two patients with primary generalized parathyroid hyperplasia were found to have superimposed neoplastic lesions: multiple adenomatous nodules in one, adenocarcinoma in the other.

these observations add new dimensions to the diagnosis and therapy of parathyroid disorders. they indicate the necessity of examining all four

parathyroid areas at time of surgery. they also emphasize that hypercalcemia developing in patients with chronic renal disease is a manifestation of autonomous parathyroid function.

.I 674

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experimentelle nierenvergroberung nach unilateraler nephrektomie bei ratten
untersuchungen mit 3h-thymin

in this paper it is attempted to clarify certain questions as to the mechanism of compensatory renal hypertrophy by means of histological, cytological, and autoradiographical examinations in nephrectomy experiments on young and grown rats. based on the results of this investigation the process of compensatory renal hypertrophy must be imagined as follows:

as early as two hours after unilateral nephrectomy, a distinct increase of the mitosis index without a simultaneous increase in dna-synthesizing cells was observed in the remaining kidney. it is assumed that a cell division of polyploid cells is involved, which were in a prolonged premitotic rest phase. after a latent period of 48 hours, the dna-synthesizing cells and dividing cells start to increase. the maximum of the regenerative processes is reached between the 3rd and 4th day after nephrectomy. twenty days after unilateral nephrectomy, the regenerative processes are largely concluded.

all tubule sections participate in the compensatory renal hypertrophy.

although the regenerative processes are most marked in the central section, one cannot speak of the development of an actual indifference zone in the regenerating kidney.

in young test animals, compensatory renal hypertrophy is determined more

by mitotic cell division, in older test animals more by polyploidization processes.

the results of these investigations provide no certain indications for the assumption that amitotic nuclear divisions play a major part in compensatory renal hypertrophy.

proliferation processes which in extent and localization run parallel to the regeneration of the parenchyma, are also observed in the cells of the connective tissue of the renal vessels.

.I 675

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abscopal effects of whole-body
x-irradiation on compensatory hypertrophy
of the rat kidney.

the weight and dna content of normal growing (i.e., intact), and hypertrophying (i.e., following uninephrectomy) rat kidneys were obtained from several hundred sprague-dawley white rats. the effect of whole body x irradiation with 500 rad and local irradiation to the kidney with 1000 rad, was then determined by following the rate and degree of hypertrophy and the dna content of the kidney. when calculated on the basis of body surface area, a constant ratio of kidney weight and of kidney dna was found in the normal, non-hypertrophying kidneys of 5-12 week old rats. after 21 days of hypertrophy these values increased approximately 50 per cent over normal in rats 4-6 weeks old at the time of nephrectomy. for animals 6-14 weeks old at the time of nephrectomy the corresponding increase was only about 20 per cent.

following uninephrectomy and x irradiation with 1000 rad to the

exteriorized remaining kidney, 4 week old rats whose bodies were lead-shielded during irradiation showed no body weight growth retardation, no significant difference in the dna content of the kidney, and a small but significant decrease in weight increment of the hypertrophying kidney after 21 days.

rats exposed to 500 rad of x rays with the kidney shielded during irradiation, when compared with nonirradiated controls, showed body weight growth retardation, a reduction in the dna content of the kidney, and a reduction in the amount of kidney hypertrophy 21 days following uninephrectomy. a still greater inhibition of both kidney compensatory hypertrophy and the increase in dna content of the kidney occurred after 500 rad whole body irradiation.

food restriction in nonirradiated 4 week old rats resulting in body weight growth retardation, elicited a marked reduction in kidney weight and in dna content of the hypertrophying kidney 21 days after uninephrectomy.

it is concluded that the reduction in kidney hypertrophy following whole body x irradiation with 500 rad is due in some measure to an abscopal or indirect effect, secondary to decreased body weight.

.I 676

.W

radiation effects renal enlargement in the mouse
three hours following unilateral
nephrectomy weanling female cf-1 mice were
subjected to local abdominal or total body
exposure to either 500 or 600 r. other
groups were given 1350 r to half the abdomen

with and without prior nephrectomy. significant decreases in renal weight gain compared to controls were obtained in the 600 r total body group and in the locally irradiated animals given 1350 r. when the renal weight changes are compared on the basis of the ratio of renal weight to body weight in per cent, an increase from .64% to .95% is seen in animals subjected to nephrectomy alone. the final value in all of the irradiated and nephrectomized groups was similar, ranging from .93% to 1.0%. the results suggest that irradiation in these dose ranges does not exert a direct inhibitory effect on renal weight increase but it limits body weight gain which influences kidney weight.

.I 677

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renal hyperplasia and neoplasia
in rats given dimethylnitrosamine
multiple foci of hyperplasia and neoplasia were induced in the kidney
of rats that had been dosed orally with dimethylnitrosamine. the younger rats
and the male sex had a greater incidence of renal tumors. the hyperplastic
or neoplastic lesions were classified into two groups on the basis of their
histogenesis, namely that of tubular epithelial origin and that of interstitial
cell origin. dimethylnitrosamine is recommended as a useful chemical
compound for the study of renal carcinogenesis.

.I 678

.W

the role of age and x-irradiation on kidney

function in the mouse

female mouse kidneys show a decline with respect to age in the ability to concentrate the urine during a 24-hour water fast. x-irradiation early in life has no measurable long-term effect on this process.

kidney cortex slices of old female mice can concentrate p-aminohippuric acid against a concentration gradient equally as well as slices from young mice. there is no loss in this ability by cortex slices from young or old female x-irradiated mice.

it is uncertain whether compensatory renal hypertrophy after unilateral nephrectomy declines with age in nonirradiated mice. x-irradiation does cause a reduction in the degree of compensatory renal hypertrophy in the aging mouse. this reduction may represent a loss in the ability of kidney cells to undergo cell division.

the administration of testosterone propionate to old mice during compensatory renal hypertrophy results in an increased hypertrophy. the increase is relatively the same for irradiated and nonirradiated mice, indicating the lack of a long-term effect of x-irradiation to reduce the ability of a target organ to respond to a hormone.

the over-all conclusion of this study, with respect to "radiation-induced aging," is that x-irradiation of the female swiss mouse early in life does not have a pronounced effect on kidney function late in life but may have a long-term effect on those processes concerned with cell division.

.I 679

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hyperaldosteronism, hyperplasia of the juxtaglomerular complex, normal blood pressure, and dwarfism: report of a case

a patient with the syndrome of hyperaldosteronism, hyperplasia of the juxtaglomerular complex, dwarfism, and normal blood pressure is reported in detail. in this patient, the aldosterone secretion rate increased significantly and the serum potassium rose slightly with sodium deprivation. with a low-sodium diet urinary sodium fell to zero. spironolactone with a low-sodium diet raised serum potassium to normal. infusion of albumin, however, resulted in a rapid increase in serum potassium and a fall in aldosterone secretion rate. the unique features in this patient are the response to albumin and the lowering of urinary sodium to zero in response to a low-sodium intake. in all other essentials, the case resembles the two previously reported cases. treatment by subtotal adrenalectomy was not curative.

.I 680

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the juxtaglomerular cells of the kidney and the

zona glomerulosa of the adrenal cortex in the sodium losing and the hypertensive forms of virilizing adrenal hyperplasia

pathological and biochemical observations are presented in two cases of virilizing adrenal hyperplasia: one of the sodium-losing type and the other of the hypertensive type. examination of the kidneys revealed hypertrophy of the juxtaglomerular cells in the case exhibiting excessive sodium loss. the adrenal cortex showed hypertrophy of the zona glomerulosa. it is hypothesized that the chronic state of sodium loss caused changes in the intravascular compartment which led to compensatory activity of the juxtaglomerular cells with resultant stimulation of the zona glomerulosa.

examination of the hypertensive case (known to involve a different enzyme deficit) showed hypertrophy of the zona glomerulosa without hypertrophy of the juxtaglomerular cells. the intrinsic overproduction of sodium-retaining steroids associated with the genetic defect in this clinical form could account for both the hypertension and the absence of hypertrophy of the juxta-

glomerular apparatus.

.I 681

.W

studies on eperythrozoon infection in sheep

the intravenous inoculation of blood from sheep in the parasitaemic stage of eperythrozoon infection produced detectable parasitaemia in recipient sheep within 7 days. the parasitaemia lasted from 3 to 12 weeks and was accompanied by anaemia and occasionally by icterus. no other symptoms developed and in a controlled experiment on hogs there was no significant difference in weight gain between infected and control animals.

a concurrent attack of tick-borne fever led to the disappearance of eperythrozoon from the circulating blood. it is suggested that this phenomenon may be caused by the pyrexia.

the incubation period following the inoculation of infected blood in ten 3 to 4 week old lambs varied from 3 to 6 weeks. in eight of these animals the symptoms were less severe than in adult sheep, but the two smallest lambs developed a profound anaemia and failed to gain weight.

culture of the organism on sheep blood agar or on sheep kidney monolayers was unsuccessful as was the attempted transmission of the infection to mice.

the transference of keds and lice from infected to uninfected sheep failed to transmit the infection, but a sheep was infected by the intravenous inoculation of ground-up lice from an infected animal.

the only characteristic histopathological changes in infected sheep were lymphoid hyperplasia of the malpighian corpuscles in the

spleen and deposition of haemosiderin in the cells of the proximal convoluted tubules in the kidney cortex.

.I 682

.W

age differences in cellular

proliferation in rat kidneys

the hyperplastic response to unilateral ne-

phrectomy after 48 hours in the cortex and

medulla of the remaining kidneys of weanling

and young adult rats was studied by means of

autoradiography. tritiated-thymidine, which

is destined exclusively for nucleoprotein synthe-

sis, was administered to 11 control and 11 ex-

perimental rats 4 hours prior to sacrifice.

labeled tubular cells were rare in control

tissues, especially in medulla, where the per-

centages did not differ greatly for the two age

groups. in the cortex of controls such cells were

three times more frequent for weanling rats

than for adults. significant increases in per-

centages of labeled cells over control levels

were found in both regions of the remaining

kidneys for both age groups. the percentage of

increase was greater in medulla than in cortex

and most pronounced in medulla of the young

adult rats.

.I 683

.W

phospholipids of the sexual segment of the kidney of the

indian house lizard, *hemidactylus*

flaviviridis ruppell

the indian house lizard, *hemidactylus flaviviridis* breeds seas-

onally. in a sexually mature male lizard, from october to

may of the following year, the secondary and tertiary collecting

tubules of the kidney are hypertrophied forming the sexual seg-

ment. the development of the sexual segment is synchronous with

the testicular cycle and maximum development occurs during the

period when the testes are spermatogenically active. the sex-

ual segment is not developed in the females in any season of the

year; it is completely regressed in males during sexual quiescence

(june and july). injection of 4.0 mg of testosterone propionate

over two weeks stimulated the regressed sexual segment to hyper-

trophy in males during quiescence and also in females. the

apical portions of the cells of the sexual segment are loaded

with granular secretions which are stained with baker's acid hae-

matein and phosphomolybdic acid-stannous chloride, indicating the

presence of choline - containing phospholipids. the composi-

tion of the phospholipids of the sexual segment, which is a unique

feature of the lizards and snakes, is unknown. this preliminary

communication describes the isolation and quantitative estimation

of phospholipids present in the sexual segment of the indian house

lizard, *hemidactylus flaviviridis ruppell*.

.I 684

.W

(on the erythropoietic effect of different

tissue suspensions)

the stimulating effect on erythropoiesis of regenerated liver and hypertrophic kidney tissue after partial hepatectomy and unilateral nephrectomy respectively was studied in the rat by means of the erythrocyte count, haemoglobin determination, reticulocyte count and ^{59}Fe utilization. the reticulocyte count and ^{59}Fe utilization increased significantly after treatment with normal liver and renal tissue and more strongly after regenerated liver and hypertrophic kidney tissue. the same effect was seen after treatment with the sera of rats which had undergone partial hepatectomy or unilateral nephrectomy.

.I 685

.W

hemihypertrophy and medullary sponge kidney

congenital hemihypertrophy is an overgrowth of one side of the body which is associated with an asymmetry beyond the expected range. it is to be distinguished from hemiatrophy in which atrophy or withering of one half of the body has occurred, usually because of neurological lesions.

this condition of hemihypertrophy, though rare, is very frequently associated with other congenital abnormalities. these include several in the urogenital tract, such as hypospadias, cryptorchidism, unilateral renal hypertrophy and an increased incidence of wilms' tumour.

.I 686

.W

chemical aspects of compensatory renal hypertrophy

the effect of unilateral nephrectomy on the size and composition of the remaining kidney has been investigated in rats. in normal rats the right kidney is, on the average, significantly heavier than the left and has a higher total content of dna and rna. the 2 kidneys have almost identical ratios of rna/dna and protein/dna. after unilateral nephrectomy the surviving kidney increases steadily in wet and dry weight for the 1st 4 days after the operation. this is accompanied by a much slower increase in total dna content and by a dramatic increase in rna/dna ratio.

the rna/dna ratio in kidney is also affected by diet, being higher on a high-protein than on a low-protein intake. moreover, the rise in rna/dna ratio that follows unilateral nephrectomy is greater in animals fed a high-protein diet. the changes in kidney weight and in total contents of dna, rna, protein, and lipid phosphorus resulting from the feeding of a high-protein diet were found to be of approximately the same magnitude as those in the remaining kidney 4 days after unilateral nephrectomy. the rna/dna and protein/dna ratios are also greater in rats fed a diet containing 10% urea, but the increase is much less than that in the remaining kidney after unilateral nephrectomy.

.I 687

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the antidiuretic mechanism of hydrochlorothia-

zide in the treatment of diabetes insipidus

the changes in water and electro-

lyte balance during hydrochlorothiazide

therapy in 2 patients with vasopressin-deficient diabetes insipidus were studied. in 1 case, under fixed daily sodium intake, the urinary sodium excretion markedly increased on the first day of treatment, but the urinary volume began to fall on the second day and persisted low for 3 days after discontinuation of the drug. in the other case the urinary volume markedly decreased when the daily sodium intake was strictly limited. it further decreased on hydrochlorothiazide therapy but after sodium intake was restored it returned to the pretreatment level despite continued use of the drug.

the antidiuretic action of hydrochlorothiazide in the treatment of diabetes insipidus is believed to be related to the sodium depletion state of the body brought about by increased output or decreased intake of sodium. sodium and water reabsorption in the proximal convoluted tubules in the kidney increases and the amount of glomerular filtrate reaching the distal convoluted tubules decreases. thus the final

urinary volume falls.

.I 688

.W

the action of oral diuretics

in diabetes insipidus

chronic administration of chlorothiazide and

other thiazide analogues in diabetes insipidus

results in a striking reduction in urinary volume

with increase in urinary osmolality. this curious

antidiuretic action was first described by

crawford & kennedy (1959), and though it has

since been widely confirmed in both the pituitary

and nephrogenic forms of the disease, its precise

mechanism remains obscure. a number of

investigators have sought to explain the phenom-

enon entirely on the basis of the renal actions of

these drugs (earley & orloff 1962, goodman &

carter 1962), whilst others have contended that

abatement of polyuria may be secondary to a

central effect of the thiazides in decreasing thirst

(robson & lambie 1962, skadhauge 1963).

over the past two years, we have conducted

detailed in-patient studies of the action of

various diuretic drugs of the thiazide and other

series in a group of 7 patients with pituitary

diabetes insipidus.

.I 689

.W

investigations into the thiazide-induced antidiuresis in patients with diabetes insipidus plasma sodium, osmolality and serum chloride, together with creatinine clearance, were studied before and during thiazide treatment of 7 patients with diabetes insipidus.

the diuresis was reduced by 28-39%.

the urine osmolality was increased by

7-128%. an average decrease in plasma

sodium of 4 meq/l, in plasma osmolality

of 21 mosm/kg, and in serum chloride of

8 meq/l was observed. only in one pa-

tient was the creatinine clearance re-

duced significantly. the thirst-feeling was

reduced even from the first day of treat-

ment. the diuresis was not minimal until

the third to fourth day. if the diuresis was

corrected for the extra electrolyte ex-

cretion initiated by the thiazide, the

antidiuresis was found to be operating to

the full extent even on the first day of

treatment.

it is concluded that the antidiuresis is

mainly secondary to the natriuresis and to

a certain degree due to a decreased thirst-

feeling; but there seems also to be a direct renal action, involving at least a reduction of the glomerular filtration rate. a pronounced antidiuresis was found by a water deprivation test after thiazide treatment in one patient.

.I 690

.W

salt and water

the antidiuretic effect of thiazides is thus the result of the induced sodium deficit. the fall in serum osmolality may be contributory by reducing thirst. as depletion of body sodium will be self-limiting the major hazard to the use of thiazides is potassium depletion. treatment of patients with vasopressin insufficiency type of diabetes insipidus with thiazides is only indicated for those who are intolerant of hormone replacement. in nephrogenic diabetes insipidus thiazides have a more important therapeutic application.

.I 691

.W

nephrogenic diabetes insipidus

chlorothiazide has been found of value in establishing and maintaining adequate hydration in some patients; its exact mechanism of action is not known. the antidiuretic effects

of chlorothiazide and its analogues have been studied in six patients with ndi, two of whom were infants less than six months of age. dehydrated infants showed a dramatic response to treatment. with those unable to achieve an optimal fluid intake prior to treatment, the initial beneficial response was associated with an increased fluid intake. following this initial antidiuretic response, a variable degree of "escape" or resistance to the action of the drug commonly occurred. despite the unpredictability of a prolonged antidiuretic response, a therapeutic trial of chlorothiazide in ndi seems warranted if diet alone is not sufficient to maintain hydration. it must be remembered, however, that this drug is potentially toxic.

.I 692

.W

fluid and electrolyte metabolism in nephrogenic diabetes insipidus the body fluid volumes have been followed in two infants with nephrogenic diabetes insipidus. without treatment both patients had a low extracellular fluid volume (ecv) and a normal to low-normal total body water (tbw). following thiazide therapy (case 1) and during a

fluid deprivation test (case 2) a further reduction of ecv and tbw was found. untreated both patients revealed a severe hypernatremia without any increase in the urinary aldosterone excretion. the first patient had a cerebral atrophy and a rightsided hydronephrosis, a higher diuresis and a lower concentration capacity was found on this side. the patient was treated continuously with thiazide. when an ordinary house diet was given this drug could only maintain normal electrolytemia in combination with spiro lactone. a considerable increase in height and psychic development took place during this combined treatment. it is noted, that nephrogenic diabetes insipidus may be present in infants with unexplained fever and vomiting in the absence of polydipsia and polyuria. the urine may even be hypertonic.

.I 693

.W

diuretics in pediatric practice
clinical notes and comments
with the development of more and more potent oral diuretics in recent years, these

drugs which were once looked upon as being of only limited usefulness in pediatrics are now receiving clinical application. they permit a new approach to the management of edematous states. that most of them can be given orally is a significant advantage, particularly when coupled with their relative lack of toxicity. although the number of patients in the pediatric age range who require these agents is relatively small, they are valuable adjuncts in the management of chronic renal disease, refractory heart failure, and hypertension. this discussion reviews their pharmacology and clinical indications.

.I 694

.W

the role of aldosterone and vasopressin in the postural changes in renal excretion in normal subjects and patients with idiopathic edema
the effects of the upright posture
(leisurely walking for 2 hours) on half-hourly urine volume, and excretion of sodium and creatinine were studied in 13 normal subjects and 13 patients with idiopathic edema, while they drank 150 or 300 ml. of 0.14 per cent sodium chloride solution every half hour. when

the 2 hours of walking were compared with a preceding recumbent period of 4 hours, both groups were found to show a significant antidiuresis upright. the administration of ethanol during the last half hour of recumbency abolished the fall in urine flow and in free water clearance during the first hour of walking in the normal subjects and significantly reduced this fall in the patients with edema. sodium excretion in the normal subjects was slightly but not significantly lower when upright than when recumbent, but in the edematous patients was significantly lower when upright and fell progressively over the 2 hour period. administration of spironolactone or d-amphetamine increased sodium excretion during recumbency in both groups but increased sodium excretion upright only in the edematous patients to equal that of the normal subjects. creatinine excretion was not changed in either group by posture or drug therapy. similar studies were performed on 5 patients with untreated diabetes insipidus and on 6 patients with adrenal insufficiency treated

with hydrocortisone alone. lack of aldosterone (in adrenal insufficiency) did not increase the amount of sodium excreted above that of normal subjects in recumbency and did not prevent the occurrence of significant sodium retention in the upright posture. however, lack of adh (in diabetes insipidus) delayed the antidiuresis upright for 30 minutes. the results indicate that adh release is probably responsible for the reduction in urine volume during the first 30 minutes after assuming the upright posture, but not thereafter. the excessive magnitude of the orthostatic antidiuresis in idiopathic edema probably results from a cause other than adh release, since it is not completely overcome by ethanol. reduced na excretion during 2 hours in the upright posture can occur in the absence of circulating aldosterone, but the abnormal magnitude of the na retention in the patients with idiopathic edema probably results from hyperaldosteronism.

.I 695

.W

the use and mode of action of ethacrynic acid
in nephrogenic diabetes insipidus
the use of diuretic agents in the treatment
of nephrogenic diabetes insipidus had been re-
ported to result in decreased urine volume
and decreased clearance of free water. a
study of the use of ethacrynic acid, a potent
saluretic agent, was instituted in patients
with nephrogenic diabetes insipidus in an
attempt to achieve a significant antidiuretic
response while allowing a liberal sodium diet.
intravenous ethacrynic acid resulted in de-
creased urine volume, decreased clearance of
free water and decreased rpf and
gfr. prolonged oral administration of ethacrynic
acid promoted a significant antidiuretic re-
sponse when the daily sodium intake was
limited to 60 meq. the effect of ethacrynic
acid on renal function, potassium and chlo-
ride excretion, and uric acid metabolism are
discussed.

.I 696

.W

the treatment of pituitary responsive
diabetes insipidus

in evaluating therapy in diabetes insipidus, it is important to note we
are altering only ten per cent of the reabsorption function of the kidney.

the kidney function in a case of diabetes insipidus is as efficient in its activity as are biological tests. the purpose of therapy is patient convenience, economy, and normal function in society. the diabetes insipidus itself does not alter the life span, however, secondary factors may introduce it into a health problem.

lysyl-8-vasopressin nasal spray is effective, offers a maximum of convenience, and has produced no untoward reactions.

it is, as expected, ineffective in the treatment of extrapituitary (pituitary unresponsive) diabetes insipidus.

.I 697

.W

antidiuretic effect of hydrochlorothiazide

in diabetes insipidus

and ch'iu-an-lu

12 cases of diabetes insipidus

were studied during hydrochlorothia-

zide therapy under a fixed diet. the

symptoms, blood pressure, urinary

volume, blood and urinary electrolytes,

plasma volume, electrocardiogram and

hypertonic saline intravenous drip test

were compared before and after treat-

ment.

a daily dose of 100-150 mg

brought down the urinary volume to

about 50% of the pretreatment value.

the initial antidiuretic effect was noted

8 hours after medication and the maximal effect after the fourth or fifth day. owing to the kaluretic action of the drug, 2-4 gm of potassium salt was also given each day. satisfactory results were obtained with dietary sodium ion at not more than 200 meq daily, but ingestion of excessive table salt frequently diminished or even destroyed the therapeutic effect.

the physical signs, blood pressure and ecg were essentially unchanged and the plasma volumes were altered after treatment. the hypertonic saline test was improved in some of the patients.

low salt syndrome was frequently encountered as the therapy continued over 1 month. but this and even secondary failure could be prevented by timely use of intermittent or alternative regimen.

the therapeutic mechanism, indications and side effects of the drug were briefly discussed. the drug might possibly act through the mechanism of salt depletion, contraction of extracel-

lular fluid volume and decrease of renal glomerular filtrate, and in consequence urinary volume decreases and thirst is alleviated.

.I 698

.W

the effect of hydrochlorothiazide on water intake and plasma osmolality in diabetes insipidus in the rat

a fall in plasma osmolality accompanied the reduction of urine volume in rats with hypothalamic diabetes insipidus, given hydrochlorothiazide and an otherwise normal diet. the plasma concentration was not reduced with a high sodium intake, although urine volume still fell. normal rats and hypothalamic obese rats increased their water turnover after hydrochlorothiazide, yet their plasma concentration fell. moreover the antidiuretic response to vasopressin, which is purely renal, was also accompanied by plasma dilution; although it is self-evident that rats which drink less are less thirsty, the reduction in thirst after hydrochlorothiazide may not be a direct result of the change in plasma osmolality.

as previously shown in patients (kennedy and hill, 1963) a high sodium intake increased free water clearance in diabetes insipidus but did not interfere with the reduction of polyuria by hydrochlorothiazide, whereas a high potassium intake reduced free water clearance and prevented any effect of the drug on urine volume.

.I 699

.W

antidiuretic properties of chlorothiazide

in diabetes insipidus dogs

chlorothiazide was found to decrease urine volume and increase urine concentration in diabetes insipidus dogs.

there was no change in gfr, rpf, tmpah, plasma volume, extracellular fluid or total body water. the one consistent altered function was a decrease in "free water" clearance. diazoxide and mercurhydrin were not antidiuretic. it is believed that the antidiuretic action is dependent on the chlorothiazide-induced saluresis. although the mechanism of this antidiuresis has not been clearly defined, it seems best explained by postulating a decrease in filtrate reaching the distal nephron (giving a decreased final urine volume) coupled with inhibition of solute reabsorption in the distal tubule (preventing the selective reabsorption of solute in the distal tubule that is normally seen, accounting for the increase in urine concentration). the possible role of the mineralocorticoids in the antidiuretic response to chlorothiazide therapy was investigated in diabetes insipidus and adrenalectomized dogs. ad-

ministration of sodium-retaining steroids to diabetes insipidus dogs did not re-produce the urinary changes associated with chlorothiazide therapy. in addition, the antidiuretic response to chlorothiazide was not altered by adrenalectomy or spironolactone administration. therefore, the presence of the sodium-retaining steroids are not essential for the antidiuretic response of chlorothiazide in diabetes insipidus.

.I 700

.W

stable strontium in human bone: geographical and age differences in the united kingdom and their correlation with levels of strontium-90

a re-assessment has been made of published data of other workers on sr and 90sr in human bone. in different parts of great britain the mean ratio of stable sr to ca in adult human bones ranged from 240 to 475ug/g. extreme values were found even as close as 40 miles apart (carlisle v. westmorland).

perinatal levels of stable sr were correlated with adult levels. an estimate of placental discrimination may be derived from the ratio, perinatal level: adult level of about 0.7. the concentration of stable sr in bones of children from 2 to 5 years old or more was not demonstrably different from that of adults except in one area, carlisle. with the striking exception of london and south-east england the

change from perinatal to adult levels occurred in the 2nd year of life: there was no particular change during the first 9 months or so. in london and south-east england the pattern of change with age was quite different: there was a progressive rise in sr level from shortly after birth to the end of the 1st year by which time adult levels were reached. it is concluded that geographical differences need to be taken into account when making physiological deductions about turnover of bone salt from changes with age in the level of stable

sr. when children in the south-east of england and the rest of the united kingdom were compared, there seemed to be a broad inverse correlation between levels of stable sr and of

⁹⁰sr. detailed analysis of perinatal results from one area suggested that the level of stable sr in bone was somewhat higher in summer than in winter and somewhat higher in anatomically normal babies than in babies dying with gross congenital defects. ⁹⁰sr showed the seasonal change only.

.I 701

.W

fibrin and thrombosis in the central nervous system

in children with particular reference to

congenital hydrocephalus

while rare metabolic and degenerative diseases of

the central nervous system in children are reported

at great length, the much commoner diseases

relating to vascular incidents are rarely discussed.

only those aspects of disease of the central

nervous system related to thrombosis and the

deposition of fibrin will be discussed here; diseases

related to general vasculitis and aneurysm are omitted. the conditions discussed here fall into two main categories: first, the presence of thrombosis in small blood vessels or in the large superficial veins draining the brain, and second, the deposition of fibrin either in the ventricles or on the membranes overlying the brain in association with thrombotic lesions, haemorrhage, or infiltration.

.I 702

.W

hydrocephalus due to unrecognized cerebellar astrocytoma treated by ventriculoatrial shunt for four years

a case of a 9-year-old girl is presented in whom prolonged palliation of signs of increased intracranial pressure, presumed to be due to aqueductal obstruction, was achieved by means of a ventriculoatrial shunt. four years after placement of the shunt, signs of a cerebellar mass became apparent. the neoplasm, a cystic astrocytoma, was subsequently totally resected and the shunt was removed. air studies demonstrating diminution of ventricular size within this four year period are compared.

.I 703

.W

hydrocephalus

the problem of hydrocephalus, formerly a hopeless one, has in recent years begun to yield to clinical research. the indications for the new forms of treatment, and their drawbacks, are clearly delineated in this discussion by a leading authority in the field.

.I 704

.W

a case of unilateral hydrocephalus secondary to occlusion of one foramen of monro

a unique case of unilateral obstructive hydrocephalus secondary to occlusion of one foramen of monro by gliomatosis in a 3-day-old infant is reported.

.I 705

.W

calcification within congenital aneurysms of the vein of galen

thirty-one cases of aneurysm of the vein of galen had been reported previously. calcification within the wall of the aneurysm was visible on plain skull roentgenograms in 6 of this number. the present communication describes an additional case in which calcification of the aneurysm was discovered at the age of 9 years, the youngest patient heretofore reported.

.I 706

.W

ventriculo-venous shunts for infantile hydrocephalus
a review of 48 hydrocephalic patients treated with atrioventricular shunts during a 5-year period has been presented. we have

discussed function of the shunt, complications of the procedure, and revisions necessitated by nonfunctioning. the overall 75 per cent survival rate and 14.3 per cent infection rate is comparable to that in other series. the major cause of death in our patients has been infection.

our experience to date supports the observation that spontaneous arrest of the hydrocephalic process does not occur once a ventriculo-venous shunt has been established.

meticulous introduction of a ventriculo-venous shunt appears to be the present treatment of choice for patients with severe hydrocephalus. results are only satisfactory when the patients are carefully followed and complications recognized and treated promptly.

.I 707

.W

congenital malformations of c.n.s.

it seems that only a small proportion of malformations of the central nervous system can be explained in simple genetical terms and that most are dependent, to some extent at least, on environmental factors. the nature of these has yet to be determined. dr. williamson found that the maternal aunts,

uncles, and cousins of her index cases of anencephalus and spina bifida were more frequently affected than the paternal relatives were. she suggested that mothers of affected children had some genetic factor which modifies the intra-uterine environment and thus predisposes the embryo to these malformations. such a hypothesis opens up interesting possibilities, but before accepting it one would have to be satisfied that the higher incidence in maternal relatives is not merely due to the fact that the history is obtained in most cases from the mother.

.I 708

.W

experimental studies on cerebrospinal
fluid flow

a mixed suspension of kaolin and lyco-
podium was injected into the cisterna magna
of dogs. blockade of csf space was produced
successfully in 63 of 75 dogs; in 48 of the 63,
ventricular dilatation of more than interme-
diate degree was observed.

in these hydrocephalic dogs experimental
shunting was performed either between the
lateral ventricle and the lumbar cistern or be-
tween the unilateral lateral ventricle and the
contralateral cerebral subarachnoid space. uni-
directional, steady csf flow averaged 0.15 ml. per
hour in the cases of the former shunting,

and the flow averaged 0.25 ml. per hour in the cases of the latter shunting.

csf flow rate from the ventricle toward the cerebral subarachnoid space was larger when intraventricular pressure was higher. this increase in flow rate parallel to increasing pressure probably results from an increase in csf absorption. there seems to be an upper limit of the flow rate as the pressure is raised.

transient reflux of csf flow was induced by jugular or abdominal compression.

following intravenous administration of hypertonic solutions, csf flow rate decreased parallel to the fall of csf pressure and regained the original value as the pressure was recovered. when the pressure fell as low as 50 mm. of water the flow almost stopped.

.I 709

.W

the dandy-walker syndrome

the dandy-walker syndrome is a specific morbid entity in which the fourth ventricle is grossly dilated and there is a congenital malformation of the cerebellar vermis. it is nearly always associated with atresia of the foramen of magendie, and in many cases with atresia of the foramina of luschka also. the

lateral and third ventricles are usually dilated.
figure 1 illustrates a specimen of the condition.
most cases present in infancy, but others are
discovered in childhood and in adult life. the
oldest patient recorded to have had this anomaly
was aged 59 years. the first recognized case
was published by dandy and blackfen in 1914,
but the best early description of the condition
is that of taggart and walker (1944), who
concluded that the cerebellar lesions were
consequent upon the atresia of the foramen of
magendie. in 1954 benda proposed the term
"dandy-walker syndrome".

.I 710

.W

a probable epidemic of congenital
hydrocephalus in 1940-1941
a peak in the incidence of congenital hydrocephalus in 1940-41 is described;
reasons are given for believing it to be a genuine phenomenon, though it is too
late to find the cause.
epidemics of malformations are to be detected promptly only if the incidence
of malformations in a defined population is studied continuously; and for some
epidemics the population studied must be very large indeed.

.I 711

.W

functional craniology: an aid in
interpreting roentgenograms

of the skull

analysis of the form of the skull is

facilitated by considering it to be composed

of a number of functional components. for

the roentgenologist's purposes, division into

the facial or somatic skeleton and the neu-

ral skeleton is valuable, as is the recognition

of three functionally separate portions

within each calvarial bone: the inner table,

the diploe and the outer table.

the base of the skull is the only por-

tion that is preformed in cartilage. this ac-

counts for the unusual appearance of the

skull in achondroplasia. in addition, the

base apparently is more closely related to

facial and general somatic growth than to

neural growth.

calvarial bone forms directly from

membrane within the cerebral capsule.

consequently, the size and shape of the cal-

varia directly reflect the form of the grow-

ing neural mass.

the inner table of the calvaria at all

ages is intimately related to the dura mater

and directly reflects the form of the dura

mater. consequently, the inner table re-

flects the form of the arachnoid mater and,

usually, of the brain as well.

the outer table of the calvaria serves not only to protect the brain but also to anchor many of the intrinsic and extrinsic muscles of the skull. its form, particularly in thick-skulled mammals such as the pig, is determined more by the demands of these muscles and of the scalp than by the form of the brain.

the principal function of the diploe is to form a lightweight yet rigid separation of the two osseous tables. in addition, it serves as a site of hematopoiesis; for this reason it may tend to a specific volume at a given age.

the calvarial sutures oppose separation of the bones of the calvaria while allowing relative motion between them.

when the calvarial bones are passively carried apart with the expanding cerebral capsule by the growth of the neural mass, their areas are increased by the deposition of bone in the suture margins. the sutures, however, do not function as epiphyses and have no innate growth potential: removal of a suture does not disturb final skull form. because the calvaria represents ossi-

fication of the cerebral capsule, it is small when the neural mass is small. the deformity of the skull and the secondary changes that occur in the air sinuses and the diploe can be explained in terms of the functional cranial components. the opposite changes occur when the neural mass is abnormally large.

the correlation between skull size and intelligence is only fair. the presence of a brain of distinctly abnormal size, however, may be inferred from plain roentgenograms of the skull.

premature closure of the cranial sutures may be due to an abnormal form of the cranial base and possibly of the primitive chondrocranium that precedes it. the abnormality is mediated through the dural fiber tracts that underlie the major calvarial sutures.

.I 712

.W

hydrocephalus: changes in formation and absorption of cerebrospinal fluid within the cerebral ventricles
formation, flow and absorption of cerebrospinal fluid were measured in normal

and progressively hydrocephalic dogs by steady-state studies during ventricular perfusion. the formation of cerebrospinal fluid was found to be constant, independent of hydrostatic pressure, and unaffected by the development of hydrocephalus. the normal dog produced 0.016 ml. cerebrospinal fluid/min. in the lateral ventricles, 0.011 ml. cerebrospinal fluid/min. in the 4th ventricle and 0.20 ml. cerebrospinal fluid/min. in the subarachnoid space. the intraventricular formation of fluid was calculated to be 0.24 ml. cerebrospinal fluid/min./gm. of choroid plexus, and 0.3×10^{-3} ml. cerebrospinal fluid/min./cm.² of ependymal surface.

absorption of cerebrospinal fluid was found to take place within the ventricles as well as in the subarachnoid spaces. the resistance to absorption of cerebrospinal fluid in the normal ventricle was much higher than in the hydrocephalic ventricle. the decrease in resistance occurred as the ventricular volume increased and the ependyma became flattened so that in chronic hydrocephalus the resistance was not significantly different than in the normal dog. the theory of restricted diffusion was applied to the data to

calculate the diffusive permeabilities of creatinine and urea, and from this the mean pore radius within the ventricle.

using formation of cerebrospinal fluid

and data on absorption, the hydrocephalic

animals could not be distinguished from the

normal with sufficient accuracy to suggest

using this as a clinical test. the reason for

this is that intraventricular pressure has

always been considered as if it were constant

when, in fact, it is changing constantly. the

problem of ventricular enlargement concerns

the ability of the craniospinal contents to

adjust to and absorb the small but very rapid

changes in intracranial contents that occur

with each beat of the pulse.

.I 713

.W

dural sinus pressure

in normal and hydrocephalic dogs

simultaneous measurement of cerebro-

spinal fluid pressure (csfp) and venous

pressure in the anterior (ssvp) and poste-

rior sagittal sinus (tvp) has demonstrated

that in the normal dog the mean pressures are

related as follows:

csfp>ssvp>tvp. the statistical relationship between the pres-

tures has shown a poor correlation of ssvp and tvp with changes in csfp. on the other hand, in the hydrocephalic dog, ssvp rises to meet csfp and is related to fluid pressure in a 1:1 fashion. this could be expected to cause a "non venting" of acute changes of csfp and a decrease in fluid absorption. it is postulated that the mechanism of ssvp elevation is a partial occlusion of the sinus.

.I 714

.W

intraventricular papilloma

a case of intraventricular papilloma of the left lateral ventricle is reported. craniotomy was performed and removal of the tumor was accomplished without incident.

the literature is reviewed.

an unusual although perhaps relatively unimportant observation in the reported case was that for four or five days postoperatively the patient, a 17-month-old female, kept her head tilted to the right but at the time she left the hospital she was holding it erect and unsupported and was sustaining weight satisfactorily on both feet.

.I 715

.W

five-year comparative study of hydrocephalus in children with and without operation (113 cases) on the basis of a 5-year study of 113 hydrocephalic children of whom 65 were operated on early with ventriculo-atrial shunting and 48 were not operated on, all of them having been studied periodically in a similar manner to determine mortality, morbidity, intelligence, and related factors, the following conclusions are justified:

the program in which shunting operations were done apparently gives significant advantages to the children over the program in which no shunting operations were done (based on life-table data projected from birth to 10 years)

survival: 61.8 per cent as compared to 22.2 per cent;

number of competent children (i.q. of 75 or better): 33.8 per cent vs. 5.5 per cent;

number of noncompetitive children (i.q. below 75): 27.6 per cent vs. 16.7 per cent.

the major cause of death and morbidity in both groups is infection.

in the operative group, morbidity

associated with the shunting procedure is related to obstruction of the shunt and septicemia. the early occlusions show a correlation with abnormal, inflammatory type of spinal fluid being shunted into the blood stream. the late obstructions are associated with mechanical breakage of the shunt or factors of growth causing retraction of the cardiac end from the atrium. prompt re-establishment of a functioning shunt has been possible in all instances. periodic follow-up examinations, irrespective of symptoms, have proved invaluable in early recognition of malfunctioning shunts. septicemia usually required removal of the shunt.

from the program of periodic evaluations, including "bubble" ventriculograms, studies of clearance of risa, and psychological testings, correlations showed: intellectual ability seemed associated with width of cerebral mantle; width of cerebral mantle in hydrocephalus decreases with ventricular pressures of 120 or over; it increases with pressures less than this; prolonged shunting of cerebrospinal fluid can give dramatic increase in

width of cerebral mantle, apparently
irrespective of basic etiology of the
hydrocephalus;
intellectual capacity could not be cor-
related with the basic etiology of the
hydrocephalus, but did correlate in-
versely with duration of increased in-
tracranial pressure.

the many etiologies of hydrocephalus
require large numbers of patients in each
group for thorough evaluation. factors
favoring such studies should be carried out in
medical centers where appropriate disciplines
can study in depth. prevention should be the
ultimate goal.

in the operative group, only 1 patient
compensated his hydrocephalic process and
no single patient demonstrated "arrest" of or
recovery from the basic hydrocephalus-pro-
ducing process in spite of numerous attempts
to demonstrate this. this might imply a
necessity for life-long shunting of cerebro-
spinal fluid in these cases.

.I 716

.W

hydrocephalus

any present day definition of

hydrocephalus is very loose. the authors would rather adopt the concept that hydrocephalus is an abnormal condition characterized by excessive amount of cerebrospinal fluid with or without enlargement of the head.

the most common cause of hydrocephalus is arachnoiditis followed by congenital anomalies. a neoplasm is a rare cause.

the ideal surgical procedure is the placement of a ventriculo-atrial shunt, using either pudenz or halter valves. where these valves cannot be availed of the choice is between a conservative waiting with medical support and ventricular tapping from the older surgical shunting procedures, like, ventriculo-peritoneal, choroidoplex-ectomy, thecal-fimbria, subarachnoid-ureteral, and others.

.I 717

.W

recognition and treatment of hydrocephalus following spontaneous subarachnoid hemorrhage

eight adult patients with hydrocephalus secondary to spontaneous subarachnoid hemorrhage have been presented with a discussion of diagnosis and treatment. a number of possible mechanisms for the development of ventricular dilatation in this condition have been advanced and pathological data have been presented in 2 cases.

.I 718

.W

congenital malformations.

clinical and community considerations

two of the most significant medical

events of the century, the epidemic of

post-rubella anomalies in australia

during 1940 and 1941 and the pan-

demic of thalidomide embryopathies

in europe and elsewhere during 1960

and 1961, have demonstrated clearly

the importance of monitoring programs

to record the occurrence of congenital

malformations at group (for example,

hospital) and community (especially

city) levels. the principle of report-

ing malformations and utilizing the

data for service programs or, better

still, for prevention, is not new, but

the methodical use of vital statistics in a scientifically constructed surveillance system is new. so also is the joint endeavor on the part of clinicians, public health workers and basic scientists to reconstruct an epidemiology of deformity on the basis of time, place, person distributions of malformations. a primary need has been for standardized methods of classifying and reporting congenital malformations.

.I 719

.W

the family history of spina bifida cystica the family histories of 722 infants who were born with spina bifida cystica were studied.

the index cases were referred for surgical treatment and were not selected in any way from the genetic point of view.

intensive inquiries were made to obtain a complete family pedigree, including a prospective follow-up of siblings born after the index case.

of 1,256 siblings 85 or 6.8% had gross malformation of the central nervous system: spina bifida cystica in 54, anencephaly in 22,

and uncomplicated hydrocephalus in 9.

of 306 children born after the index

case 25 (8%) or 1 in 12 were affected.

there was a progressive increase in

multiple cases in the family with increasing

family size. in sibships of five or more, mul-

tiple cases occurred in 24.1%.

in 118 families cases of gross malfor-

mation of the central nervous system were

known to have occurred among members of

the family other than siblings. cases oc-

curred in three generations.

it is possible that spina bifida cystica

might be a recessively inherited condition.

.I 720

.W

pulmonary vascular changes complicating

ventriculovascular shunting for hydrocephalus

a patient is described in whom pulmonary hypertension and cor

pulmonale were noted 3 years after placement of a ventriculovascular

shunting apparatus for treatment of hypdrocephalus. in addition,

the histologic sections of lung tissue obtained from 65 patients with hy-

drocephalus who died at various intervals following placement of a

ventriculovascular shunting apparatus were reviewed with regard to vas-

cular alterations. a high incidence of "old" and "multiple" pulmonary

vascular lesions was found in this group compared to the incidence

in control subjects. this difference can be attributed to the operative

procedure. the lesions in postmortem material were not widespread and did not suggest the diagnosis of pulmonary hypertension on purely histologic grounds.

.I 721

.W

etiology of trypan blue induced antenatal

hydrocephalus in the albino rat

wistar strain albino rats were injected with 1 cm³ of a 1% solution

of trypan blue. three types of dye were used: matheson, coleman and bell,

chroma-gesellschaft and a highly purified sample. the dyes were injected on

days 6, 7, and 8 of gestation. fetuses were excised from days 16 through 20,

fixed, decalcified where necessary, embedded in paraffin, serially sectioned

and stained. newborn young were treated similarly. chroma-gesellschaft

trypan blue was without reproductive or teratogenic effect at the above doses.

increasing the dose did not increase the teratogenicity but did yield a

decrease in litter size. both matheson, coleman and bell trypan blue and the

purified sample were teratogenic. the most frequent neural defect observed

was hydrocephalus. serial sections of the newborn hydrocephalics showed an

occluded or extremely stenotic aqueduct of sylvius in 31 of 33 sectioned

animals. the fetuses collected from days 18 through 20 also had occluded or

stenotic aqueducts if hydrocephalic. aqueductal stenosis or occlusion was

present in 17-day-old fetuses, but hydrocephalus was not conclusively

demonstrated at this age. sixteen-day-old fetuses did not have aqueductal

occlusion in any of those examined, but stenosis was evident. it is concluded

that the defect predisposing to hydrocephalus in the young of trypan blue

treated rats of this strain is aqueductal stenosis or occlusion.

.I 722

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bilateral papilloma of the choroid plexus

a rare case of bilateral papilloma of the choroid plexus in a five-and-a-half-year old hydrocephalic girl is presented.

the tumor encountered at autopsy was not suspected during life, the existing hydrocephalus being attributed to either cytomegalic inclusion disease or toxoplasmosis. after post mortem examination, it was evident that the hydrocephalus was due to two factors; hypersecretion from the tumor itself, and obstruction at the level of the sylvian aqueduct by a delicate, tense, translucent membrane.

an interesting and uncommon additional feature of this case was the presence, within the choroidal papilloma, of well-formed haversian bone.

a plea is made for regularly considering papilloma of the choroid plexus in the differential diagnosis of hydrocephalus in children, for here, early diagnosis and treatment might conceivably result in total cure.

.I 723

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the diagnosis of hydrocephalus

the early diagnosis of hydrocephalus is imperative if definitive steps for its correction are to be effective.

transillumination is a fairly accurate

procedure that may offer the earliest means of determining whether or not the infant's head is enlarging. however, serial head measurements constitute the easiest and most accurate method for early detection of hydrocephalus. charts of normal head size of full-term and premature infants are available to aid the physician in evaluating any deviation from normal. once the condition has been detected, it is up to the neurosurgeon to determine the treatment plan. the operative procedure most widely used for shunting the excessive cerebrospinal fluid is insertion of a spitz-holter valve. early detection and improved treatment methods will help prevent irreversible intellectual damage likely to develop if hydrocephalus continues unchecked.

.I 724

.W

infantile hydrocephalus and hematoma in the posterior fossa we have presented a case of hydrocephalus in an infant, the basic cause being intracranial hemorrhage in the perinatal period. surgical re-

removal of a hematoma in the posterior fossa did not give permanent relief of the raised intracranial pressure. a lumbar air study at this stage disclosed information that the passage through the intracerebral cerebrospinal-fluid pathways was normalized whereas the extracerebral ones still were occluded by arachnoiditis. the condition necessitated a ventriculo-atrial shunt.

.I 725

.W

urinary excretion of ¹³¹I-diodrast injected intraventricularly in communicating hydrocephalus and aqueduct stenosis in nine cases of expansive infantile hydrocephalus were investigated by injecting small amounts of ¹³¹I-diodrast intraventricularly. urinary excretion of the tracer was determined during the first 4-5 hours after injection. the cumulative excretion of diodrast from the c.s.f. differs in cases with communicating hydrocephalus from those with stenosis of the aqueduct. the investigation is rapid and easily performed and has not produced any side effects.

.I 726

.W

gastrointestinal

ulceration and central nervous system lesions

there is both a real and an apparent increase in the incidence of severe gastrointestinal ulceration due to central nervous lesions. some of this increased incidence reflects recently devised iatrogenic measures including new drugs and surgical therapy.

in adults, cerebrovascular lesions are the commonest single cause of acute peptic ulceration found at autopsy. in children, we found 25 instances of upper gastrointestinal ulceration due to central nervous system lesions in 1,750 autopsies. two general anatomical categories could be recognized: acute ulceration and malacias.

a variety of causative central nervous system lesions was responsible in these 25 cases, the commonest being bacterial meningitis.

other causes were poliomyelitis, brain tumor, hydrocephalus, etc. theories of pathogenesis are presented.

more experience with both drug and surgical therapy is needed. the recent development of local freezing techniques offers promise for reduction of mortality.

.W

mansonia crassipes as the natural vector of filarioids, *plasmodium gallinaceum*

and other plasmodia of fowls in ceylon

it would appear from these

observations that

m. crassipes is the natural vector of

p. gallinaceum of fowls

in ceylon and possibly of other

species of *plasmodium* of

fowls or of related avian hosts.

if one of the other

plasmodia from *m. crassipes* is

in fact *p. lophurae*

then this will be the first record

of *p. lophurae* from

this part of the world. we are,

however, not certain

whether the fowl is the natural

vertebrate host of

p. lophurae in ceylon.

we have seen crithidial forms in

the midgut of engorged

wild-caught *m. crassipes*. this

mosquito may, therefore,

prove to be the vector of the

trypanosome as well. the

trypanosome differs from

trypanosoma gallinarum and
t. calmettei which have previously
been reported from
fowls.

.I 728

.W

filariasis in portuguese timor, with observations on a new microfilaria
found in man

the results are described of an
investigation into filariasis in portuguese timor.

two types of microfilariae were
found in blood films: one was wuchereria bancrofti
and the other, referred to as the timor
microfilaria, is probably a new species.

blood surveys showed that
w. bancrofti and the timor microfilaria were widely
distributed in the territory but that infection
rates were usually low.

clinical lesions were few and mild;
elephantiasis was confined to oedema of the
lower limbs below the knee.

the timor microfilaria resembles
that of brugia malayi in general staining
reaction and appearance and in the possession
of two nuclei in the terminal thread, but
differs in over-all length, in cephalic-space ratio,
and in failure of the sheath to stain with

giemsa. it is nocturnally periodic. it was rapidly removed from the peripheral blood by treatment with diethylcarbamazine citrate in daily doses of 9.3-13.3 mgm. per kgm. body weight or 3.3-5.0 mgm. per kgm. body weight for seven days. only damaged fragments of adult female worms were recovered.

the timor microfilaria was not found in cats, dogs or monkeys.

the vectors of filariasis in timor are still unknown.

.I 729

.W

dipetalonema obtusa (mccoy,1936) comb. n. (filarioidea: onchocercidae) in colombian primates, with a description of the adult microfilaria obtusa mccoy, 1936, was identified in the blood of 29 (31%) of 93 cebus capucinus and c. albifrons from northern colombia, but was not found in an additional 42 c. apella and 99 saimiri sciurea from other areas in colombia. the adult male and female, recovered from the periesophageal connective tissue of the infected animals, are described in detail. dipetalonema obtusa (mccoy, 1936) comb. n. resembles tetrapetalonema marmosetae faust, 1935, but is smaller and the right spicule is complex, not simple.

.I 730

.W

experimental onchocercal ocular lesions in the chimpanzee

this is the first attempt to produce

onchocercal eye lesions with microfilariae of

O. volvulus in the chimpanzee.

live microfilariae, once in the anterior

chamber of the eye, could penetrate the an-

gle of the anterior chamber, the iris, the

ciliary body, the choroid and the vitreous.

most of the microfilariae injected alive

into the anterior chamber of the eyes of the

chimpanzee died within a short time. com-

parison, therefore, could not be made be-

tween the effects of live and dead micro-

filariae.

microfilariae debris was demonstrated

within giant cells for the first time.

subconjunctival and limbal infiltration

with incipient pannus, inflammation within

the trabecular meshwork of the angle of the

anterior chamber and extensive active iri-

docyclitis were demonstrated in histologic

sections, although the conditions were clini-

cally quiescent.

the posterior segment lesion of oncho-

cercal chorioretinal degeneration could not

be reproduced.

subcutaneous and intravenous injections of worm extracts, derived from human onchocercomas, may have contributed to the onset of active choroiditis. this sensitization alone, without the intraocular injection of microfilariae, had no effects on the eye. various aspects of the pathogenesis of human onchocerciasis are discussed on the basis of present experimentation.

.I 731

.W

the occurrence of *dirofilaria magnilarvatum* price and *brugia* sp. in philippine monkeys of 356 *macaca philippinensis* examined, three were found infected with *dirofilaria magnilarvatum* price, 1959. one of these was infected also with a species of *brugia*. both species showed a sub-periodic type of microfilarial periodicity. these observations suggest that philippine macaques may serve as reservoirs for sub-periodic *b. malayi* on palawan, where high rates of infection have been found in people living in small villages in the forests. *mansonia bonneae* was found naturally infected with third stage larvae of *d. magnilarvatum*. it is suggested that monkeys may serve as reservoirs for sub-periodic *b. malayi* on the island of palawan, where high rates of infection with this species have been observed in people living in small villages in the forest.

.I 732

.W

the filarial parasites of the eastern gorilla in the congo

a survey for parasites has been undertaken in 20 mountain

gorillas (*gorilla gorilla beringei*) from the eastern congo kivu province.

six full-grown (two males and four females),

three adolescents

(one male and two females), and eleven

young gorillas were

examined, some of them during several

consecutive months. nine

autopsies were performed.

no protozoa were discovered in the blood.

plasmodium parasites

which are common in gorillas and chimpanzees

from west africa

were never found in the eastern congo primates,

including ten

other gorillas examined previously and some fifty chimpanzees.

severe diarrhoea with a balantidiasis picture developed in two

young gorillas. autopsy revealed however an intensive infection

with *oesophagostomum stephanostomum* and resulting fatty degenera-

tion of the liver. *oligotrichida* belonging to the genus *trogloodytella*

were commonly found in the intestinal tract. *oesophagostomum*

stephanostomum eggs were consistently present in the stools of

the gorillas and autoinfection caused the death of several young

gorillas 4 to 6 weeks after their capture.

many microfilariae were found in the blood and the skin. preliminary communications were published mentioning the existence of four different microfilariae in the blood of gorillas and of three others in the dermal layers of the skin. after a detailed study seven species have been identified and described: *dipetalonema leopoldi*, *d. gorillae*, *d. vanhoofi*, *d. streptocercum*, *microfilaria binucleata*, *loa loa gorillae* n.subsp. and *onchocerca volvulus*. three of the worms described have so far been discovered only in gorilla gorilla, namely *dipetalonema leopoldi*, *d. gorillae* and *loa loa gorillae*. two of them were previously known from the chimpanzee, namely *d. vanhoofi* and *microfilaria binucleata*. one species, *d. streptocercum*, first discovered in man and later described from the chimpanzee, is now also known from gorilla gorilla. *onchocerca volvulus* has been found in only one of the 20 gorillas examined. gorilla gorilla beringei in eastern congo might become through close contact with man and his filarial vectors an abnormal or accidental host of *d. streptocercum* and *onchocerca volvulus* or else might be considered as an original reservoir of these filarial parasites of man.

.I 733

.W

a pilot project for the control of filariasis

in thailand

in a village in kanjanadit district of surat-thani province, south thailand, where a field station for filariasis studies had been established by the bangkok school of tropical medicine, blood films were examined from 977 persons (95.5 per cent. of the total population of 1,023). two thick films (each of

20 c.mm.) were prepared from each person and stained with giemsa. it was found that 21.1 per cent. of the people harboured microfilariae (all *brugia malayi*). elephantiasis was found in 5.3 per cent. of the population. microfilarial periodicity was studied in 25 persons; in every case it was found to be markedly nocturnal. the blood of 98 cats, 52 dogs and two monkeys was also examined. no *b. malayi* larvae were recovered. mosquitoes were caught and identified. in an initial survey, 4,557 mosquitoes were examined, of which 568 were *mansonia* spp. in 4,136 dissections, *b. malayi* larvae in stage ii were found in one *m. uniformis* and in stage iii in another; the infection rate for *m. uniformis* was 0.6 per cent. spraying with ddt was carried out in all the houses during the last phase of the investigation. it resulted in a slight decline in the numbers and percentage of *mansonia* mosquitoes caught. diethylcarbamazine was administered to as many of the villagers as possible, in a dose of 5 mgm. of the citrate salt per kgm. body weight once weekly for six weeks. eight hundred and eighty-eight persons received the drug (86.8 per cent. of the population). considerable side-effects were observed in nearly all microfilaria-carriers. blood examinations were repeated one month and again one year after cessation of the drug. it was found that the proportion of microfilaria-carriers had decreased from 21.1 per cent. to 2.2 and 2.2 per cent. respectively, the filariasis infection rate from 26.1 per cent. to 8.6 and 8.5 per cent., and the mean microfilarial density of all films from 4.8 per 20 c.mm. blood to 0.48 and 0.12. larvae of *b. malayi* were not found in mosquitoes dissected one month and one year after the mass therapy.

.I 734

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studies on loiasis in monkeys.

iv.--experimental hybridization of the human and

simian strains of loa

in the cameroons rain-forest there exist two strains of loa, each apparently evolving in its own host-vector complex (duke and wijers, 1958). the natural simian parasite which is found most abundantly in the drill (*mandrillus leucophaeus*), is characterized by the large somatic size of the adult worms and microfilariae and by its nocturnal microfilariae periodicity. it is transmitted among the monkey population by the crepuscular canopy-dwelling *chrysops langi* and *c. centurionis*. the natural human parasite has diurnally periodic microfilariae and is transmitted by the day-biting anthropophilic *c. silacea* and *c. dimidiata* (bombe form). it can also be transmitted experimentally to the drill, in which host the parasites are of small somatic size and maintain their diurnal periodicity.

as the two strains of contrasting periodicity can be maintained in drills, it was decided to try cross-mating them to produce hybrids. the present paper describes the methods by which this was done, records the characteristics of the hybrid parasites, and suggests that, when interbreeding, the two strains segregate according to a simple mendelian pattern as regards periodicity and somatic size.

.I 735

.W

development of *dirofilaria immitis* in *anopheles quadri-*
maculatus after exposure of the microfilariae to a
freezing temperature
blood samples containing *dirofilaria*
immitis microfilariae were stored frozen for

periods ranging from 24 hr to 4 months,

thawed at 38 °C and

fed through an animal-derived bandrodie membrane to laboratory-reared *Anopheles quadrimaculatus*. the microfilariae were capable of developing to the third or infective larval stage and migrating to the head and labium of the mosquito.

.I 736

.W

advances in filariasis

especially concerning periodicity of microfilariae

a review is given of some advances in our knowledge about filariasis during the past ten years.

it is urged that investigations should be continued on methods to facilitate the control of filariasis in large populations, by means of

diethylcarbamazine--e.g. incorporation of the compound in cooking salt, as was done with chloroquine against malaria. furthermore, steps should be taken to protect young people against filariasis by systematic treatment in the schools.

in order to understand the cyclical disappearance of microfilariae from the peripheral blood and their accumulation in the lungs, the movements of microfilariae in the pulmonary capillaries has been studied by cinematography. apparently their accumulation in the lungs is not due to mechanical retention, but perhaps they migrate round and round in the pre-capillary network of arterioles.

the periodicity of microfilariae is best considered as a biological rhythm.

apparently the microfilariae have a circadian rhythm of their own which is entrained and synchronized by stimuli from the circadian rhythm of the host.

judging by experiments with monkeys containing microfilariae of *Edesonfilaria*

malayensis, the most effective of these stimuli from the host seems to be the rhythmic variation of body temperature which occurs every 24 hours.

.I 737

.W

attempts to transmit wuchereria bancrofti to cats and to a toque monkey there are no records of the larval development of wuchereria bancrofti in experimental animals. in attempts to transmit periodic w. bancrofti to domestic cats and to a toque monkey we recovered from one of the cats an infective larva that had undergone some development. this finding was reported in a preliminary note (dissanaike and nils, 1963); the present paper gives the experimental details and describes the larva.

.I 738

.W

the periodicity of microfilariae.

x. the relation between the circadian temperature cycle of monkeys and the microfilarial cycle.

monkeys were used whose blood contained the microfilariae of edesonfilaria malayensis, which has a nocturnal periodicity.

artificial lowering of the body temperature during the daytime caused the microfilaria count in the blood to rise; and artificial raising of the body temperature during the night caused it to fall almost to zero, i.e. inversion of the normal circadian temperature rhythm of the body was followed by inversion of the microfilarial rhythm.

the hypothesis is put forward that the circadian rhythm of the microfilariae of e. malayensis (but probably not of the microfilariae of some other species) is entrained by the circadian rhythm of body temperature, which thus provides the "effective stimuli" to which these microfilariae respond.

.I 739

.W

the periodicity of microfilariae

ix. transfusion of microfilariae (*edesonfilaria*) into

monkeys at a different phase of the circadian rhythm

this paper reports experiments in which microfilariae at one phase of their

circadian rhythm were transfused into a host at another phase of the circadian

rhythm, in an attempt to analyse the relative importance of the rhythms

inherent in the microfilariae and of those in the host for the production of

the well known periodic migrations. the experiments were performed with

edesonfilaria malayensis (yeh, 1960) present in a macaca monkey from thailand.

.I 740

.W

biliary tract morphology and prognosis

of biliary atresia

in 86 infants who did not have extrahepatic "hepatic" ducts, present

observation after use of artificial

bile ducts suggests that the presence of the

gallbladder may be of good prognostic significance in biliary atresia.

there are 11 long-term survivors (as of october 1965) up to 8 1/4 years of

age (100 months) after use of artificial bile ducts in 86 babies. a

gallbladder was identified in 10 of the 11 infants.

other specific factors for this prolonged survival pattern in these infants

with biliary atresia have not yet been identified, although suggestive

correlations among minimal hepatic fibrosis, maximal bile ductule

proliferations and the presence of the gallbladder were noted.

it is suspected that if any opportunity for long-term survivals exists for

infants to overcome the tragic occurrence of biliary atresia that the surgeon should avoid trauma to the hepatic pedicle.

we may be able to provide a "guarded" rather than a "pessimistic" prognosis when the gallbladder is found in the babies with biliary atresia.

.I 741

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current concepts in the management
of congenital biliary atresia
the current management of congenital
biliary atresia at the university of cali-
fornia, los angeles is reviewed.

biliary enteric decompression was
performed on 18 of the 27 patients, eight
of whom are presently alive (29.6%).

these figures are higher than the cure rate
of 8% previously reported.

described recently. five additional patients
with extrahepatic atresia underwent biliary
decompression by means of a hepatic
lymphaticojejunostomy.

early diagnosis of biliary atresia is im-
perative in order that any corrective sur-
gery may be performed before advanced
biliary cirrhosis develops.

.I 742

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congenital atresia of

the extrahepatic bile ducts

because congenital atresia of the extrahepatic biliary tract is almost always fatal, exception to this course becomes of interest.

the remarkable history of one such infant was reported in 1960 when he had attained the age of 2 1/2 years and, after three operations, he was in good health developing normally and free of jaundice. since he is now 8 1/2 years of age, has had two more operations, is still free of jaundice, and is again in good health, his further course since 1960 should be of interest.

.I 743

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neuroaxonal dystrophy in congenital biliary atresia

neuroaxonal dystrophy has been described in 8 patients with congenital biliary atresia. the characteristic changes include axonal dystrophy, a mild loss of nerve cells and a variable degree of astrocytic reaction, mainly in the gracile, cuneate and trigeminal nerve nuclei in the medulla, and rarely in other parts of the central nervous system.

the neuroaxonal dystrophy in these patients is remarkably similar to that in patients with prolonged mucoviscidosis and in experimental vitamin e-deficient rats.

it is strongly suggested that the neuroaxonal dystrophy in these patients with congenital biliary atresia is a manifestation of prolonged vitamin e

deficiency.

the neuroaxonal dystrophy in these patients is also similar to that seen in aging and bears resemblance to the axonal change encountered in a group of heredo-degenerative diseases, the various forms of "hallervorden-spatz disease". the pathological similarity between these diverse conditions warrants further investigation as to the possible metabolic relationship between them.

.I 744

.W

extrahepatic biliary atresia: comments on the frequency of potentially operable cases in a 10 year period, 35 infants with extrahepatic biliary atresia were encountered. twenty-eight babies, who were subjected to surgery and operative liver biopsy, are discussed. although an operable lesion was detected at laparotomy in only one baby, 5 further potentially correctable lesions were discovered in the 14 necropsies performed. review of the literature revealed that few authors have discussed necropsy findings and that confirmation of the diagnosis by liver biopsy has been neglected in many cases, including some of those claimed as surgical cures. it is concluded that the frequency of potentially operable forms of biliary atresia is not really known.

.I 745

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metabolism and excretion of c14-labeled bilirubin in children with biliary atresia and judson g. randolph radioactive bilirubin was injected intravenously into 3 children with biliary atresia. the isotope

over a period of ten to fourteen days was recovered principally in the urine. sixty per cent of the label in the urine was found to be in the form of bilirubin. distribution of the radioisotope was observed to be principally extravascular but not, as in other forms of jaundice, in the same distribution as albumin. daily turnover of bilirubin was several times greater than the calculated normal daily production of bilirubin. this was assumed to be due to increased hemoglobin breakdown, confirmed by survival studies of ⁵¹Cr-tagged red cells. the serum half-life of intravenously administered radioactive bilirubin may have useful prognostic value in children with biliary atresia.

.I 746

.W

central regulation of enzyme activity and synthesis in embryonal and adult mammalian tissues activity of non-specific hexokinase (hk) in soluble fraction and, particularly, in mitochondria of embryonal liver is much higher than in the adult rabbit; it decreases in the prenatal period, gradually approaching adulthood values postnatally (fig.1). embryonal liver lacks specific glucokinase (gk) (1,2), although during the second half of embryonic development there occurs incretion of insulin, known to induce gk synthesis in the liver of alloxan diabetic animals (3,4). activity of glucose-6-phosphate dehydrogenase (g6p dh) in soluble liver fraction is subject to quite similar changes during embryonic development.

.I 747

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ribonuclease activity in hepatic nuclei during development
mammalian liver undergoes marked qualitative and quantitative changes
during the development from the embryonic to the adult stage. many of these
events are associated with the derepression or repression of certain enzymes
which may be related to specialized subcellular activity. the involvement
of ribonucleic acid in the transcription of the information from the genome
into the construction of a finished protein molecule has prompted a study of
biosynthesis of the rna during differentiation. although considerable effort
in this regard has been expended in amphibian¹⁻⁵ and avian^{6,7} systems, as well
as in the sea urchin⁸⁻¹¹, a paucity of literature exists with mammalian liver.
accordingly, an investigation of the alterations in rna metabolism which
occur during the development of the rat embryonic liver has been undertaken.
this report concerns the fluctuations in nuclear ribonuclease during hepatic
development and some of the properties of the enzyme.

.I 748

.W

an electron microscopic study of developing gall
bladder epithelium in the rabbit
the gall bladder epithelium of the
adult rabbit consists of two types of cells.
the first and more common type shows features associated with absorption,
notably microvilli, limited pinocytosis, some lysosomes and an elaboration of
the lateral cell membrane and intercellular spaces. the mitochondria are
concentrated in a subapical band.
the second and more infrequent type is a dark rod-shaped cell of unknown

function but which may be a dehydrated epithelial cell.

foetal epithelial cells lack the functional adult characteristics; the mitochondria are uniformly distributed. in addition they display basal granules and apical apocrine bullae.

epithelial cell damage and white cell infiltration occurs between 24 days after birth or just after.

just before birth some epithelial cells are very large and pale with smooth outlines, others are more dense and display vigorous pinocytosis.

adult characteristics are acquired at or immediately after birth and pinocytosis subsides. it is believed that water resorption occurs before the functional changes which allow continuous passage of water into the circulation.

.I 749

.W

congenital anomalies of the cystic duct

and phineas rabinovitch

anomalies of the cystic duct, of four different types, are reported. the characteristic anatomic appearance and embryonic development of each of these anomalies are described and the clinical and surgical significance discussed.

.I 750

.W

lesions of the liver in hereditary

metabolic diseases

whether the various cells of the liver, both parenchymal and stromal,

receive genetic misinformation in all hereditary diseases caused by gene mutation is unknown, but the metabolic capabilities of these several cell types are so diverse that it is not surprising that their involvement in many such diseases can be demonstrated by clinical, pathological, or biochemical methods. repetitive abnormality of the liver has apparently not been defined for any disease caused by quantitative (i.e., chromosomal) gene anomaly, whether produced by nondisjunction, translocation, or major deletion, perhaps because relatively few such diseases have been described. as a result, the genetically determined disorders of the liver surveyed in this paper appear to be the result of conventional "single gene" abnormalities, and to be transmitted in affected families by mendelian mechanisms.

.I 751

.W

acid catabolic enzyme activity in relation to accessory limb and cancer initiation in amphibia cathepsin and acid phosphatase were determined in livers and kidneys of adult rana pipiens and triturus viridescens. organ-specific and species-specific differences in distribution of these enzymes were found, as well as considerable differences in the effect triton x-100 on the two enzymes. a heterogeneous population of lysosomes in respect to enzyme content and stability is deduced.

we have found positive correlations between catheptic activity of the implant and host tissue dissociation, and between acid phosphatase and inducibility, as features of the phenomenon of implant-induced accessory limb formation in urodeles. further, we have found a positive correlation between catheptic activity and resistance to virus-induced renal adenocar-

cinoma development in rana pipiens.

.I 752

.W

neonatology

considerable progress has been made in the knowledge of bilirubin metabolism since the characterization of "direct" (conjugated) bilirubin as an ester glucuronide. the metabolic pathway involved in this hepatic conjugation is now well established and has been the subject of excellent reviews by sherlock and billing.

sherlock's diagrammatic representations of bilirubin metabolism (fig. 1) and of the possible mechanisms of jaundice (fig. 2) are reproduced here because they furnish a clear picture to serve as a reference point for the discussion to follow.

it is interesting to re-examine current concepts of the etiology of physiologic jaundice with this diagram in mind. jaundice may occur for a number of reasons, described below.

.I 753

.W

red cell glucose-6-phosphate dehydrogenase deficiency--a newly recognized cause of neonatal jaundice and kernicterus in canada seven male newborns of chinese, greek and italian origin presented with severe hemolytic jaundice due to red cell glucose-6-

phosphate dehydrogenase (g-6-pd) deficiency. In five, the hemolysis was precipitated by inhalation of mothball vapours in the home. Kernicterus was evident upon admission in six infants and was fatal in four of these.

g-6-pd deficiency should be suspected as a cause of jaundice in all full-term male infants of these ethnic groups. The diagnosis can be confirmed in any hospital by the methemoglobin reduction test. In areas similar to Toronto, Canada, where these high-risk ethnic groups prevail, the following measures are recommended: (1) detection of g-6-pd deficient newborns by screening cord bloods of all infants of these ethnic groups; (2) protection of affected infants from potentially hemolytic agents such as naphthalene, certain vitamin K preparations, and sulfonamides; and (3) observation of serum bilirubin levels to assess the need for exchange transfusion for hyperbilirubinemia.

.I 754

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trisomy 17-18 syndrome with congenital extrahepatic biliary atresia and congenital

amputation of the left foot
the phenotypic characteristics of
the 17-18 trisomy syndrome have been well
described. among the most recently docu-
mented cases of this syndrome are those
with findings of agenesis or aplasia of various
bones of the forearm and hand, in addition
to the more classical symptoms.

we have recently studied a case of trisomy
17-18 syndrome with congenital absence of
the left foot, and congenital extrahepatic
biliary atresia.

.I 755

.W

differentiation of explanted fragments of
early chick blastoderm
ii. culture on protein-deficient medium
enriched with rna
posterior fragments of head process
blastoderms were cultured in vitro for two
days on a protein-deficient medium sup-
plemented with various rna's, after which
they were grafted over the chorio-allantoic
membrane for eight to nine days.
pancreatic (adult) rna enhanced
the development of the entodermal epi-
thelium.

heart (adult) rna caused hyper-
plasia of the epidermis with, in some cases,
keratinized papillary projections.

brain (embryonic) rna produced a
papillomatous epidermis with giant epi-
dermal cysts that were keratinized and
fibrillar as in feather formation.

liver (embryonic) rna had no vis-
ible tissue modifications.

in the controls there was no keratini-
zation, nor papillary formation of the epi-
dermis. the epidermal cysts were very
small, unkeratinized and devoid of fibrillar
organization.

the results are discussed in terms of
relationships of proteins from brain, mus-
cle and skin.

.I 756

.W

the inhibition of cell aggregation by a pure
serum protein

the aggregation of embryonic chick and quail limb bud, heart and liver cells
in a shaker system has been investigated in order to elucidate the mechanism of
cell adhesion.

a new method of assessing aggregation is described and evaluated; this
method involved measurements of aggregation kinetics. it was found that the
measured kinetics agree closely with flocculation kinetics, which provides a

direct quantitative measurement of adhesiveness in terms of the probability of an adhesion forming on contact between two cells. using this technique it was confirmed that aggregation is inhibited at 1-2 c. in the presence of serum but not in its absence. the kinetics of aggregation in the presence of serum at 37 c., the lack of inhibition of aggregation at 1-2 c. by serum which has been 'conditioned' by the presence of cells, and the similar lack of inhibitory power of serum which has been pre-treated with antiserum antibodies, all suggest that serum contains a factor which inhibits aggregation until destroyed by cellular metabolism.

.I 757

.W

les icteres du nouveau-ne en dehors

de l'incompatibilite foeto-maternelle

statistical data pulled off a study of 30 haemolytic neonatal icteri not linked to a foeto-maternal incompatibility, and of 200 non haemolytic neonatal icteri. among this latter, the two most important groups are the malformative icteri (69 cases) and the neonatal hepatitis (109 cases). the difficulties of the diagnosis frequently encountered between these two groups clearly appear in the comparative statistical analysis of the clinical, histological and evolutive data.

.I 758

.W

the immunological development of the human

fetus

the normal human fetus is said not to be engaged in the formation of immunoglobulins; the immunoglobulins present in the serum of the fetus and the newborn are considered to be of maternal origin. in favor of this opinion is

the observation that directly after birth the serum of the newborn contains an appreciable amount of iga, with gm groups identical with those of the mother (68-70). the level of the iga of the neonate decreases gradually during the first 3 months (3,27,71), which is generally explained by the catabolism of the maternal iga, whereas the formation by the newborn infant is still inadequate to maintain the original level (16,27). the best evidence for the transplacental passage is the almost complete absence of iga in the serum of newborn infants from mothers with agammaglobulinemia (3,27).

the transfer of the immunoglobulins appears to be a selective process (13, 15). while iga is readily transferred, there is little, if any, transfer of igm and igg, as has been shown by ultracentrifugation and immunoelectrophoretic studies of the serum (12, 16, 19, 20) and the analysis of maternally-transferred antibodies (31-33). with more sensitive techniques such as the double diffusion test in agar or quantitative immunochemical techniques, however, minute amounts of both igm and igg have been detected in fetal blood as well as in cord blood from mature and immature neonates (12, 19, 20, 23, 26). since large molecules do not pass the placenta, this may indicate that the trace amounts of igm originate in the fetus itself, but transplacental passage has not been completely excluded.

the absence of immunoglobulin formation has been associated with the absence of plasma cells in the lymphoid tissues and bone marrow of the normal human fetus and the newborn. it has been reported that these cells do not appear until a few weeks after birth (2, 3, 14, 25, 34). however, in pathological conditions such as congenital syphilis and toxoplasmosis the human fetus has been found to respond to the antigenic stimulus with intrauterine formation of plasma cells after about the sixth month of gestation (24,25).

.W

galactosemie congenitale

this observation of a case of congenital galactosemia with a particular familial incidence gives the opportunity of a brief review on the subject.

of a certain point of view we must consider that galactosemia is much more frequent than we suppose, that there are many severe cases with a reserved prognosis, that even with very slight degree of galactosemia, the disease must receive the most careful attention from the pediatrician.

.I 760

.W

postnatal changes in the portal circulation

during foetal development a large portion of the oxygenated umbilical blood flows through the umbilical recess directly into both main portal branches. accordingly, these are exposed to the umbilical blood pressure and have a wide by contrast, the trunk of the portal vein is narrow and there is probably only a small blood flow through it from the inactive digestive tract, though the pressure in it is approximately the same as in the umbilical vein or perhaps somewhat higher.

immediately after birth the liver is deprived of the substantial umbilical blood flow. the portal venous pressure falls to about one-quarter of the umbilical venous pressure at birth. however the

pressure gradient between the portal veins and inferior vena cava remains constant.

.I 761

.W

pattern of serum transaminase activity in neonatal jaundice due to cytomegalic inclusion disease and toxoplasmosis with hepatic involvement the pattern of serum transaminase activity that evolved in a newborn infant with congenital toxoplasmosis and in another newborn infant with congenital cytomegalic inclusion disease is described. this enzymatic pattern was unlike that found in infants with any other cause of neonatal jaundice studied to date.

.I 762

.W

impaired development of rat liver enzyme activities at birth after irradiation in utero development of activity of three liver enzymes at birth was studied in rats receiving 180 rads of x-rays on day 15 of gestation. at 20 days of gestation, activities of lactic and glycerophosphate dehydrogenases and glucose-6-phosphatase were not altered. the subsequent increases in enzyme activities in the 3 days between 20 days of gestation and 1 day of age were only 30 to 60% of those observed in controls. this finding suggests that irradiation in utero may alter later development of enzyme activity in the perinatal period.

.I 763

.W

(cytological and cytochemical study of

hepatic cells in the human embryo)

changes in golgi apparatus and mitochondria as well as in the contents of

nucleic acids, proteins, polysaccharides, lipids and iron in the hepatic cells

of developing human embryo were studied; the data obtained in human embryos and

adults were compared. it was found that during the developmental process some

changes in localisations of golgi apparatus and iron salts were taking place.

the contents of rna and polysaccharides in the cytoplasm increased:

mitochondria in the form of granules were revealed throughout the embryonic

period and in adults. no essential alterations in the contents of dna,

proteins, and lipids were noted.

.I 764

.W

risk of severe jaundice in

glucose-6-phosphate-dehydrogenase

deficiency of the newborn

the incidence of g.-6-p.d. deficiency and neonatal

jaundice in all male infants born in one year in an area of

the island of lesbos was studied.

of 634 infants tested, 29 (4.6%) were found to be

g.-6-p.d. deficient. hyperbilirubinaemia of 16 mg. per

100 ml. or over was observed in 34% of g.-6-p.d.-

deficient newborn males and in 9.1% of those with normal

enzyme activity--in more than half of them in the absence

of incompatibility or prematurity.

this is the first time that such a high incidence of severe neonatal jaundice has been reported in both a g.-6-p.d.-deficient and a g.-6-p.d.-normal group. it is postulated that in the population of lesbos a second factor increases the incidence of neonatal jaundice, especially when this factor is combined with g.-6-p.d. deficiency.

.I 765

.W

studies of b-glucuronidase activity in bile and liver of developing chick embryos and chicks in search for the reason of the occurrence of unconjugated bilirubin and biliverdin in chick-embryo and in chick bile the possibility of a b-glucuronidase function must be taken into serious consideration.

.I 766

.W

jaundice in infancy most causes of jaundice in infancy are discussed. the emphasis has been on those syndromes solely or usually encountered in the neonate and infant.

.I 767

.W

absence of the cystic duct

a case of congenital absence of the cystic duct is described, the 18th reported case in the literature. the embryogenetic basis of anomalies of the extrahepatic biliary tree is discussed. methods of early operative recognition and surgical management of the anomaly are suggested.

.I 768

.W

familial extrahepatic biliary atresia
a fifth family with familial congenital extrahepatic biliary is described.
clinically and pathologically familial and nonfamilial biliary atresia are similar except for a predominance of males in the familial condition.
the sex incidence and association of other congenital anomalies is discussed in relation to a possible etiology. further information must be correlated and new facts uncovered before the nature of this syndrome will be known.

.I 769

.W

linfangiografia no estudo da filariase linfatica
in the first part of the present paper a study is presented of the lymphangiogram of the normal african; the author has

noticed that it is coincident with the one of the white individual.

the second part includes the lymphangiographic examination and the observation of lymph circulation (via risa) during the several stages of lymphatic filariasis.

even during the asymptomatic stage, lymphangiography shows ganglial hypertrophy with a slight fibrosis and occasional discreet alterations of the lymphatic trunks.

in the symptomatic stage, the lymphangiographic aspects vary according to the disease's different stages and there is not always a relationship between the duration period of the symptoms and the changes observed.

in lymphangites, there are frequent alterations of the lymphatic trunks, i.e., increase in caliber, extensive and segmentary dilatations, numerical decrease with visualization of anastomoses and higher permeability. circulatory trouble evidences itself not only by a decrease in the rate of the lymph flow, but also by a very marked ganglial retention.

in adenites, in spite of the marked ganglial hypertrophy due to intense sclerosis, there may be no considerable alterations in the lymphatics, but risa already shows clear circulation troubles leading to lymphatic stasis.

in adenolymphoceles, the obstruction at the primitive-iliac level causes the lymph flow to deviate through the pre-sacral anastomoses and reflux to the inguinal glands, thus causing their dilatation and the formation of varicosities in the afferent lymphatics.

in lymphedemas, our lymphangiographic results together with risa's allow us to assume that the pathogeny is chiefly influenced by three factors: lymphatic obstruction due to lymphangitis, insufficiency of the collateral ducts, and ganglial sclerosis.

.I 770

.W

adjuvant chemotherapy in cancer of the large bowel

the completeness of reporting, the availability of continuous statistical analysis to warn of adverse effects, and the accumulation of 300 cases a year have demonstrated that this cooperative study group can provide a relatively quick assessment of a new approach to treatment of cancer of the large bowel. it is hoped that a study begun in january, 1962, on the use of 5-fluorodeoxyuridine as an adjuvant to adequate excisional surgery may demonstrate that, with a drug known to produce objective remissions in 20 per cent of a group of unresectable cases of colon carcinoma the five year survival rate in curative resections may be improved.

.I 771

.W

cancer chemotherapy by prolonged arterial

infusion

our current experience is reported with 136 patients treated by prolonged arterial infusion chemotherapy. the patients presented a variety of far advanced cancers unsuitable for conventional surgical or roentgen therapy. antimetabolite solution, either methotrexate or a fluorinated pyrimidine, was injected continuously through a small plastic catheter into the unobstructed artery to provide a high regional drug concentration for days to weeks. the patients have received drug infusion for up to 45 days. their course has been followed for up to 37 months after treatment.

methotrexate with antidote therapy by systemic administration of citrovorum factor was used preferentially in most patients. a fluorinated pyrimidine, most commonly, 5-fluoro-2'-deoxyuridine, was preferred for hepatic artery infusion of liver metastases.

.I 772

.W

the montgomery tube to palliate hypopharyngeal cancer

three cases of advanced, incurable cancer of the hypopharynx have been presented. in each instance, the simple procedure of insert-

ing an available prothesis served as an effective palliation for an otherwise difficult or hopeless situation.

.I 773

.W

adjuvant cancer chemotherapy

development of a dosage schedule for adjuvant cancer chemotherapy in surgical cases

an account is given of the development of a dosage schedule for adjuvant cancer chemotherapy for surgical patients.

this treatment was administered for two purposes:

as an adjuvant to radical surgery to reduce the risk of blood-borne metastases.

as a palliative measure for non-radically operated and inoperable patients.

for these purposes 3 dosage levels were fixed:

a maximum tolerated dose for adjuvant therapy.

a maximum tolerated dose for parenteral palliative therapy.

a maximum tolerated dose for oral palliative therapy.

for this treatment the authors used

2 antimitotics, sp-i and sp-g, both of which are podophyllin derivatives.

.I 774

.W

surgical palliation for lung cancer
the results of resecting incurable lung cancer
in an effort to improve the terminal course of a
small number of patients are briefly presented.
this is not a comparative study and no in-
ferences or conclusions are justified regarding
the choice of this form of therapy as palliation
in preference to other forms of palliative ther-
apy; however we do believe that the terminal
course of the patient with lung cancer is bene-
ficially effected by removal of the primary
tumor whenever this is technically feasible.

.I 775

.W

management of advanced endometrial
adenocarcinoma with medroxyprogesterone
acetate
a basis for progestin therapy for patients
with advanced endometrial adenocarcinoma
is presented. the criteria for selection of
patients for hormone therapy and the sched-
ule of administration of medroxyprogester-
one (provera) is discussed. evaluation of

patients for objective changes only, i.e., by visual, palpable, histologic, or roentgenologic means, revealed complete or partial remission with significant palliation in 8 of 20 patients (40 per cent). response to medroxyprogesterone therapy is apparently related to degree of differentiation of the primary neoplasm, the well-differentiated lesions being more responsive. documentation of tumor effect by serial biopsies during treatment provides an index to the histologic changes this progestin produces in susceptible cases. the effects of therapy upon serial urinary hormone excretion rates is documented in several patients.

on the basis of our experience, the treatment of patients with advanced endometrial adenocarcinoma with the potent progestin medroxyprogesterone seems justified.

.I 776

.W

chemotherapy of breast cancer

the majority of cancer patients who are referred for chemotherapy are in far advanced stages of the disease. the difficulty in delivering an effective dose of an oncolytic agent to the involved areas may limit the results of

treatment unless the patient's tumor is an unusually responsive one. the variability in response between apparently similar cases of cancer of the same cell type has become increasingly evident, and is as puzzling as the fact that 20 per cent of patients with breast cancer will live 5 years with no treatment. the decisions as to the choice between chemotherapy and hormone therapy, as well as to the choice of the chemotherapeutic agent to be employed, may be difficult.

as experience increases, the usefulness of chemotherapy in the treatment of cancer is becoming increasingly apparent. it also has become apparent that chemotherapy cannot be regarded as a curative procedure in advanced cancer even though an occasional patient appears to have been cured. however, the value of the oncolytic agents in prolonging useful survival time, ameliorating many of the distressing symptoms associated with cancer, and providing the physician with an extra tool for a positive program in the care of the cancer patient is now established.

.I 777

.W

clinical experience with palliation

of metastatic adenocarcinoma with 5-fluorouracil chemotherapy chemotherapy of solid tumors is becoming a more and more helpful therapeutic tool. it is probable that within a few years chemotherapy will become firmly established as an adjunct to the primary treatment of solid tumors. perhaps someday a cancerocidal chemical will be devised that can actually act as antibiotics do on bacteria. for this reason it is important for all surgeons interested in the treatment of cancer to try to keep abreast of the recent advances in the field of chemotherapy. surgeons should also begin to use some of the technics for palliation of incurable patients so that when these drugs are added to the armamentarium of primary treatment of cancer, they will be familiar with the various technics and the mode of actions of the drugs.

5-fluorouracil (5-fu) has had extensive clinical use and has produced significant palliation in breast and colon cancers with about a third of these patients receiving palliation for five to six months.

.I 778

.W

pelvic perfusion and carcinoma

of the rectum

a method of regional chemotherapy through

isolation of the pelvis has been presented.

all of the subjects were near the terminal

stage at the time of perfusion. the survival

time and degree of palliation have been en-

couraging.

.I 779

.W

carcinoma of the esophagus

a survey of fifty-seven patients with cancer

of the esophagus occurring over a twenty year

period is presented. the presenting complaints

of the disease, methods of diagnosis, and char-

acteristics of the disease are discussed. three

equal treatment groups consisting of no treat-

ment, x-ray treatment, and surgical resection

were compared and the results were extremely

poor. only one patient in all three groups sur-

vived longer than two years. it was our con-

clusion, supported by the opinion of others,

that x-ray therapy gave the best palliation in

most cases and that surgical resection for cure

should be used in only the most suitable pa-

tients.

.I 780

.W

carcinoma of bladder: cobalt therapy

from 1959 to 1962, 202 patients have received radiotherapy for carcinoma of the bladder. radical therapy with cobalt-60 has been done in 121 of these cases. these patients received tumor doses in excess of 5000 rad in 3 weeks. of 49 patients followed for 2 years after radical treatment, 28 are alive. sixteen out of 32 patients with stage b2, c or d tumors are alive; while 15 patients survived out of 30 with tumors of grades 3 and 4 (broders'). four of the 28 survivors had cystectomy performed and none showed residual disease in the bladder or lymph nodes. the complications of radiotherapy presented were not considered to be excessive.

we believe that radiotherapy should be the initial treatment for patients with infiltrative carcinoma of the bladder. the survivals presented at 2 years are better than those quoted for radical cystectomy (whitmore and marshall) and useful bladder function is preserved for the majority of survivors. we reserve cystectomy for specific indications.

.I 781

.W

polyposis of colon

as seen in

private practice

familial polyposis of the colon may present itself in a variety of clinical entities. from the cases discussed in this paper the following forms may be enumerated:

(1) an asymptomatic phase with discrete polyposis.

(2) a mildly asymptomatic stage with diffuse polyposis.

(3) a premalignant phase with carcinomas in situ.

(4) grossly malignant phase characterized by anemia and carcinomatosis, possibly of multicentric origin.

to secure a complete cure it is imperative that the clinician discover and the surgeon treat the disease in its premalignant state.

worthwhile palliative results may be obtained by surgery in incurable cases by extensive resection of the primary lesions and subsequent resection of any recurrences or metastasis, whether local or distant by second and third looks is necessary.

special emphasis should be paid to

the emotional problems of the patients.

an encouraging, sympathetic attitude on

the part of the surgeon is essential and

rewarding.

.I 782

.W

systemic chemotherapy

for cns metastases

of solid tumors

of the 13 cases studied, remissions were ob-

tained in eight. this 62% remission rate is not

significant because of the number of variables

present. however, we believe that chemother-

apy for this type of patient is indicated, as sup-

ported by the reported data. the results suggest

that the blood supply to solid tumors is different

from that of tumors associated with hematopoi-

etic disorders. the latter respond very poorly,

if at all, to systemic therapy. although we were

not able to measure the central nervous system

(cns) lesions exactly, the regression of the

cns symptomatology was significant. in pa-

tients who had other demonstrable metastatic

disease, those lesions also regressed. with this

evidence we feel that patients with metastatic

cns lesions, even when these have recently

resulted in paralysis or seizures, should be con-

sidered for systemic chemotherapy.

.I 783

.W

combined 5-fluorouracil and supervoltage
radiation therapy in the palliative manage-
ment of advanced gastrointestinal cancer:
a pilot study

malcolm y. colby, margaret a. holbrook

5-fluorouracil in combination with supervoltage radiation
therapy was employed in the palliative treatment of 44 pa-
tients with advanced gastrointestinal carcinoma.
a total dose of from 40 to 50 mg. per kilogram of body
weight of 5-fluorouracil given by rapid intravenous injection
at the onset of radiation therapy was found to be relatively
safe and tolerable. larger doses were associated with excessive
toxicity and mortality.

a sufficient number of patients achieved objective and
subjective palliation to justify controlled study of the possible
additive or synergistic role that 5-fluorouracil may have when
combined with radiation therapy.

.I 784

.W

palliation by radiotherapy
the purpose of radiotherapy in the management
of cancer of the lung is first to cure the disease;
second, to prolong useful and comfortable exist-
ence; and third, to provide comfort and relief of

suffering to those who are symptomatic and incurable.

cancers of the lung vary quite widely in their response to radiation. those of glandular origin, the adenocarcinoma, are more often than not of modest susceptibility and sometimes quite resistant. the very undifferentiated, the so-called oat-cell cancers, are often of exquisite sensitivity, responding to irradiation almost like lymphomas.

most cancer of the lung, however, is squamous-cell carcinoma and as such may be considered to be moderately radiosensitive in much the same order of magnitude as squamous-cell carcinoma of the skin, cervix or larynx, and should, in theory, be curable by this means in the same degree. unfortunately, this has to date not been found to be true. the reasons are principally two: first and foremost, by the time a diagnosis is made, cancer of the lung has more often than not, estimated at 80% and more, spread beyond the site of origin, thus making cure by any effective means presently available unlikely. second, the substrate in which the cancer grows, the lung, tolerates radiation less well than do the tissues which surround the highly radiocurable epithelial cancers such as carcinoma of the skin, cervix, and larynx, thus making an unfavorable therapeutic ratio.

.I 785

.W

chlorambucil-prednisolone therapy
for disseminated breast carcinoma
over a 7 1/2-year period, 71 patients with
disseminated breast cancer were treated
with combined alkylating-agent-cortico-
steroid therapy. chlorambucil and pred-
nisolone were the drugs of choice. these
agents, administered orally, produced no
serious or disagreeable toxic effects. twen-
ty-four patients (33.8%) had objective
regression of six months' duration or long-
er; average survival time after therapy
was 23.9 months. results are statistically
similar to those obtained with sex-steroid
and endocrine-ablation therapy, presum-
ably because the three modalities have a
similar mechanism of action, ie. suppres-
sion and/or eradication of endogenous
estrogen.

.I 786

.W

recent advances in the treatment of
cancer of the esophagus
whether combining surgery and supervoltage radiation therapy will
noticeably improve the 5-year survival rate for carcinoma of the esopha-

gus remains to be seen. it is encouraging, however, to observe at the time of operation that the previously irradiated esophagus is firmly encased in fibrous tissue, which gives the impression that the danger of disseminating tumor at the time of resection is diminished. in addition, the fibrosis suggests that the tumor that had spread locally, beyond the limits of surgical excision, may have been destroyed.

.I 787

.W

cyclophosphamide in the management of advanced bronchial carcinoma
forty patients suffering from advanced bronchial carcinoma who were treated with cyclophosphamide are reviewed. the selective effect of the drug in tumours of the oat-cell type is noted. it is suggested that relapses which occur while the patient is on oral maintenance therapy may be controlled by a further intravenous course of cyclophosphamide.

full clinical and statistical details of all the patients referred to in this paper are available on application to the author.

.I 788

.W

esophageal obstruction
the use of an endoscopically inserted tube in the care of esophageal carcinoma
our experience suggests that the en-

doscopy insertion of intraluminal tubes provides a relatively simple and reasonably safe method of dealing with some of the problems which arise in the management of patients with esophageal carcinoma. such tubes would appear to be of particular use in handling the problems of obstruction and regurgitation in patients with incurable tumors, but may also be helpful in preparing severely debilitated patients with esophageal carcinoma to withstand the rigors of operation and radiation therapy.

.I 789

.W

palliative radiation therapy

the care of the patient with "incurable" cancer may be directed by physicians of various backgrounds and persuasions. if this physician has little experience in such care, he is prone to be influenced by still prevalent attitudes of therapeutic futility or by equally unjustified premature claims for widely publicized methods recent on the scene. surgery and radiation therapy remain the dominant treatment forces for the patient with cancer. it is unfortunate that lack of demonstration of good radiation therapy has led to unjustified condemnation of the method rather than the user, with resultant loss to the patient's

welfare. to obtain maximal benefit, radiation therapy must be allowed indications and contraindications like any therapeutic modality. these must be the responsibility of the therapeutic radiologist. application of realistically stringent indications and contraindications does not lessen useful accomplishment, but avoids unnecessary morbidity, waste of time, money and effort, and delay in seeking suitable treatment.

.I 790

.W

carcinoma of the middle ear
the results of radiotherapy in a relatively large number of cases of carcinoma of the middle ear are reported. the crude 5 year survival rate of 100 cases is 29%. there is no difference in survival between those cases who had a preliminary mastoidectomy and those who did not. the use of megavoltage x-rays probably increases the survival rate.

.I 791

.W

sustained palliation in
ovarian carcinoma
management of 64 cases of advanced ovarian carcinoma has been analyzed.
an attempt is made to compare the
value of radiation and the value of chloram-

bucil, using salvage time and sustained palliation as end points.

chlorambucil, an outpatient oral medication, appears to be as efficacious as radiation in advanced ovarian carcinoma.

chlorambucil may be used before or after irradiation therapy.

pleural and peritoneal effusion respond favorably to chlorambucil 80% of the time.

the possibility of using a different dosage schedule is discussed.

.I 792

.W

clues in dealing with cancer patients

it is clear that the patient with cancer changed his pattern of communication at different stages of the disease. these patterns in communication were the basis or clues for the doctor and paramedical personnel to consider in making total care more effective. the bedside clinician of past days knew these clues instinctively in his wise ministrations. thanks to a gifted social worker these have been now made manifest to help all of us in dealing with cancer and perhaps other chronic relentless diseases.

.I 793

.W

radon and radioactive seed volume implants
for extensive recurrent vaginal-pelvic cancer
radioactive seed volume implants for
extensive recurrent vaginal-pelvic cancer
result in extended control of otherwise
untreatable disease. immediate and early
reactions are practically nonexistent. late
complications are also rare, the most
serious being severe hemorrhagic cystitis
in 2 of the author's 13 patients.

.I 794

.W

terminal cancer nursed at home
perhaps the most difficult part of mrs. brown's illness,
was that she herself knew all about it. she had been a
nurse for most of her working life, and was only too aware
of the deteriorating process of carcinoma. there were
times, of course, when she would try to deceive herself, say-
ing that there was always hope that something new in the
way of treatment would turn up, and life would then be
worth living again.

.I 795

.W

advanced cancer of the breast
treated primarily with irradiation
the five-year results in 109 patients

treated primarily with irradiation for cancer of the breast, mostly in the late stages, have been analyzed.

in all cases, the initial intent was to control with x radiation alone the primary tumor involving the breast and its entire lymphatic drainage. irradiation remained essentially the sole method of treatment in 84 cases. postirradiation mastectomy was performed in the 25 other patients, who initially had been considered inoperable.

the plan of treatment has consisted of a single continuous course of radiation therapy, protracted over a period of seventy-five to one hundred days and administered in 3 closely integrated phases. tissue doses, superficial and deep, must be brought to the highest levels required for maximum biological effects within the tolerance of the structures involved.

the immediate effects of irradiation alone have been remarkable. the regression of neoplastic manifestations in the breast and palpable nodes, the degree of healing of ulcerated carcinoma, and the incidence of recurrence have been recorded and assessed to determine the

efficacy of treatment.

.I 796

.W

the management of disseminated

cancer of the breast

when mammary cancer has spread to tissues beyond

the breast and axilla, the disease is incurable by present

day methods. however the patient may be greatly helped

and tumor growth retarded by skillful and sympathetic

application of irradiation, surgical ablation, hormone ad-

ministration, and chemotherapy. given in conjunction

with analgesics, sedatives, and ataractic drugs, these

measures can frequently reduce disability and pain and

prolong the period of useful comfortable life.

.I 797

.W

toilet training of an autistic eight-year-old through

conditioning therapy: a case report

operant conditioning techniques have been successfully

used in the treatment of a wide variety of be-

havioral problems including hysterical blindness (brady

and lind, 1961), tics (barrett, 1962), psychotic

symptoms (lindsley, 1956; 1960, 1961), reading disabilities

(rachman, 1962) stuttering (flanagan et. al.,

1958) enuresis (mowrer and mowrer, 1938; lovibond,

1961, 1963a, b) and encopresis (neale, 1963;

madsen, 1965). neale (1963) successfully treated three

out of four encopretic children using operant training techniques. in the case of one 9-yr-old boy, with an 18 month history of encopresis, going to the toilet was rewarded by a candy, praise and recording the event in a special book in the boy's presence. soiling was not inadvertently rewarded (e.g. attention) or punished; the boy would be given a clean pair of pants without comment. neale reports that response to treatment was rapid and complete and 6 months after toilet training there had been no relapse in bowel habits. procedures similar to those used by neale were used in the case reported here. positive and, in a small number of instances, negative reinforcement were used to toilet train an 8-yr-old boy diagnosed by a child psychiatrist/neurologist as having infantile autism.

.I 798

.W

incidence of symptoms of early infantile autism in subsequently hospitalized psychiatric patients this study was concerned with the relationship between the occurrence during the first two years of life of symptoms of early infantile autism, as retrospectively reported by the mothers of s's and subsequent adjustment. the mothers of 69 unmarried young hospitalized psychiatric patients were interviewed to deter-

mine the presence or absence of each of 28 different signs contained in a check list. the signs represent characteristic features that are reportedly often found in conjunction with early infantile autism. as a control, 50 mothers of high school students residing in the community and presenting no significant adjustment problems were questioned in regard to the very same items.

the results indicated that there were significantly more symptoms reported for patients than for normals, and that this finding applied to the overall number of symptoms as well as to several subcategories of symptoms. the items classified under the heading of "social withdrawal" appeared to be the most sensitive in differentiating the groups. it was also found that 11 of the 28 signs distinguished between the patients and normals, with all except one occurring more frequently in the former group. it was concluded that a significant relationship existed between the reported presence of symptoms that are often associated with severe and early ego impairment and subsequent status as

a mental hospital patient. this study does not provide any direct answer to the question of what proportion of children with infantile autism are later able to make an adequate adjustment outside of a mental hospital.

.I 799

.W

eeg abnormalities in early childhood schizophrenia:

a double-blind study of psychiatrically disturbed and normal children during promazine sedation

eeg tracings during promazine sedation

were obtained on 58 children who had

autistic or symbiotic childhood psychosis.

for comparison eeg's were done under

identical conditions on 4 other groups of

children: 44 with chronic undifferentiated

schizophrenia; 37 non-psychotic children

with severe, acting-out behavior disorders;

10 with neuroses; and 13 psychiatrically

normal children. final clinical diagnoses

were made without knowledge of the eeg

readings as determined for this study, and

the eeg's were all placed in random order

and read without any knowledge of the

clinical diagnosis. eeg abnormalities ac-

cepted were focal slowing, focal spikes,

paroxysmal spikes and waves, and paroxysmal spikes and waves with independent spikes.

among the 149 patients 51% had abnormal records. none of the psychiatrically normal children had eeg abnormalities. except for the neurotics, the eeg abnormalities were qualitatively and quantitatively similar in the psychiatric patients. the most frequent abnormalities were irregular paroxysmal spike and wave complexes, often best seen during the transition from wake to sleep. of the 149 patients, 33% had this complex, either alone or with independent spikes. although these complexes were most frequent in the autistic-symbiotic group, the incidence was not statistically significantly different from the higher performing, chronic undifferentiated schizophrenics who had communicative speech or the non-psychotic children with acting-out behavior disorders.

of the 58 autistic-symbiotic children, 19% had seizures, which is similar to the 13% seizure incidence in the remaining 91 psychiatric patients.

whether the cerebral dysfunction im-

plied by this study is a primary disorder or is secondary to some factor such as the effect of prolonged anxiety on body chemistry cannot be decided at this time. nevertheless, an organic concomitant has been demonstrated in 51% of the psychiatrically disturbed children. by increasing the amount of time included in the eeg sample, the incidence of electrical abnormalities might be even higher.

.I 800

.W

on early infantile psychosis.

the symbiotic and autistic syndromes

in conclusion, i wish to state that the

core of child psychosis must

be sought in one or the other of the

described distortions of the sym-

biotic phase. in the first case, what lay

at the heart of the psychotic dis-

turbance was the marked emotional

unavailability of the mother,

which alternated with a purely physical

extreme closeness during the

breast-feeding situations, and particularly

with the destructiveness of

the mother's unpredictable rage attacks.

the contrasting experiences
drove the child to the autistic warding
off of any human contact and
the de-animation of the world of reality.
constitutional factors could
not, in this case, be evaluated with any
degree of accuracy.
in the second case, it was, by contrast,
the mother's ever-presence
that created an unendurable intrusion
upon and interference with
the structuralization of the budding ego,
which constitutionally and
perhaps predispositionally may have been
very vulnerable. this made
it impossible for the infant to experience
the normal alternation of
the gratification-frustration sequences at
his own pace; it also made
the process of individuation in the
separation-individuation period
one which was beset with abysmal panic.
in both instances, we can see that it was
primarily in the severe dis-
tortions of the normal symbiosis that the
child psychosis had its roots.

.W

autopathy:follow-up of cases

the publication of two papers

recently in the acta paedopsychiatrica by

d. arn. van krevelen on the subject of "autistic

psychopathy", has stimulated the author

to present 5 cases which appear to conform to

his description. the only value of this brief

contribution lies in the fact that they have all

been followed up for at least 10 years, and

this may give some idea of the eventual results

in this type of cases.

.I 802

.W

sensory dominance

in autistic imbecile children and controls

in a previous experiment (hermelin and

o'connor, 1964) it was found that autistic

and control imbecile children responded most

frequently to a light stimulus in conditions of

bimodal, simultaneous stimulation. however,

the role of the relative intensity level of the

stimuli remained to be determined. in the

present experiment a light and a sound, or a

light and a verbal command were presented

simultaneously in various intensity combina-

tions. all responses, irrespective of the stim-

ulus to which they were made, were rewarded. autistic, mongol, and nonmongol imbecile children were tested. in addition to a tendency for visual dominance results showed that independent of modality, high intensities affected all groups. nonmongol imbecile children also responded significantly more frequently to the verbal than to the sound stimulus, while the other two groups did not.

.I 803

.W

dreaming sleep in autistic twins
each of 5-year-old identical autistic twins was observed during one spontaneous all night sleep session during which their electroencephalogram, eye movement, heart rate, and chin muscle potential were recorded. these autistic twins showed a similar patterning and amount of dreaming sleep to each other and to that reported for normal children of the same age.

.I 804

.W

twins discordant
for early infantile autism
a pair of heterozygous twins discordant

for early infantile autism is reported and the relevant literature reviewed. although manifest organic factors were ruled out, the twins' physical development was different. a specific emotional etiology was not demonstrated. the few available twin studies offer findings consistent with the hypothesis that genetic factors are relevant to the development of childhood autism. evidence is also presented that impaired acquisition of language may have hereditary determinants. a second set of probably homozygous twins are reported who were also discordant for autism. this second case suggests that, although genetic factors may play a part, in some cases the syndrome of infantile autism appears to be a reversible one. in view of this set of twins and of kanner's sibling data, the role of genetic factors remains obscure, and more twin studies properly documented with blood typing are needed.

.I 805

.W

evaluation and treatment planning

for autistic children

infantile autism is considered to be a re-

action on the part of an immature organism

at a primitive and undifferentiated stage of ego development. little choice of defensive reactions is available; the possibility of sublimation does not exist and, even though other object relationships are gradually developing, the mother is still the child's primary object. at this vulnerable developmental stage, a wide range of pathological circumstances, ranging from the most severe family psychopathology to the most adventurous physiological traumata or the most unfortunately malignant circumstances, may constitute an acute or cumulative catastrophic stress. the primitive organism tends to respond to this overwhelming stress with a paranoid reaction which is directed at the mother (regardless of the actual etiological variables) because the mother is still the child's primary object. we believe that the child then responds with an autistic reaction and shows varying degrees of simple withdrawal, obsessional behavior, magical or delusional thought processes, and consequent disruption of developmental skills, speech, and relationships with others.

many families can and do make every effort to counter the paranoid reaction of the

child and do not respond to his rejection with counterrejection and counterwithdrawal. some of the child's autistic symptoms may abate without formal treatment. yet, since the mother (and family) are the primary objects of the child's paranoid attitude, it is felt that formal therapeutic intervention is necessary to modify the paranoid core of the autistic reaction.

.I 806

.W

a twenty-five year view of therapeutic results

thus this group of ten patients shows a complete range of chronic schizophrenia from a bright pseudoneurotic never hospitalized, to an inaccessible patient chronically hospitalized for 20 years.

physiological therapy in the form of metrazol-induced convulsions given in the course of a puberty schizophrenic psychosis, has been helpful to some by making them more accessible for the total treatment program in the hospital or by raising their margin of tolerance sufficiently so that they could live at home and attend public schools at least for a time and at best, indefinitely.

several of the most regressed, deteriorated patients in state hospitals for many years, have been brought back to some level of meaningful living again by the current drug therapy program, and are still improving.

now we have not determined who the sinner may be. there are

many who will believe that the mother is always the sinner; is she not schizophrenogenic? there are others who will believe that the individual himself is the sinner since, after all, is he not the one whose behavior and fantasies are schizophrenic? however, there will be many of you attending this fifty-second annual meeting of the american psychopathological association, who will judge the speaker to be the sinner, for have i not given you this wealth of clinical material without charts, graphs, or statistical evaluation?

.I 807

.W

group psychotherapy with preschool

psychotic children and collateral

group therapy of their parents:

a preliminary report of the first two years

a group approach in the treatment of preschool-aged psychotic children is reported. autism is a defense against loss of the symbiotic partner. the group of children penetrates this defense and forms a "group ego," which constitutes one pole of a new therapeutic symbiosis from which separation-individuation can occur.

.I 808

.W

autistic reactions in early childhood:

differential diagnostic considerations

the term "autism" is frequently used today

in the differential diagnosis of the severe

emotional disturbances of early childhood.

however, to label a child as "autistic"

presents some formidable problems with regard to definition of the term, the specific etiological-diagnostic implications, and treatment considerations for any given child so designated. the purpose of this paper is to briefly review some of the historical psychiatric background of the term "autism", its more recent ramifications, and our clinical experiences in this field.

.I 809

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infantile autism: a family approach

the autistic child appears to be unable to integrate or to respond to stimuli, both from an internal source, the body, as well as from external sources, such as human contact. we have noted in the children at our residential treatment center how in their preliminary period with us they appear to be unaware of their body; they give the impression of being insensitive to pain, display little autoerotic behavior, inflict injury on themselves, such as hitting their heads against objects and biting their own bodies, with little outward display of distress. in working with these children in therapy, one of the guideposts for change and for growth is a display on the child's part of an increased body awareness and autoerotic behavior. for example, one child who developed polio during his early stay at the clinic residence did not communicate this to anyone and it was only made known by observing the child's dragging one leg (memorial guidance clinic, 1959). later, he was able to point to his body and to indicate pain. another child, who at first seemed to be quite unaware of both himself

and others, concurrent with his growing display of affective expression toward the therapist also manifested pleasure through genital stimulation, was quite ticklish, and when injured would display the area of pain quite readily.

.I 810

.W

an analysis of the language of fourteen
schizophrenic children

fourteen schizophrenic (autistic) children were studied by means of detailed behavioural histories and observations.

the language recorded in history and observation protocols was analysed and compared with available data on normal children.

all schizophrenic children were grossly retarded in their language development and all measures of this correlated highly with a previous overall clinical assessment of the severity of illness.

the most striking abnormalities in the language of the children studied were stereotyped repetition of utterances appropriate to an earlier developmental level or to a previous environmental context, accompanied by a lack of normal expressions of curiosity and of responsiveness to changing environmental cues.

.I 811

.W

a behavioural and electroencephalographic
study of autistic children

short biographies are given of 10 children,
age 3 to 6 years, diagnosed as suffering from
kanner's syndrome (early infantile autism).

an analysis was made of the free-field acti-

vities of these children compared with a group of normal children of similar age. electro-encephalographic studies were also carried out on all 10 children, and in two it was possible to carry out simultaneous behavioural and eeg observations by means of telemetry. the children were observed for three minute periods in four environments of varying complexity: a. an empty room; b. the same room with toy wooden blocks present; c. blocks plus passive adult; d. blocks plus active adult. except in a the visual fixations and manipulatory activities were of significantly shorter duration in the autistic children than in the normals, lacked clear 'cut-off' points and showed relatively little variability between environments. the autistic children as a whole showed virtually no constructive play in contrast with the normals, though more time was spent in contact with play materials in the social environments. changes in the time spent in locomotion, gesturing, block-play and manipulation of other objects in the environment showed that the autistic children were acutely responsive to changes in their environment, including the presence of the social stimulus. if the autistic children were

subdivided into those who characteristically showed stereotypies and those who did not, the latter sub-group showed a behaviour structure which was very similar to that of the normals, whereas the stereotypy sub-group was clearly differentiated from both the normal children and the non-stereotypy sub-group.

eight autistic children had waking eeg records characterized by low voltage irregular activity without any established rhythms; one child, a record containing irregular alpha and another unstable theta activity. two of the children with 'flat' laboratory eegs showed more rhythmic, higher voltage records when their eegs were telemetered in environment a. they also showed less stereotyped behaviour. in environments b and d they showed progressively more irregular eeg activity and more stereotypy.

the hypothesis is advanced that autistic children are in a chronically high state of physiological arousal. the findings of the present study and those of other workers are discussed with respect to this hypothesis.

.I 812

.W

the autistic child in the school and the

school-nurse teacher responsibility

autistic children demonstrate a more persistent pattern of retreating from reality than is apparent in those children categorized as normal.

some psychologists have established the cause of symptoms in the autistic child as extreme anxiety which forces withdrawal from social contact.

such anxiety is reported to have its initial occurrence during the age range of one to five years. a sense of security which is considered essential for a child is gained through overt manifestations of love, care and approval of those adults most closely associated with him. when this need is not satisfied, the child's attempts at self-realization and esteem are deterred or thwarted, and a state of anxiety may result. the severity of the anxiety may be the forerunner of a schizophrenic disorder. such a condition can develop in a child, an adolescent or an adult. schizophrenia, a serious mental illness, is considered to be a major cause for admitting patients to mental institutions.

another school of thought has placed infantile autism in the category of a disturbance resulting from abnormalities of development during the intrauterine period. such a congenital condition is not categorized as mental retardation.

yet another concept of autism conceives of the problem as the absence of an innate ability or capacity for developing meaningful contacts with other people. a detachment of varying degrees persists where human contacts are concerned.

.l 813

.W

the autistic child

the conditions most frequently mistaken

for autism are speech disorder, brain damage and mental deficiency, each a prominent symptom of the psychotic child. careful history and close observation to disclose symptoms of withdrawal, lack of ego, compulsion for sameness, and displays of intelligence give incomplete clues to the diagnosis.

the etiology of autism is uncertain. several factors seem significant. the important role of organic damage of the brain is underscored by the coincidence of epilepsy, eeg and neurological abnormalities in these children. in our series seizures of various types occurred in 25%, eeg abnormalities in 58%, and minor neurological deficits in 70% of the cases. environmental factors are quite obviously important in many instances. the emotional and behavioral pattern of the parents toward the infant is often incriminated. separation, inattention, coldness, rejection, etc. have been found in many situations. familial incidence of psychoses is low; so is that of autism in siblings.

.l 814

.W

shadow therapy

shadow therapy was developed at sunland

training center in gainesville, florida, because of communica-
tion difficulties with disturbed, psychotic children. it was con-
jectured that subjects would reveal their anxieties and conflicts
more readily in a simulated night situation.

the therapy was conducted in a darkroom with projector
light used to produce silhouettes and their accompanying
shadows as additional stimuli. twelve subjects attended. in
this article, the reaction of a child who was autistic and severely
disturbed is used as an illustration of subject reactions. in the
playroom, he exhibited static behavior; in the darkroom, re-
gressive-transcendental behavior. he also transcended his usual
level of vocalizing and socializing.

.I 815

.W

language training in the treatment

of the autistic child

functioning on a retarded level

a preliminary study to

determine the effect of language and

speech therapy on the development of

communication and the lessening of un-

relatedness in a group of non-verbal,

autistic children functioning on a retarded

level is reported. on the basis of the re-

sults of the study, it is suggested that the

inclusion of language and speech therapy

techniques be considered in developing a

treatment program for such children.

.I 816

.W

the convergence and interaction of visual,
auditory, and tactile responses in human
nonspecific cortex

the relation between the electrical responses in the human brain and
mental processes of integration and association is perhaps the most chal-
lenging of all the problems facing neurophysiologists today. until quite
recently the prospect of unifying physiological and psychological concepts
by electro-encephalographic (eeg) techniques seemed to be receding
because of the baffling complexity of the intrinsic electrical rhythms, and
this difficulty has still not been overcome. the most intriguing, and at
the same time most elusive, of the properties of these rhythms is that,
although often remarkably constant in their variations with respect to
time, they fluctuate also, in a much less regular manner, within the three
dimensional space of the brain. the continuous analysis and display of
such a phenomenon presents serious difficulties, and no method has yet
given entirely satisfactory results.

the incentive to construct adequate equipment and to design and per-
form crucial experiments is undoubtedly limited by the uncertainty as
to whether the information likely to be obtained in this way is essential
to understanding brain mechanisms; few experimenters imagine that it
would be sufficient.

.I 817

.W

infantile autism and the schizophrenias

in a paper published in 1943, entitled "autistic disturbances of affective contact," i reported from the children's psychiatric service of the Johns Hopkins Hospital observations of 11 children (8 boys and 3 girls) who had in common a pattern of behavior not previously considered in its striking uniqueness. The symptoms were viewed as a combination of extreme aloneness from the beginning of life and an anxiously obsessive desire for the preservation of sameness. I concluded the discussion by saying: "we must assume that these children have come into the world with an innate inability to form the usual, biologically provided affective contact with people, just as other children come into the world with innate physical and intellectual handicaps. If this assumption is correct, a further study of our children may help to furnish concrete criteria regarding the still diffuse notions about the constitutional components of emotional reactivity. For here we seem to have pure-culture examples of inborn autistic disturbances of affective contact."

In my search for an appropriate designation, I decided in 1944, after much groping,

on the term early infantile autism, thus
accentuating the time of the first manifesta-
tions and the children's limited accessibility.

.I 818

.W

autistic children

autism is a form of childhood schizophrenia. a sudden
separation from his mother or traumatic shock in
early life causes the child to reject the world of nor-
mal relationships. leading him back to the original
traumatic situation is part of the treatment described
in this article.

.I 819

.W

gilles de la tourette syndrome in an autistic child

a case of gilles de la tourette syndrome

presenting an early infantile autism is
described. the treatment applied is outlined.

.I 820

.W

psychodrama for disturbed children

psychodrama is especially adaptable to the treat-
ment of mentally ill children. it evokes a degree
of spontaneity and involvement that is difficult to
attain with many group therapies, and it offers situa-
tions in which the children can participate as actors
or as observers. competition and restriction are

minimal: the child can do what comes naturally. indeed, much of children's natural play is in the form of dramatic activity. their make-believe is, however, more intense than acting, for a child becomes the person or thing he pretends to be: a fireman, an indian, a horse, a tiger.

.I 821

.W

the speech and language abilities of emotionally disturbed children the speech and language disorders of these severely disturbed children can be divided into two categories which relate to the type of psychiatric disturbance. the autistic-schizophrenic children used bizarre forms of language or did not use communicative language at all. the non-autistic-schizophrenic, the neurotic, the primary behaviour disorder, and the minimally brain-damaged children as a group, had similar speech and language problems to normal children but of a more severe and frequent nature. their problems were predominantly in the areas of speech and language development, articulation, rate of speech and fluency. the children with primary be-

haviour disorders had the more severe
speech and language problems.

.I 822

.W

a study of childhood schizophrenia
and early infantile autism
(part i--description of the sample)
following a period of observation of
three months' duration, a group of twelve
autistic schizophrenic children were se-
lected for a treatment program. the
group was selected on criteria which
would allow a reasonable chance of suc-
cessful treatment in a group homo-
geneous enough to allow statistical con-
siderations to be valid.

younger age, average intellectual func-
tioning, presence of an intact family in
or near to metropolitan toronto and a
firm diagnosis of autistic schizophrenia
were the limiting factors.

rather distinct differences were noted
in this treatment group as opposed to the
larger observation group. the dis-
tinguishing characteristic was undoubted-
ly the speech abnormalities present.

.I 823

.W

discussion sur les pseudo-tumeurs osseuses
des hemophiles
doctors queneau and josso each described one
case of pseudo-tumour of the calcaneum analagous
to that described by trillat and favre-gilly; they
demonstrated x-rays; dr. alagille referred to a
haemophilic cyst of the maxilla and dr. favre-gilly
to a cyst of the perineum; dr. kugler had seen a
case where an erroneous diagnosis of osteosarcoma
had been made.

.I 824

.W

the effect of joint position on the pressure
of intra-articular effusion
it is known that joints with symptomatic effusions are held spontaneously in
characteristic positions and that movement of these joints increases pain. in
the study reported here, a correlation was made between the hydrostatic
pressure of a joint effusion and the joint's position. the results indicate a
possible relationship between intra-articular pressure and pain.

.I 825

.W

haemophilic blood cyst
a mongol boy of ten, a known haemophiliac, was seen in the orthopaedic
department of southmead hospital in may 1962 with a swelling of the left foot.
the parents were aware of a steady increase in size since the swelling was
first noticed two months before. on examination, a cystic swelling was seen to

occupy the forefoot, the skin on the dorsum being stretched over it and a dusky red in colour (fig. 1). radiographs showed destruction of the proximal two-thirds of the third metatarsal bone, an appearance consistent, it was thought with destruction from within by an expanding lesion (fig. 2). the diagnosis of a haemophilic blood cyst was made.

.I 826

.W

treatment and prevention of chronic haemorrhagic

arthropathy and contractures in haemophilia

orthopaedic treatment of joint deformities in thirteen patients with

haemophilia is reviewed over a period of seven years.

forms of treatment discussed include open operation, manipulation under general anaesthesia, continuous traction, splintage and physiotherapy. the amount of intravenous therapy required for each form of treatment is indicated.

in discussing prevention of joint deformity the histories of a further eighteen patients have been taken into account. it is concluded that initially painless haemarthroses provide the main threat to joint deformity in haemophilia.

the best preventive treatment is early immobilisation followed by prolonged splintage and physiotherapy; intravenous therapy with antihemophilic factor plays a less important role here than in other forms of haemorrhage.

evidence is presented that joint deformity in severe haemophilia can often be entirely avoided.

.I 827

.W

osteopatia in emofilia

the aa. present the case material of the literature and one

personal remark of extrarticular osteopathy in

hemophilia. they examine the anatomic and clinical picture of the illness in its most important and less known peculiarities and they dwell upon the curative medico-surgical problems of the affection.

.I 828

.W

la plasmatherapie a minima dans le traitement de la douleur des hemarthroses hemophiliques

some fifty clinically similar cases of hemophilic hemarthrosis were, after immobilization, either treated with placebo and plasma perfusion or else with corticoids and analgesics.

a very small quantity of plasma is sufficient to stop the pain for the following few hours.

it is attempted to give a physio-pathologic explanation which would seem in accord with the pathogenic studies on hemophiliac by r. marx et al.

.I 829

.W

effet analgesique immediat des injections de plasma pour hemarthroses recentes du genou des hemophiles

a single injection of 20 ml of lyophilized fresh plasma per kg body weight is proposed as a treatment in recent cases of knee hemarthrosis with an important distension of the capsule, so as to achieve hemostasis, and reduce the evolutive period. pain is always acute and permanent in such cases of hemarthrosis; it subsides during the plasma injection, or immediately afterwards.

.I 830

.W

hip disarticulation in a
patient with hemophilia
disarticulation of the hip in a hemophiliac patient
was performed because of a severe osteomyelitis
involving the entire right femur and was lifesaving.
the following are suggestions for hemotologic management: (1) infected wounds in hemophiliac patients should be left open initially. (2) electrocautery should not be used in an infected wound of a hemophiliac patient. (3) a safe fibrinogen preparation potent in the antihemophilic factor is now available in this country and is a highly significant advance in the surgical treatment of hemophilia.

.I 831

.W

haemophilia in sweden

vii. incidence, treatment and prophylaxis of
arthropathy and other musculo-skeletal
manifestations of haemophilia a and b

the clinical material consisted of 242 of the 308 known haemophiliacs (a and b) in sweden. the investigation included clinical examination of all major joints in 95 of 116 patients with severe haemophilia, in 38 of 65 patients with moderate haemophilia, and in 24 of 127 patients with mild haemophilia, and roentgen examination of practically all joints found to be abnormal at the clinical examination. in addition information about 7 patients with severe haemophilia, 21 with moderate haemophilia, and 57 with mild haemophilia was obtained by questionnaire only.

the degree of arthropathy (grades 2, 3 and 4) was classified largely according to depalma and cotler (1956). evaluation of general disability was made with regard to ability to manage (walk, dress, eat, toilet) without help. this latter evaluation comprised also extra-articular manifestations of haemophilia.

.I 832

.W

interet de la radiotherapie dans les hemarthroses
recidivantes du genou chez l'hemophile
radiotherapy was delivered at a dose of 100 r
repeated from 7 to 10 times, to 22 knees of haemophilic children presenting recurring arthropathies.
irradiation had no harmful effect on growth of patients; it was beneficial in two thirds of the cases, reducing considerably the number per annum of haemarthrosis onsets; one third of the patients showed no significant result: the number of onsets was the same in the following year.
totally the average of infirmary stays due to knee haemarthrosis was 175 days in the year before radiotherapy and 25 days in the following year.
the authors think that these results justify this therapeutic method.

.I 833

.W

discussion sur les donnees radiologiques
dans les arthropathies des genoux

professor marchal acts as moderator.

dr. le coeur wonders if the fringed appearance of condyles has really a pathological significance; that appearance could be normal in young children, but, in the opinion of dr. queneau, it seems to be pathological in older children.

it seems to dr. favre-gilly and dr. queneau that scalariform traits occur more frequently in haemophiliac children than in normal ones.

dr. le coeur thought that fibrillary decalcification was the ultimate stage of decalcification, whereas dr. favre-gilly has the impression that it represents in haemophiliac subjects an early stage anterior to homogeneous decalcification.

according to brinkhous, densification of synovial membranes are a result of an infiltration of the joint cartilage due to haemosideraemia; this is also the opinion of dr. favre-gilly and dr. izarn.

dr. izarn asks if geodes are caused by intra-osseous haemorrhages or necroses; dr. queneau and dr. de mourgues think that anatomical data concerning haemophiliac subjects are insufficient for that question to be answered.

.I 834

.W

etude radiographique des genoux de 100 hemophiles
de 7 a 15 ans

radiographic examination of the knee were systematically performed in 100 haemophilic subjects aged from 7 to 15 years, 64 of whom had a bilateral haemarthrosis, 30 had only one knee affected and 6 were uninjured.

an intra-articular opacification, observed in 29 knees, corresponded to a recent haemarthrosis. densification of the synovial membrane was observed in 25 knees and corresponded to iron deposits.

an interlinear pinch was present in 52 knees. erosions of articular surfaces are especially frequent (78 knees) or homogeneous (28 knees). hypertrophy of condyles or knee-caps, broadening of intercondylar space, crushing of internal tibial disk, genu valgum and posterior subluxation of tibia are osseous deformations that are encountered. atrophy of femur diaphysis explains the frequency of fracture of femur.

some of these aspects seem to occur early (interlinear pinch, erosion of the surfaces), others are tardier (geodes, decalcification).

a relation between the intensity of abnormal radiological findings and the severity of sequelae does not always exist, but one can observe major radiological alterations only when there is a major biological disturbance.

.I 835

.W

blood vascular disorders in

connection with the nose,

throat and ear

these disorders include (1) those having lesions

primarily in the nose, throat or ear, and (2) those

producing symptoms and signs in nose, throat

and/or ear only as a part of their symptomatology

and involve other organs as well. we will con-

sider the lesions in connection with the nose,

throat and ear separately.

.I 836

.W

volkmann's ischaemia

volkmann's ischaemia is the name given to a sequence

of events originally described by volkmann in 1881.

basically the condition consists of the replacement of

the limb flexor muscles by fibrous tissue following injury or

occlusion of the main arterial supply of blood to these

muscles. the condition is rare fortunately--mainly because

of improved methods of prevention. the flexor muscles of

the toes are sometimes affected, but the commonest group of

muscles so damaged are the flexor muscles of the forearm.

total arterial occlusion to a limb for several hours usually

causes frank gangrene; partial or total occlusion for shorter

periods may give rise to ischaemic contracture. the muscles,

being deprived of their blood supply, die and are subsequently replaced by fibrous tissue. like all scars, the fibrous tissue contracts, producing the complete picture of volkmann's ischaemic contracture. the forearm is thin and wasted, and the fingers are held in flexion owing to the overall shortening of the flexor muscles. in severe cases, if the nerves are also affected or if the entire muscle mass is replaced by fibrosis, the fingers may be totally paralysed as well.

.l 837

.w

linik der polyarthrosen

among the degenerative affections of joints

the symptoms of the arthrosis of

the joints of the fingers with heberden-nodes,

the bouchard-nodes of the inter-

digital joints, the polyarthrosis - on those subjects

coste and forestier wrote about

and how they were described by lffb too - and the

arthropathies of chronic gout are

more thoroughly discussed. the rare conditions,

as the arthrotic changes in hemo-

philia, psoriasis and metabolic disorders are

mentioned. a wider area is dedicated

to the differentiation between degenerative and

inflammatory diseases. it is refer-

red to, that gout more often occurs in our days

and one is forced to calculate with
it more than some years ago. it is also referred
to the significance of the serological reactions for the differential diagnosis.
the most important diseases are
enumerated, which do not belong to degenerative
polyarticular affections of joints,
but which very often get mixed up with them.

.I 838

.W

major surgical procedures,
including amputation,
on a hemophiliac
various surgical procedures in a hemophilia patient, including amputation above
the knee, are reported. human cohn fraction
i (fibrinogen/ahg) was used to ensure
normal hemostasis. the patient's ability to
form a firm clot within a normal time was
measured and treatment was prescribed in
accordance with serial studies with the
thrombelastograph.

.I 839

.W

the prevention of crippling
in haemophilic children
children who are severely affected with haemo-

philia or christmas disease suffer repeated haemorrhages into joints and muscles after trivial injuries. these episodes of bleeding produce cumulative crippling. the haemarthroses tend to be recurrent; each episode produces some damage to the joint surface and the immobility during convalescence leads to muscle weakness. thus after recovery the joint becomes increasingly liable to renewed bleeding. the deep muscle haematomata can produce crippling by actual destruction of muscle tissue, by pressure on important nerves or arteries, by contractures which develop during healing and by failure of resolution of the original haematoma leading to chronic cyst formation.

.I 840

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throat and nose surgery in patients with constitutional haemostatic defects successful surgery in patients with defective haemostasis is becoming possible and it is of interest to detail the problems encountered in nose and throat surgery.

.I 841

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hemophilic arthropathy

jaromir priborsky, zora antalovska

the authors report their experience with joint diseases in 54 patients suffering from hemophilia, 49 of them being cases of hemophilia a, 5 of hemophilia b. 21 patients were children up to the age of 14 years. bleeding into the joints occurred in 66.6% of patients. in the age group over 14 years the cases of bleeding into the joints were more frequent (78.8%) than in the age group up to 14 years (47.7%). there were no differences as to bleeding into the joints and the seriousness of articular changes between the cases of hemophilia a and hemophilia b. in most cases the bleeding into the joints began between the 6th and the 14th year of age. bleeding into the joints as the first manifestation of a hemophilic condition occurred only in 9.3% of patients; in most cases other hemophilic manifestations preceded. in spite of this fact the joint manifestations were often wrongly diagnosed as tuberculous arthritis, rheumatic fever, progressive arthritis, and were treated accordingly. most usually the large joints (knee, elbow, ankle) were affected with bleeding and in them the changes were also the most serious. the joints of both halves of the body were affected uniformly. in most cases several joints were affected while monoarticular localization

was observed in 16.6%. the seriousness of articular changes was dependent mainly on the number of repeated bleedings into one and the same joint, although other factors (weight bearing of the joint, complexity of the joint, treatment) may be of decisive importance in the individual cases as well.

according to clinical (especially from the functional point of view) and x-ray criteria the articular findings were classified into three groups: in the first group the function of the joint is preserved, in the second limited and in the third practically extinguished. the following laboratory tests were carried out: erythrocyte sedimentation reaction, latex test for the rheumatoid factor, c-reactive protein, mecoprotein tyrosine and weltmann's coagulation test.

the findings were normal even in cases of irreparable articular changes unless acute bleeding into the joint or in some other localization, or some other complicating disorder was present simultaneously.

the therapy of hemophilic arthropathy remains troublesome owing especially to a frequent occurrence of articular bleeding.

a close cooperation of the hematologist and the rheumatologist or the orthopedist may con-

tribute to the improvement of the fate of
these patients.

.I 842

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prevention and treatment of joint deformity in haemophilia
experience in treating established joint deformities in 27 patients, and
preventing the development of deformity in 10 younger patients, during the last
8 years, has shown that there are two types of haemorrhage, which require
different treatment to prevent chronic deformity.

.I 843

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the haemophilic pseudotumour
or haemophilic subperiosteal haematoma
the case history of a haemophiliac in whom a large haematoma of the thigh was
treated by amputation of the limb is described.
examination of the available radiographs and of the histology led to the
conclusion that the cyst was subperiosteal in origin.
evidence is presented to support the hypothesis that haemophilic pseudotumours
are always associated with subperiosteal haemorrhage, and that those
haemophilic cysts which are confined to muscle have little or no effect on the
adjacent bone.

.I 844

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actinomycin d and the response to parathyroid hormone
actinomycin d inhibits the effect of
parathyroid hormone upon bone, as measured
by ca mobilization, without altering

its effects upon the renal excretion of phosphate and ca in rats.

.I 845

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aspects of circadian periodic changes in phosphorus metabolism in mice kinetic studies on the p32 content of mouse brain phosphorus fractions following the intraperitoneal injection of p32-labeled orthophosphate were performed during two selected segments of the 24-hour time scale. the results of these studies suggest that the circadian periodicity in relative specific activity of brain phospholipids is probably a consequence of a variation in the extent of p32 incorporation into brain inorganic phosphate and is not indicative of a periodicity in the rate of intermediary phospholipid metabolism. data on the postinjection time course of the specific activities of plasma inorganic phosphate, liver inorganic phosphate, and liver phospholipid suggest a similar explanation for the circadian periodic changes in relative specific activity of liver phospholipids. a circadian rhythm of inorganic phosphate concentration in mouse plasma is demonstrated.

consideration of a mathematical model suggests that the observed within-day variation in p32 distribution and the circadian periodicity of phospholipid relative specific activity in liver and brain are a consequence of this periodicity in plasma phosphate content. a significant within-day variation in total phosphorus content of liver was observed. the disturbance of mice incident to p32 injection has a marked effect on the plasma content of inorganic phosphate and corticosterone.

.I 846

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specificity of the inhibition of tubular phosphate reabsorption by certain amino-acids the inhibition of tubular phosphate reabsorption by certain amino-acids is a highly specific one in which differentiation between such closely related compounds as the d and l isomer is clearly possible.

.I 847

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localization of phosphaturic effect of parathyroid hormone in nephron of the dog the renal mechanism and tubular site of the phosphaturic action of parathyroid hormone were investigated by clearance and stop-flow

techniques in one intact and seven thyroparathyroidectomized dogs. administration of hormone caused a significant increase in the excretion of phosphate without increasing the filtered load. stop-flow analysis indicated that in the absence of parathyroid hormone most of the filtered phosphate was reabsorbed in the proximal tubule, and that the hormone increased the rate of phosphate excretion by inhibiting this reabsorptive mechanism. ^{32}P injected during stopped flow showed no significant transport across the renal tubule despite the presence of excess parathyroid hormone. significant ^{32}P activity appeared in the stop-flow collections simultaneously with the appearance of new filtrate. there was no evidence that parathyroid hormone mediated a secretory process for phosphate excretion.

.I 848

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the regulation of growth hormone secretion
in the present communication we summarize
our investigations on the control
of secretion of hgh using radioimmunoassay
for the measurement of plasma
gh. the assumption, implied throughout this
presentation, that changes in
secretory rate are responsible for acute
changes in plasma concentration of
hgh appears reasonable since the
fluctuations in plasma hgh concentration
are often too rapid to be caused solely by

alterations in hormonal degradation or excretion. for slower changes in plasma hgh concentration, however, alterations in the rate of removal of hormone from the body fluids might play a contributory role. however, there is no evidence that important changes occur in the rate of removal of hgh from the circulation except in patients who have developed antibodies to hgh following treatment with hgh.

.I 849

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early infantile autism and receptor processes the syndrome of early infantile autism is examined as a function of deviation in near-distance receptor usage. these receptor deviations are compared with normal receptor hierarchies developing from near to distance receptor dominance. the available information is consistent with the view that early infantile autism involves early sensory deprivation. this sensory deprivation results from an interaction between a constitutional deficiency inhibiting certain reticular arousal functions and mothering tending to understimulation.

treatment of the young autistic child is suggested including stimulation and communication via the available near receptor systems. in the framework of sensory development, directions for the study of early diagnosis and treatment are indicated.

.I 850

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studies on compensatory renal hypertrophy. i. effect of unilateral ureteral ligation and transection data are presented comparing the relative rate of compensatory renal hypertrophy and hyperplasia of the control kidney of rats following either unilateral ureteral transection, ligation, or nephrectomy. the growth of the control kidney on the unoperated side was strikingly slower after ureteral transection and ligation when compared with that resulting from the removal of one kidney. progressive hydronephrosis was observed on the operated side following ureteral transection and ligation and was more pronounced in the latter. degree of hypertrophy of the control kidney showed a close correlation with degree and duration of the hydronephrosis of the kidney on the operated side. these observations

have been interpreted as indicating the operation of a control system regulating kidney growth in response to changes in some way related to kidney size.

.I 851

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studies of the changes in growth and dna synthesis in the rat kidney during experimentally induced renal hypertrophy there is a high rate of accumulation of newly synthesized dna in the kidney after folic acid injection, compared with the small increase during the first few days after unilateral nephrectomy. there is a large increase in the water content of the kidney after folic acid which does not occur after unilateral nephrectomy. the changes in the wet and dry weight and the rna and dna content of the kidney have been compared after administration of folic acid, unilateral nephrectomy and unilateral nephrectomy followed by folic acid 24 hr later in an attempt to study the nature of these differences. after unilateral nephrectomy there was a steady increase in wet weight, dry weight and rna content of the kidney, each parameter reaching about 35 to 40% above normal by 14 days, by which time the dna content had increased

by only about 25%. an increased rate of dna synthesis was found between 2 and 4 days, returning almost to normal by 7 days. after folic acid injection there were very large increases in wet weight (60%), rna content (100%) and dna content (70%) during the first 4 days accompanied by a smaller increase in dry weight (30%). thereafter these parameters declined, relative to body weight, returning almost to normal by 14 days. the rate of dna synthesis was greatly increased as early as 24 hr after injection and reached a much higher level than that found after unilateral nephrectomy, before returning to the normal level by 7 days. when unilateral nephrectomy was followed 24 hr later by folic acid injection, the increases in weight, nucleic acid content and rate of dna synthesis were greater than at the corresponding times after either treatment alone. marked differences were found in the labeling indices of kidney cells after either unilateral nephrectomy or folic acid injection. the latter treatment resulted in very large increases in all three zones of the kidney, whereas after unilateral nephrectomy the responses of the cortex and outer medulla were much lower, with no significant increase in the inner medulla. when both treatments were combined, the response of the remaining kidney was similar to, though

more exaggerated than, that of the normal kidney
after folic acid injection.

.I 852

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renal and adrenal relationships
in compensatory hyperplasia
the compensatory renal hyperplasia that
normally follows unilateral nephrectomy
is abolished by bilateral adrenalectomy if
rats are maintained on fresh drinking
water, but is restored when saline drinking
water is provided or if such animals are
injected with doca. the adrenals are also
important for the increased proliferation
caused by unilateral hydronephrosis. these
experiments suggest that the role of the
adrenal cortex in renal hyperplasia may be to
secrete mineralocorticoids, which
promote the retention of sodium and thereby
stimulate cell division in the kidneys.

.I 853

.W

a genetic study of neonatal obstructive jaundice
58 children with extrahepatic biliary atresia, 7 with intrahepatic
biliary atresia and 50 with 'neonatal hepatitis' were analysed
concerning diagnostic criteria, natural history, familial, clinical
and pathological data. in extrahepatic biliary atresia, there is no

evidence of a familial tendency, influence of maternal age, birth order or disturbance of foetal development. in 'neonatal hepatitis', there were 4 consanguineous parents, suggesting a mutant autosomal gene in homozygous form. some infants with the genotype for 'neonatal hepatitis' may manifest a very mild or a very severe form, so, a diagnosis was not made. an apparent excess of males over females may be another evidence of failure of manifestation of the genotype. but 'neonatal hepatitis' may be a manifestation of more than one disease. in 'neonatal hepatitis' the birth weight shows a marked decrease, perhaps as a sequence of disturbed liver function in the foetus.

.I 854

.W

parathyroid extract-induced changes in the oxidation of citrate, succinate and other organic acids by liver.

parathyroid extract (pte) or partially

purified parathyroid hormone administered in

vivo markedly altered the oxidation

in vitro by rabbit liver minces of citrate, -keto

glutarate-c, succinate-c, fumarate-c

and lactate. with Ca^{++} present in the

incubation medium, minces from pte

treated animals produced more CO₂ and had

a greater O₂ consumption than did control

minces. this stimulation was due, in part

at least, to a more rapid decline in metabolic

activity of the control tissues. when

ca++ was absent, total metabolism was increased and the tissue derived from pte treated animals was less active than the control tissue. the effect was detected as early as 4 hr after injection (750 u/kg) and could be elicited with as little as 200 u (at 14 hr). the action of pte could not be duplicated by the injection of cacl into the animal. the data suggest that one effect of treatment was a general inhibition of oxidation. the stimulation of metabolism could be a consequence of this inhibition or a separate unrelated alteration.

.I 855

.W

actinomycin and erythropoiesis and the production of erythropoietin in mice.

in b6d2f female mice a single dose of 10 of actinomycin will suppress normal erythropoiesis (fe erythrocyte uptake). in polycythemic mice 2 is enough to prevent the stimulatory effect of 0.25 a units of erythropoietin. the curves of suppression and recovery versus time support the hypothesis that erythropoietin acts for a short time in an early stage of erythropoiesis; after this early stage developing

cells are no longer so sensitive to actinomycin.
recovery, even from repeated
doses, is rapid and adequate. amounts of
actinomycin which are adequate to abolish
erythropoiesis do not prevent the new appearance
of erythropoietin in the plasma of
hypoxic mice.

.I 856

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the ultrastructure, histopathology, and
histochemistry of the parathyroid glands of pregnant
and nonpregnant cows fed a high level of vitamin d.
the parathyroid glands of pregnant and
nonpregnant cows were studied by light and
electron microscopy following the daily
feeding of 30 million units of vit d for 30
days and compared to untreated controls.
in both the pregnant and nonpregnant cows
the parathyroid glands became markedly
atrophic with a diminution in the amount of
parenchyma compared to the untreated controls.
after vit d feeding the number of
actively secreting dark and intermediate
chief cells was reduced and the percentage
of inactive (light) and atrophic chief cells
was increased. the parathyroid glands
of the vit d-fed, nonpregnant cows were

dominated by severely atrophic chief cells. these cells were characterized by their highly irregular shape, shrunken nucleus and cytoplasm, widened intercellular spaces traversed by numerous cytoplasmic processes, increased electron density, few secretory granules, inactive ergastoplasm and golgi complexes. atrophic chief cells were not present in the untreated controls. the predominating cell type in the parathyroids of the vit d-fed pregnant cows were the inactive chief cells. in contrast to the atrophic chief cells, they were larger and more regular in shape with relatively straight cell membranes. they were comparatively electron-transparent, containing more glycogen and fewer secretory granules. organelles concerned with protein synthesis and packaging into secretory units were poorly developed. inactive chief cells were observed only occasionally in the parathyroid glands of untreated pregnant cows where the actively secreting dark and intermediate chief cells predominated.

.I 857

.W

effect of heparin and parathyroid extract on acid phosphatase in bone.

to test the theory that heparin might stimulate acid phosphatase in the bone of young rats, heparin, pte, or a combination of both were injected. after an appropriate time interval acid phosphatase activity of bone of treated animals was compared with controls. it was found that heparin enhanced the pte-stimulated acid phosphatase activity of both calvaria and metaphysis but not diaphysis. the possible relation of these facts to the presence of lysosomes in osteoclasts was discussed.

.I 858

.W

the isolation of thyrocalcitonin and study of its effects in the rat.

the thyroid secretes a polypeptide hormone (thyrocalcitonin) which is effective in lowering plasma calcium and phosphate. the hormone

can be extracted from
the thyroid of the rat, dog,
pig, goat, ox, and monkey.
the isolation of the hormone
from pig thyroid by a combination
of salt fractionation
and gel filtration is described.
one microgram of
the pure material is very
active in the rat. thyrocalcitonin
remains effective after
parathyroidectomy, after
nephrectomy, after overdosage
with vitamin d, during vitamin
d deficiency, and during
calcium or magnesium deficiency.
its action is not prevented
by prior administration
of actinomycin d. a
single injection does not change
soft tissue calcium but
infusion for 12 hr lowers cardiac
muscle calcium. it is
concluded that this new thyroid
hormone acts on bone
and that it probably plays an
important role in normal physiology.

.I 859

.W

the effect of actinomycin d on parathyroid-induced change in bone and kidney.

actinomycin d (amd), an antibiotic known to inhibit dna-directed rna synthesis, was used to study parathyroid-induced changes in ca mobilization in vivo and in vitro as well as renal excretion of ca and phosphate in rats. intact and parathyroidectomized rats subjected to peritoneal lavage were administered amd, and changes in ca, p, and mg in lavage and serum were examined. amd consistently lowered the ca transfer into the peritoneal rinse in both the intact and parathyroidectomized animals, although the drop in ca was more acute if the animals were pretreated by subcutaneous injections of amd than if amd was administered as a component of the rinse. pretreatment of lavaged animals with amd prevented the expected increase in osteoclast numbers in the distal metaphysis of the femur but had no effect if administered as a component of the peritoneal rinse. the incubation of femora removed from both intact and parathyroidectomized

animals resulted in media ca levels that were significantly lower after 4 hr. incubation when amd was added in vitro. however, transfer of recently injected ca into the incubation medium from animals treated with amd was increased. in addition, parathyroidectomy of animals subsequent to administration of amd still resulted in expected changes in ca and p in the urine although amd significantly increased p excretion in both intact and parathyroidectomized animals. it was concluded that endogenous parathyroid hormone requires the continuous production of enzymes ultimately responsible for its action on bone and kidney, but that this action is not necessarily related directly to the production of m-rna.

.I 860

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inhibition by actinomycin d of bone resorption induced by parathyroid hormone or vitamin a. actinomycin d inhibits cell proliferation in control cultures of embryonic rat bone and prevents the stimulation of bone resorption by parathyroid hormone (pth) or vit. a. with a dose of 0.004 /ml. of actinomycin

d, pth effects are only partially inhibited
and this inhibition can be overcome
by increasing the dose of pth. these
findings suggest that these agents act competitively.

.I 861

.W

j. clin. endocr. 1965, 25/4 (457-464).

antagonism between parathyroid extract and adrenal
cortical steroids in man.

metabolic balance studies were done in 2

patients with hypoparathyroidism who

received hydrocortisone or prednisone

during the administration of parathyroid

extract. administration of prednisone was

associated with phosphate retention,

decreased urinary ca, decreased serum

ca, citrate and glycoprotein concentrations,

and increased serum phosphate.

excretion of parathyroid activity in the

urine of 1 patient was uninfluenced by the

administration of prednisone. it is concluded

that the antagonistic effect of the

adrenal cortical steroids was expressed

at the biochemical sites of action of the

parathyroid extract in bone and kidney,

that the steroids reduce parathyroid secretion

but that their administration probably does not

result in degradation or inactivation of
the hormone.

.I 862

.W

tissue distribution of electrolytes, ca and mg in experimental
hyper- and hypoparathyroidism.

the effects of experimental hyper- and

hypoparathyroidism on plasma and tissue

distribution of electrolytes and tissue

exchangeability with ca and mg were studied

in dogs following acute renal pedicle

ligation. in hyperparathyroidism, plasma concentrations

of mg and inorganic p as

well as ca were increased. a greater accumulation

of ca occurred in some tissues

and a lesser accumulation in others than

in acute hypercalcemia of comparable

severity and the fractional rate of exchange

of tissue ca was 30% more rapid than

in control and acute hypercalcemic dogs.

bone exchange of ca was not significantly

increased. cell mg concentrations were

not appreciably altered by hyperparathyroidism

except for a significant 9% decrease

in myocardium, but the fractional rate

of exchange of tissue mg was increased.

acidsoluble p concentrations were decreased

in 3 tissues and na and c1 concentrations were decreased by 10 to 25% in 4 tissues. in hypoparathyroidism, in addition to a decreased plasma ca, the increment in plasma inorganic p that usually occurs after renal pedicle ligation was 75% less than in control dogs. cell ca concentrations were decreased by 10-40% but the fractional rate of exchange of tissue ca was unaltered. although cell mg concentrations were unaltered a 40% increase occurred in the exchangeability of skeletal muscle mg. tissue na and c1 concentrations were decreased by 20% in 2 tissues. it has been previously reported that hypercalcemia increases cell ca concentrations by raising the extracellular ca concentration gradient. evidence has also been presented that hypercalcemia directly inhibits cell influx of mg and na and cell efflux of k. with altered parathyroid activity, 2 types of effects are observed: those which are dependent upon an abnormal extracellular ca concentration and those which appear to be due to intrinsic effects of parathormone on cell cation transport. the present data are compatible with the hypotheses

that parathormone stimulates bidirectional transport of cell Ca^{2+} and P^{4-} , stimulates cell influx of Mg^{2+} and opposes the effects of hypercalcemia on cell transport of univalent ions.

.I 863

.W

the inhibition of respiration and phosphorylation in kidney mitochondria by parathyroid hormone administered in vivo.

parathyroid hormone administered

in vivo to rabbits

produced a metabolic alteration

in kidney cortex

mitochondria, evidenced by

diminished respiratory rate,

respiratory control, and P/O

ratio with a series of substrates

including pyruvate plus

fumarate, succinate,

ketoglutarate, malate, citrate,

and isocitrate. the adenosine

triphosphate-inorganic

phosphate exchange reaction

rate was decreased and

adenosine triphosphatase

activity was increased compared

to control mitochondria.

these changes did not become

apparent until about 12
hr. after injection, were undiminished
by 24 hr., and could
be elicited with as little as 200
usp units of hormone.
under identical conditions liver
mitochondria were unaffected.
diphospho- and triphosphopyridine nucleotides
in combination frequently elevated
the respiration in
parathyroid-treated mitochondria
close to or above control
levels with citrate and isocitrate
but not with the
remaining substrates and had
no effect on respiratory
control with any of the substrates.
the effects of the
hormone could not be duplicated
by elevating and maintaining
in otherwise normal rabbits
serum ca concentrations
at twice normal level
for 6 hr. it is concluded
that the effects produced by
parathyroid hormone on kidney
are multiple in nature and

related to the Ca^{++}

raising potency of the preparations.

.I 864

.W

sudden hypocalcemia in normal and hypoparathyroid subjects.

serum calcium concentration was suddenly decreased

in 10 normal and 4 hypoparathyroid subjects

by the infusion of 50 mg/kg of disodium edta over a

30- to 45-minute interval. the return rate to pre-infusion

values of the serum calcium concentration was the

same in both groups. serum phosphate showed a marked,

transient decrease 30 min after the infusion in normal

individuals, but not in those with hypoparathyroidism.

the hypophosphatemia was followed by a marked

increase in phosphate clearance in the normal group and

a decrease in the hypoparathyroid group. urine phosphate:

urine creatinine $\times 10$ ($\text{up:uc} \times 10$) and urine

phosphate: urine osmolality $\times 10$ ($\text{up:uo} \times 10$) ratios

also reflected an increased phosphate excretion in the

2 groups. a simple clinical measure of parathyroid

function is suggested by determining the $\text{up:uo} \times 10$

or the $\text{up:uc} \times 10$, or both, ratios before and 3 to 6

hr after intravenous infusion of disodium edta.

.I 865

.W

parathyroid function in chronic renal failure. a statistical survey

of the plasma biochemistry in azotaemic renal osteodystrophy.

a collection has been made of 134 personal and published cases of azotemic osteodystrophy in which adequate information was available concerning the pathological state of the bones. measurements were available of the plasma calcium, plasma phosphate, and blood-urea-nitrogen in all cases, and of plasma bicarbonate and plasma proteins in a representative sample. the plasma levels of calcium and phosphate in the whole series of 134 cases were not related reciprocally but were correlated directly. these data were further analyzed by allocating each case to either of 2 sub-groups, according to the type of pathological lesions present in the bones. in one group there was evidence of defective mineralization of skeletal tissues, in the form of either rickets or osteomalacia, and the plasma-calcium was found to be statistically sub-normal. in the other group there was no primary defect of mineralization but the lesions of generalized osteitis fibrosa were present and the plasma calcium was statistically normal. there was no significant correlation between the plasma levels of calcium and phosphate in either sub-group; and the plasma phosphate was significantly higher in the group with the higher plasma calcium levels. the data indicate that in patients with renal osteodystrophy, contrary to general belief, the plasma calcium varies independently of the plasma phosphate. since these results imply differences in parathyroid function among patients with azotemic

osteodystrophy, a survey has also been made of the recorded parathyroid weights in chronic renal failure. generalized osteitis fibrosa and the accompanying normal levels of plasma calcium are associated with greater parathyroid hypertrophy than is found in most cases of chronic renal failure or cases with defective mineralization. the various data are interpreted in relation to the known metabolic disturbances and natural history of azotemic osteodystrophy. by analogy with states of simple vitamin d deficiency, it is suggested that hypocalcemia and relative unresponsiveness to the calcemic action of parathyroid hormone are related to an acquired resistance to vitamin d. the group of cases with statistically normal plasma-calcium prove that the parathyroid glands can function effectively in some patients with chronic renal failure, irrespective of the level of the plasma phosphate. the size of the glands and the effects of sub-total parathyroidectomy in patients of this group suggest that the normal plasma calcium results from an increased production of parathyroid hormone. the more advanced renal failure in the normocalcemic, as compared with the hypocalcemic, cases could mean that the development of an effective degree of secondary hyperparathyroidism is a function of the duration of the renal disease. it seems likely that when the parathyroid response is sufficient to overcome the effects of the vitamin d resistance it also entails the development of generalized

osteitis fibrosa, healing of the defect of mineralization
and increased liability to metastatic calcification.

.I 866

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albright's hereditary osteodystrophy. report of a family with studies
of bone remodeling.

two members of a single family, each representing
different forms of albright's hereditary osteodystrophy,
have been presented. the kindred pattern is
similar to those of other reported families and is consistent
with a sex-linked or autosomal dominant mode of
inheritance. the importance of a course of intramuscular
parathyroid extract for proof of parathyroid hormone
resistance is emphasized. biopsy specimens of rib,
labeled in vivo with tetracycline, were studied microscopically.
these new observations indicated cellular
defects in bone remodeling shared by the propositus and
case 2, which may explain the low rates of bone turnover
found in each. immunologic studies established the
presence of a substance antigenically similar to parathyroid
hormone in the parathyroid tissue of the propositus.
the pathogenesis of albright's hereditary osteodystrophy
and atypical forms of parathyroid hormone
resistant hypocalcemia is discussed.

.I 867

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acute hyperparathyroidism: a surgical emergency.

acute hypercalcemic crisis of hyperparathyroidism is a surgical emergency. diagnosis is often difficult because of the polymorphous character of the symptoms. the variable clinical features of the syndrome are described emphasizing the frequent occurrence of gastrointestinal symptoms, especially duodenal ulcer of recurring pancreatitis in the antecedent history as well as the better known occurrence of renal and skeletal manifestations, which precede the crisis in all but a few cases. despite the variability of the clinical manifestations, the total syndrome forms a distinctive pattern which should be recognizable once it is known. previously reported cases have been reviewed and an additional case reported. the differential diagnosis, aids in identification of the tumor and prospects for more effective control of the hypercalcemia are discussed. at the present time, early surgical removal of the tumor is the only effective treatment.

.I 868

.W

actinomycin d inhibition of intestinal transport of calcium and of vitamin d action.

actinomycin d injection inhibits the actions of vit d in increasing concentrative transport of ca across the intestinal wall in vitro and in raising serum ca concentrations of fasted vit d-deficient rats. actinomycin d blocks the transport of ca across the mucosal surface of vit d

deficient as well as vit d-treated rats so that its action is on the ca transport system, rather than on the stimulatory effect of vit d. this inhibitory effect of actinomycin d on ca transport is present within 3 hr of its s. c. injection and is less marked at 18 hr which suggests a direct interaction with the ca transport system. under the same conditions actinomycin d does not influence the transport of 1-tyrosine across the intestinal wall in vitro.

.I 869

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studies on hydroxyproline excretion and corticosteroid-induced dwarfism: treatment with human growth hormone.

two children who had been receiving large doses of corticosteroids for years and were growing at a retarded rate were treated with human growth hormone. growth rate increased 2.5 to 3-fold and urinary hydroxyproline excretion which was initially low increased to the normal level. when treatment was stopped, growth rate and hydroxyproline excretion decreased promptly.

.I 870

.W

a comparison of human placental lactogen (hpl) and human growth hormone (hgh) in hypopituitary patients.

the conclusions based on the studies reported are that placental lactogen (hpl) at a dose level of 200 mg./day did not induce a positive nitrogen balance in two hypopituitary subjects. in addition, lactogen does not augment

the nitrogen retaining effect of growth hormone

when given in a dose of 200 mg./day.

.I 871

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radiation necrosis of the brain in acromegaly.

radiation therapy of pituitary tumors can

cause necrosis of the brain (4 cases are reported),

particularly if a carefully considered schedule of

dosimetry is exceeded. the error can be due to

repeated courses of treatment or too rapid administration.

the cerebral lesions develop after a

latent period of months and are progressive and

often fatal. appropriate pituitary surgery is preferable

to multiple treatment with radiation.

.I 872

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experiences with high treatment of twelve hypopituitary

dwarfs for periods varying from 6 to 41 months

are reported. all the patients were considered to have

hypopituitarism from birth, four of them of the hereditary

type, four possibly due to traumatic birth or neonatal asphyxia,

and four from an unknown cause. in six

patients detailed information concerning growth during

the first year of life could be obtained. all of these patients

had a degree of growth retardation before one

year of age. we consider this to be the rule rather than

the exception in pituitary dwarfism. the most important

diagnostic evidence was a marked degree of growth retardation accompanied by a pronounced delay in skeletal maturation, and, in most cases, signs of secondary hypothyroidism, increased insulin sensitivity, and a poor response to metopirone administration. none of the patients who had passed the normal age of puberty had matured sexually. all twelve patients responded well to hgh therapy. during the first year of treatment the average height increment was 10 cm. ('catch-up' growth). with continued treatment a normal rate of growth, about 6 cm./year, was obtained. there was no disproportionate acceleration of skeletal maturation in any of the patients. none of them has so far become resistant to hgh administration. the oldest patient has reached normal height. whether this will be possible not only in the moderately severe, but also in the most severe cases of pituitary dwarfism, can not yet be stated. the possibility of using human gonadotrophic hormones in an attempt to produce sexual maturation in these patients is discussed briefly.

.I 873

.W

treatment of retarded growth with human growth hormone. results of treatment with human growth hormone in the following 3 cases are discussed:
female hypopituitary dwarf of 17 yr.,
who grew 10 cm. in 20 mth.; a boy

of 14 yr. with constitutional retarded growth,
in whom the growth rate increased;
and in a case of primordial dwarfism in a girl
of 10 yr. in whom the growth curve
was unaffected by the treatment.

.I 874

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genetic pituitary dwarfism with high serum concentration of growth
hormone new inborn error of metabolism?.

a description is given of three siblings with hypoglycemia
and other clinical and laboratory signs of growth
hormone deficiency but with abnormally high concentrations
of immunoreactive serum growth hormone. since
exogenous growth hormone was active in these patients,
the endogenous secretion of an abnormal growth hormone
molecule is postulated.

.I 875

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growth-hormone deficiency in man:
an isolated, recessively inherited defect.

a deficiency of human growth hormone not associated
with other pituitary deficiencies was observed in
midgets with sexual ateliosis, a form of dwarfism inherited
as an autosomal recessive trait. body proportions,
sexual development, birth weight, and postpartum lactation
are normal in this syndrome.

.I 876

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treatment of short stature in children and adolescents with human pituitary growth hormone (rhGH). Experience with thirty-five cases.

Human pituitary growth hormone (rhGH) was evaluated by longitudinal study of growth as a therapeutic agent in the treatment of short stature. Clinically significant increases in growth rate were achieved in 11 of 13 hypopituitary patients. No significant improvement in linear growth rate was noted with a dose of 2 mg 3 times weekly in children whose short stature was due to other conditions. No adverse reactions were noted; thyroidal, adrenal or gonadal activation was not observed. Growth was stimulated, probably without an undue increase in bone age, though this point demands continued scrutiny. Owing to the limited supply of this material it is recommended that it be used only in cases of documented growth failure, and a protocol for evaluation of therapeutic response is discussed. Though not a panacea for treatment of short stature, human growth hormone fulfils a unique and invaluable role in replacement therapy for the hypopituitary dwarf.

.I 877

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the development of bilateral adenomatous adrenal hyperplasia

in a case of cushing's syndrome of eighteen years' duration.

a case of cushing's syndrome of 18 years'

duration is presented. the disease

began when the patient was 8 years old and

was partially controlled by pituitary

radiation when she was 13. however, clinical

evidence indicate low grade but continuous

adrenocortical activity for the next 13

years. the probable suppression

of gh secretion by the increased steroid levels

during her growth period provides

a reasonable explanation for the dwarfism of

the patient. the administration of 8 mg

of dexamethasone per day failed to decrease

urinary steroid excretion. bilateral

nodular hyperplasia was found at surgery.

it is suggested from the evidence presented

that this patient's disease began first

as a primary pituitary process but

during the long duration of the acth secretion

it evolved into one of autonomously

functioning bilateral nodular hyperplasia.

.I 878

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hypopituitarism: a study of growth

hormone and other endocrine functions.

pituitary function was evaluated in 25 adults with evidence of hypopituitarism or enlargement of the sella turcica. growth hormone secretory function was measured by radioimmunoassay of plasma samples taken before and after insulin-induced hypoglycemia in a standardized test of growth hormone reserve. all patients exhibited significant defects in growth hormone secretion, as indicated by the failure of this hormone to rise to normal levels in response to hypoglycemia. the order of frequency of hormonal loss was: growth hormone, gonadotropin, adrenocorticotrophic hormone, thyroid stimulating hormone. no pattern of deficiency was characteristic for any particular etiology of hypopituitarism.

one patient with asymptomatic enlargement of the sella turcica (accidentally discovered) had an isolated loss of growth hormone secretory capacity. two patients in the series demonstrated intrinsic deficiency of thyroid as well as pituitary secretion, and both had elevated titers of antithyroid antibodies. this study represents the first direct evaluation, by radioimmunoassay of growth hormone function in a series of hypopituitary adults. it demonstrates a remarkably high prevalence of growth hormone loss, and suggests that the growth hormone response to hypoglycemia may be one of the most sensitive tests for the diagnosis of hypopituitarism.

.I 879

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hypoglycemia and dwarfism associated with the isolated deficiency of growth hormone.

the authors have studied a 7-year-old dwarfed boy with a history of severe, recurrent hypoglycemic episodes since age 1 and retarded bone age. hepatic, adrenal, and thyroid function were normal. he demonstrated fasting hypoglycemia with blood sugars of 30-40 mg./100 ml. he was not sensitive to l-leucine but showed insulin sensitivity and hypoglycemic unresponsiveness. glycogenolysis in response to both adrenaline and glucagon was appropriate. fasting plasma gh levels were less than 1 m g./ml. (normal 1-3), and no rise was seen after insulin-induced hypoglycemia. similarly, these low gh levels did not rise 3-6 hr. after a glucose tolerance test.

treatment with hgh reversed the alterations in carbohydrate metabolism. it is concluded that the patient suffered from an isolated gh deficiency which resulted in dwarfism and alterations in carbohydrate metabolism.

.I 880

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the effect of growth hormone in hypothalamo-pituitary dwarfism. i. the metabolic effects of human growth hormone.

human growth hormone, isolated by raben's method, was given in 2 to 5 mg. daily doses over periods from 1 to 12 days to 7 patients with pituitary-hypothalamic dwarfism.

the metabolic effects were as follows:

nitrogen retention with a variable reduction in blood urea. the plasma amino-acid concentration did not alter after i.m. injection of the hormone during fasting.

an accompanying retention of intracellular components, in such proportions required for protoplasm formation.

isotonic expansion of the extracellular compartment, without change in the plasma

electrolyte concentrations. retention of phosphorus, sometimes a rise in plasma

phosphate; increased intestinal calcium absorption, hypercalciuria, no alteration

in plasma calcium; an increase in plasma citrate and citrate urinary excretion;

the calcium and phosphate retention was reversed

on stopping treatment. mobilisation of fat stores with lipid catabolism: this

was accompanied by a well marked

increase in nefa concentration for some hours

after hormone injection in the
fasting state, after a period of hypoglycaemia
and low nefa levels. a complex,
biphasic action on glucose metabolism. fasting
blood sugar levels are altered,
as are the glycaemia in various tests such as
fasting, insulin injections, tolbutamide
administration, intestinal hyperglycaemia.
acceleration of intermediate
metabolism with increased blood citrate
concentrations and 24 hours urinary
excretion of α -ketoglutaric acid. in one test
during fasting the blood citrate increased
4 hours after hormone injection. after
an oral load of sugar the blood citrate
and α -ketoglutaric acid concentrations
did not alter. a progressive gain in
weight has been found during treatment, partly
reversible on stopping treatment,
correlating with the intracellular nitrogen retention
and expansion of the extracellular
space, despite mobilisation of fat reserves.

.I 881

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serum chorionic 'growth hormone-prolactin' and serum pituitary
growth hormone in mother and fetus at term.
chorionic 'growth hormone-prolactin' (cgp) and

pituitary hgh were measured in maternal and fetal blood obtained simultaneously at term from 29 pregnant women and their fetuses utilizing sensitive radioimmunoassay procedures. the mean concentration of serum cgp in maternal venous blood was 5.6 g/ml (sem 0.39) whereas in umbilical venous serum the mean concentration was 0.019 g/ml (sem 0.003), a 300-fold difference. contrariwise, the mean concentration of serum hgh in maternal serum was 5.9 m g/ml (sem 0.52) and in umbilical venous serum the level was 33.5 m g/ml (sem 4.6). the ratio of serum cgp/hgh in maternal venous serum was 1076 in contrast to 0.57 in umbilical venous serum. the findings strongly suggest that cgp is secreted by the syncytiotrophoblast almost exclusively in a unidirectional manner into the maternal circulation. further, it is unlikely that an appreciable exchange of hgh occurs between the maternal and fetal circulations. the data support the view that the growth hormone-like metabolic changes observed in pregnancy are attributable to the effects of cgp and are consistent with the hypothesis

that cgp is an important metabolic hormone of pregnancy exerting its actions on the mother and possibly the placenta, but only indirectly on the fetus.

.I 882

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effect of abdominal operation on glucose tolerance and serum levels of insulin, growth hormone, and hydrocortisone.

abdominal operations of moderate severity are followed by high fasting blood-glucose levels and a reduced tolerance to intravenous glucose which persists for at least 72 hours after operation. fasting plasma-insulin levels are raised after surgery. intravenous glucose produces much higher levels of serum-insulin and growth hormone in the immediate postoperative period. corticotrophin infusion increases the plasma-hydrocortisone levels and reduces glucose assimilation to a greater extent than operation, but has no effect on serum-insulin or growth-hormone levels.

.I 883

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plasma growth hormone concentration in the rat determined by radioimmunoassay: influence of sex, pregnancy, lactation, anesthesia, hypophysectomy and extrasellar pituitary transplants.

the assay used is described in detail. several experimental conditions were studied, both to validate the method and to determine factors which regulate gh secretion

in this species. in fasting sprague-dawley rats weighing 150-200 g, mean plasma gh concentration in females was 94.2 17.3, and in males, 54.9 12.0 m g/ml. gh levels in lactating rats were determined to be in the normal range for females, thereby providing evidence that this assay does not detect prolactin. gh levels were not elevated in pregnant rats. hypophysectomy led to a fall below detectable levels of gh. intraocular pituitary transplants failed to raise gh levels in hypophysectomized hosts. gh levels in male, but not in female, rats are depressed by brief periods of ether anesthesia. these findings and the results of pituitary transplantation experiments are further evidence that the nervous system is involved in the regulation of gh secretion.

.I 884

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clinical features of the alalies (russian).

the term 'alalies' is applied to the various states of absence or insufficient development of speech in children, resulting from defective development or affections of the speech centers before the development of speech. from the clinical study it is possible to distinguish between several forms: motor, sensory, and semantic alaly with signs of amnesia. the causes are multiple: trauma, perinatal

cerebral hemorrhage, inflammatory processes, metabolic disorders before the development of speech, and alimentary and trophic disorders. the alalies show varying degrees of severity. in most children suffering from alaly, neurological signs can be demonstrated on the right side, an indication of the organic nature of the condition. the presence of local symptoms in the various forms of alaly is often associated with signs indicating involvement of adjacent regions of the cerebral hemispheres in the pathological process which would explain why the alalies are often complex. the character of the alalies depends on functional disorders resulting from the lesion in the frontal, anterior, motor, temporal or parietal region of the dominant cerebral hemisphere. patients with alaly often show neurotic reactions, resulting from the disorders of the processes of inhibition and excitation of the cerebral cortex and the subcortical formations. early treatment of the alalies with drugs combined with logopedic and pedagogic measures gives good results.

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an unusual form of acquired aphasia in children.

an unusual form of acquired aphasia-both

receptive and executive is described

as occurring in 10 children, 6 girls and 4 boys.

the onset occurred between 5 and

6 yr. of age with one or more epileptiform

attacks-which were not repeated-but

were followed by some degree of hearing

loss (later improving), failure to

comprehend spoken language and finally loss

or impairment of executive speech.

examination of csf and peg yielded normal

results. eeg's were abnormal mainly

in the temporal leads. the disorder appeared

self-limiting and throughout non-verbal

intelligence was not impaired.

.I 886

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childhood echolalia in delayed, psychotic and neuropathologic

speech patterns.

some linguistic analytical procedures and

preliminary findings from controlled tape-recorded

samples of a group of echolalic

children are reported together with the

clinical and experimental rationale for the

investigation. the subjects are echolalic

3-yr. olds and a group of young clinical referrals representing a variety of pathological conditions. variables selected for study include the proportion of echo to non-echo and silence, the quality and appropriateness of the non-echoed speech, the amount of the stimulus echoed, the nature of the triggering stimulus, the deviation of echo pattern from stimulus pattern, pitch-loudness-time variations, and the child's chronological and mental ages. early quantitative results yielded very similar echo: non-echo:silence percentages with echolalia representing a mean of about 40% of the conversation of each experimental group.

.I 887

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speech as a landmark in development. it is attempted to demonstrate how observations of children's speech and language development may serve as valuable indicators of their general physical, intellectual, and emotional progress. speech lag or breakdown may corroborate other suspect areas of development or may point the way to them. speech and language disorders seldom originate in the mouth. ideas must precede

speech, and speech is a direct
correlate of intelligence.

.I 888

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the applicability of individualized programmed instruction
in the education of deaf children.

verbal behavior is learned behavior and as
such is guided by the same principles
as any other learned behavior. the parents'

role is mainly to help the young deaf
child conceive of language as a socializing
process and to help shape language behavior
toward the use of verbal symbols.

the teacher's role in the deaf child's
progress as a language user includes (1) helping
the child discover how the structure
of his language operates and (2) guiding
him in the process of acquiring clear
concepts. the learning of a language is a highly
individualized process and requires
thousands of hours of practice. efficiency
in language teaching to the deaf
has not been generally achieved by traditional
methods. the teacher of the deaf
needs extra help in order to provide the individualistic
kind of teaching to insure
verbal over-learning by the child. self-tutoring

programed materials offer this help. programs are so constructed that a child proceeds through the program step by step with a probability of maximum success because of constant feedback as to correctness of his responses. for younger children the use of a machine seems desirable while for older children the program may appear in book form, on film strip, and any other visual medium. well constructed programs should be correlated with classroom instruction.

.I 889

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the impact of individual differences on language learning. a matrix of extrinsic and intrinsic factors affecting language learning in the prelingually deaf child is considered. particular emphasis is placed on the effects of parental attitudes on both the emotional stability of the home and on the provision or restriction of experience.

.I 890

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the oral language performance of premature children and controls. fifty-one premature children born in 1955 and 1956 were compared with 55 normally

born subjects with birth weights over 2,500 grams. they were tested on tapped patterns, auditory memory span, auditory discrimination, word recognition, language comprehension, articulation, resistance to articulation disintegration, word finding, story telling, number of words used, mean length of 5 longest sentences, sentence elaboration, grammatical errors, definitions and categories. the mean age of both groups was 5.8 and the premature children's performance was inferior to that of children born at term.

.I 891

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speech and reading problems in childhood. the following communicative disorders have been discussed: functional articulation defects, delayed speech development, stuttering, hearing loss, cleft palate, neurological disorders, and reading disorders. these disorders rarely have a single cause. they are the result of an intermingling of many factors, some physiological and some psychological, some residing within the child and some in the parents and environment in general. delayed

or defective speech is a cause for great concern to most parents and teachers. the public health worker who listens with an attentive and sympathetic ear may allay some of this anxiety and thus help foster healthy emotional development in the child. the existence of a more serious condition underlying the presenting communication problem, even if sensed by the parents, is frequently denied. the public health worker can assist the parents in the painful process of facing up to their fears. a child with a communication problem is still a child and the public health worker by simply reflecting this to the parents and advising them on normal child-raising practices can, again, be of help to the child. children with speech deviations are exposed to an overabundance of well-intentioned speech correction at home. most of it is ineffective; some of it, unfortunately is harmful. while the worker may not be in a position to offer specific advice on a particular child, the manner in which the parents and teacher are handling the child's communication problem can be explored and damaging practices

possibly eliminated. the fact that there may be a diagnostic and treatment center to which the child can be referred does not vitiate the public health worker's role. the public health physician and public health nurse have a valuable contribution to make in helping the parents, school, and child accept the chronic nature of the disorder.

.I 892

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disorders of communication in young children. the normal development of spoken language is outlined. the causation, differential diagnosis, individual assessment and management of developmental disorders of communication in young children are briefly discussed.

.I 893

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acquired aphasia in children. this report concerns the cases of 21 boys and 11 girls studied over a period of several years while rehabilitation was carried out. the general conclusions fall under 3 headings: (1) symptomatology as compared with that of aphasia in the adult; (2) the course of the disorder; (3) prospects of the level of intellectual performance in the

future of the children. in 13 cases, cerebral damage had resulted from traumatic contusion; in 10 cases from an intracranial nontraumatic hematoma (vascular malformation, aneurysm or angioma); in 2 cases the aphasia followed operation for a cerebral astrocytoma; in 2 further cases occlusion of the left middle cerebral artery had occurred; and in the remaining 5 cases no precise diagnosis was made.

.I 894

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the causes of delayed development of speech. speech develops parallelly and simultaneously with psychophysical development of the child, arising from internal need and under the influence of external factors. not all children are given the chance to develop in favorable conditions and to pass through all the phases of development without some injury. the various possibilities when a child may be injured and hampered in the development of speech are discussed. the testing of the sense of hearing in children with a cleft palate is also included-out of 181 cases of cleft palate, in 72 cases there was decrease of the sense of hearing exceeding

30 db. this additional injury of the child with a cleft palate, if remaining unnoticed, may make the treatment of speech abnormality difficult. the necessity of diagnostic team investigation and the treatment of children with speech disturbances are emphasized.

.I 895

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concept learning in culturally disadvantaged children as a function of verbal pretraining.

while research indicates that verbal pretraining has a positive influence on the discrimination learning performance of subjects of normal intelligence, a comparable influence has not been shown for other types of conceptual tasks for retarded subjects.

the purpose of this experiment was to investigate the effects of stimulus pretraining on concept learning by subjects who had a 'high risk' of being classified as mentally retarded at some future time.

a group of 27 'higher risk' and 27 'lower risk' subjects was randomly divided into 3 pretraining groups: verbal label, attention, and control. subsequent to pretraining on the stimuli used for transfer task 1, subjects

in each group were presented with a concept learning task (transfer task 1). after reaching the criterion of learning on transfer task 1, subjects were presented with a second, new, concept learning task. analysis of the data revealed that there were no significant performance differences between risk groups and that pretraining had a significantly positive effect on performance.

.I 896

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concept development and language instruction. the author describes factors related to, and the errors that may occur in concept development in children. the contributions of language for the deaf child's conceptual development are stressed. included are a review of what concepts are, psychologically, and an example of how concepts may be presented, educationally, in the classroom.

.I 897

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formal speech characteristics as a diagnostic aid in childhood psychosis. the frequency of use of various grammatical units in the spontaneous conversational speech of adults and children has been

noted by many authors to be fairly stable.
the hypothesis that idiosyncratic distributions
might be found in certain specific
disorders of ego functioning was tested
in relationship to childhood psychosis. some
support was found for this, as well as
for some contemporary psychological and
psychoanalytical interpretations of phenomena
seen in childhood psychosis.

.I 898

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cerebral dominance and speech acquisition in deaf children.
in examining the prediction that left cerebral
dominance, as indexed by hand and
sighting preference, should be a positive accompaniment
of speech learning in individuals
whose cerebral speech areas are likely
to be in the left hemisphere, it was
found that over a 10-12 year period of formal
education right-handed-right-sighting
deaf students consistently earned higher speech
grades than their right-handed-left-sighting
and right-handed-mixed-sighting counterparts
matched on the basis of
hearing loss. this finding supports the hypothesis
that the cerebral mechanisms
relevant to speech acquisition are simplified,

facilitated, and/or less prone to interference when control of speech, hand, and eye is localized primarily in 1 hemisphere of the brain.

.I 899

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a color test for the measurement of antibody to the non-acid-forming human mycoplasma species.

a metabolic inhibition test for the measurement of growth inhibiting antibodies to the non-acid producing human mycoplasma species is described. the test is based upon the ability of these organisms to metabolize arginine with a resultant alkaline shift in the ph of the medium. the alkaline shift is inhibited by specific antiserum. labile accessory factor(s) present in unheated guinea pig serum potentiates the inhibitory effect of antiserum. the test is sensitive and specific for the measurement of antibody to mycoplasmas

in rabbit immune

and human convalescent serum.

.I 900

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serologic epidemiologic studies with m. pneumoniae. i. demonstration
of an hemagglutinin and its inhibition by antibody.

a new direct, specific
hemagglutination reaction
with live m. pneumoniae is described.
this requires the presence of a natural antibody

for the red cell in the

horse serum employed in the

diluent. although vervet

monkey erythrocytes generally

have been employed,

human and rabbit cells may be

used. hemagglutination

can be inhibited by specific antibody

but heat inactivation

of the sera is required,

whether they be human or

animal in origin. antibodies

persist for many years and

are passively transferred to

the fetus. a micro variation

has been devised. the test

is useful for diagnostic

and epidemiologic studies and,
in reverse, can be utilized
for the rapid serologic
identification of new isolates.

the method is limited,
at present, to *m. pneumoniae*.

.I 901

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serologic epidemiologic studies with *m. pneumoniae*. ii. prevalence of
antibodies in several populations.

the prevalence of antibodies
for *m. pneumoniae*
was determined in 6 populations
by means of a new
serologic test. among members
of a population of 'normal'
families, no one under
age 15 had antibodies.
none of the latter acquired an
infection during the following
year. of 67 children in
a home, only 3 had antibodies.
the 7 cottage mates
of one of these children
who had acquired an infection,
remained uninfected. in
a group of 124 elderly persons,

65 (53%) had antibodies.
a similar proportion of 76 persons
attending a rheumatic
fever prophylaxis clinic
was positive. in this population
it was demonstrated that
antibodies could persist
in undiminished titer for at least
10 yr. of 169 point
barrow residents, 68% had
antibodies. above age 15
the rate was approximately
90%. two companies of
naval recruits who had similar
positive antibody rates
at the beginning of training,
acquired antibodies in
rather divergent patterns, 63%
in one and 26% in the
other. m. pneumoniae infections
seem to be sporadic
and to produce epidemics only
infrequently in civilian
populations.

.I 902

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growth and survival of mycoplasma neurolyticum in liquid media.

maximal growth of *M. neurolyticum* (between 10 and 10 colony-forming units/ml) was obtained after 3 days of incubation at 36 °C in broth media containing 10% agarose horse serum. When whole horse serum was used in the medium, a complement-mediated inhibition was observed. This inhibition could only be detected when growth was followed by daily plate counts. Maximal growth was delayed for about 24 hr by the horse serum, and the inhibition was spontaneously reversed at the temperature of incubation. Penicillin G was also found to have a temporary inhibitory effect. This was detected with as little as 40 units/ml. Maximal growth was delayed until the 6th day of incubation, when 200 units/ml was present, and until the 16th day, when 1,000 units/ml was present. The survival of *M. neurolyticum* at undetectable levels in cultures during the incubation period presented an 'eclipse' phenomenon which has not been explained. The recrudescence of growth in such cultures late in the incubation period illustrates the events which may occur when mycoplasmas are isolated from clinical material by prolonged

incubation in the presence of inhibitors
survival data showed that *M. neurolyticum*
had greatest stability at pH 8.0, with
reduced viability at pH 9.0, 7.0, 10.0, and
6.0, in that order. The data on growth
and stability suggest a close relationship
between the species of mycoplasma studies
and bacteria.

.I 903

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HeLa cells resistant to bromodeoxyuridine and deficient in thymidine
kinase activity.

mutant sublines of HeLa S3 cells resistant
to growth inhibition by bromodeoxyuridine
(BUDR) have been isolated. The resistant
cell lines (HeLa BU-10, HeLa BU-15,
HeLa BU-25, HeLa BU-50, and HeLa BU-100)
proliferated in the presence of 10,
15, 25, 50, and 100 mg/ml BUDR, respectively.

Extracts from HeLa BU-25, HeLa
BU-50, and HeLa BU-100 cells exhibited
2-5% of the thymidine-H, deoxyuridine-H,
and bromodeoxyuridine-H phosphorylating
activities of parental HeLa S3 cells.

HeLa BU-10 and HeLa BU-15 cell extracts
were also deficient in thymidine kinase
activity, yielding approx. 43% and 8%,

respectively, the thymidine kinase activity of parental hela s3 cells. the deficiency in thymidine kinase activity of hela bu-100 cells was not due to negative feedback inhibition by high levels of budr or to interference with the thymidine kinase assay by inhibitors or competing enzymes in the hela bu-100 cell extracts. following 5 weekly passages in media lacking budr, the hela bu-100 cells did not exhibit increased thymidine kinase activity. moreover, mixtures of extracts from hela s3 and hela bu-100 cells displayed a thymidine kinase activity equivalent to the sum of the activities of extracts prepared, respectively, from the hela s3 and hela bu-100 cells. radioautographic studies have shown that after hela s3 cells were incubated for 6 hr with thymidine-h, 35-45% of the nuclei were heavily labeled with radioactivity. however, fewer hela bu-100 cells displayed labeled nuclei and the nuclei were only lightly labeled. hela bu-100 cell extracts contained normal amounts of thymidylate synthetase, thymidylate kinase, and uridine kinase activities. following infection by vaccinia

virus, high levels of thymidine kinase activity
were induced in hela bu-100 cells.

.I 904

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a note on the taxonomic status of strains like 'campo',
hitherto classified as mycoplasma hominis, type 2.

the classification of strains similar to
mycoplasma strain pg 27 of 'campo' as
myc. hominis type 2 should be withdrawn.

these strains have now been identified
as myc. arthritidis.

.I 905

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chromosome studies of human cells infected in utero and
in vitro with rubella virus.

a cytologic study of metaphase chromosomes
was undertaken to determine if damage
to the genetic apparatus of human cells may
be induced by rubella virus and whether
such damage produces the pathology seen
in newborns from mothers infected early
in pregnancy. fibroblast cell strains were
initiated in vitro from embryonic material
obtained by therapeutic abortion of fetuses
from rubella-infected mothers. embryonic
material from spontaneous and non-rubella
therapeutic abortions yielded similar

cell strains for infection in vitro. the results from both types of studies were as follows: (a) virus shedding cell strains were obtained from all types of organs cultivated, which indicated wide dissemination of virus in the fetuses from rubella-infected mothers. (b) chronic infection could readily be established by in vitro infection and no cytopathic effect was noted. (c) although many strains continued to shed virus throughout months of in vitro cultivation, no changes in growth properties occurred with the exception that infected strains from lung tissue showed limited growth capacities. (d) from observations of over 2,000 metaphases, neither obvious chromosomal rearrangements nor non-disjunctional changes were observed in strains infected naturally or experimentally. (e) among 17 rubella abortion-derived cell strains there was a marked elevation in frequency of chromosome breakage in 3 instances (18%, 29%, 68%,). (f) a correlation between virus shedding in vitro and increased chromosome breakage was noted although this was not complete. (g) the combined average frequency of chromosome

breakage in one set of 7 rubella-abortion strains was 18%; in the other set of 9 abortus strains, 9.8%. (h) similarly, a slight, but significant elevation in average chromosome break frequency (9.8%) was obtained in four cell strains which had been experimentally infected in vitro with rubella virus (uninfected cells: 5.2%). although effects upon the chromosomes were demonstrated, these were restricted to slight general elevations in frequency of breakage above normal values. very high increases in breaks were sporadic. it appears more likely that the general fetal abnormalities associated with rubella infection in vivo result from possible effects of the virus upon growth rather than from effects upon the chromosomes. however, the studies were restricted to fibroblasts cultured in vitro; and effects on other types of cells may have greater implications for this question.

.I 906

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fine structure of staphylococcal I-forms.

I forms of staph. aureus and bacterial cells were processed by the same technique for electron microscopy.

ultrathin sections allowed comparison of structural units and indicated that staphylococcal I form units of all sizes lack the rigid cell wall and the compact, fibrillar nuclear area of bacterial cells. the I form units are bound by a typical 'trilamellar' membrane comparable to that described for mycoplasma species. nuclear areas in staphylococcal I forms present a diffuse appearance and could not be correlated with size of any particular structural unit. many small units were seen within large bodies and possibly are involved in the reproductive process. no evidence of division by formation of septa or by pinching off of cytoplasmic fragments was obtained from the electron micrographs.

.I 907

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respiratory virus vaccines. ii. mycoplasma pneumoniae (eaton agent) vaccines.

purified and concentrated formalin-killed vaccines were prepared from m. pneumoniae propagated in serum-free artificial medium. the vaccines were aqueous or were incorporated in alum or emulsified peanut oil (adjuvant 65) adjuvant. two or 3 different concentrations of mycoplasma were included in each preparation. serum neutralizing and cf antibody responses were measured in hamsters, monkeys, and in institutionalized persons following 1,2,3 and sometimes 4 vaccinations. all of the preparations were

highly antigenic in animals and in man. alum vaccines were better than aqueous vaccines and those in adjuvant 65 appeared to give best results although the bleeding times were not always optimal for demonstrating maximal effect. persons who were without detectable antibody initially and thus would be most vulnerable to infection gave better responses to the vaccine than did those with pre-existing antibody. alum vaccine is an acceptable formulation for use in man, and only 2 doses of such vaccine were necessary to induce neutralizing antibody in 90% of the persons who were initially without detectable antibody. no local or systemic reaction of clinical consequence was noted in any of the persons vaccinated. recent unpublished findings, which indicate a high degree of effectiveness of the alum vaccine in stimulating antibody in preschool children and in protecting children and adults against the natural disease, are mentioned.

.I 908

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isolation of mycoplasma pneumoniae from adults with respiratory infections.

isolation of mycoplasma organisms from the sputum was attempted in 254 patients with various syndrome of respiratory disease. isolates were obtained in 56% of the 197 patients with pneumonia, 50% of patients with chronic bronchial diseases who were not treated with

tetracycline, and 33% of persons with acute upper respiratory infection. these differences are not statistically significant and indicate a nonpathogenic role for *m. pharyngis* and *m. salivarium* which were the strains most frequently isolated. the highest frequency of isolation was from males 15 to 30 yr. of age. isolation of *m. pneumoniae* requires one to 2 weeks:therefore, it is not useful for rapid diagnosis. also, it underestimates the prevalence of infection, especially if patients have received tetracycline. of the serologic tests, complement-fixation (cf) was the most specific. the growth inhibition test (tri) was the most sensitive and was significantly related to atypical pneumonia. the 2 tests may measure different antibodies against *m. pneumoniae*. serum cold agglutinins developed in many cases of pneumonia and were poorly discriminatory in etiologic diagnosis. *m. pneumoniae* infection occurred in a minimum of 8% and a maximum of 20% of civilian patients hospitalized for pneumonia during the season studied. serologic evidence for *m. pneumoniae* was rare in lobar pneumonia. in nonlobar pneumonia, *m. pneumoniae* accounted etiologically for 13% to 50% of cases. the incidence of *m. pneumoniae* infection was constant in different seasons but greatest relative to the occurrence of pneumonia in the fall and spring.

.I 909

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color test for the measurement of antibody to t-strain mycoplasmas.

a metabolic inhibition technique for the measurement of antibody to t-strain mycoplasmas was developed, based upon the ability of t-strain mycoplasmas to metabolize urea with the concomitant production of ammonia, and the ability of specific antiserum to inhibit this ammonia production. phenol red added to the medium served as an indicator of ph change resulting from ammonia production. specific antiserum to t-strain mycoplasma t-960 was prepared. the t-strain organism was shown to be serologically distinct from the recognized large-colony mycoplasmas. antibody to mycoplasma strain t-960 in human sera was demonstrated with the metabolic inhibition technique.

.I 910

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effect of mycoplasma on interferon production and interferon assay in cell cultures.

the influence of mycoplasma on the production and action of interferon was studied in cultures of both I and human embryonic kidney (hek) cells. m. hominis 1, the negroni agent, and the f12 mycoplasma were used for infection of I cells, and m. hominis 1 and m. pneumoniae for inoculation of hek cells. all strains were capable of multiplication in the culture systems employed. none produced detectable levels of interferon, and responsiveness of the cells to induction of interferon

by virus remained unaltered. infection with mycoplasma did not impair the sensitivity of the cells to the action of interferon, nor was the replication of vesicular stomatitis virus noticeably diminished.

.I 911

.W

recovery and characterization of a herpes-like virus from dog kidney cell cultures.

a transmissible agent was recovered from primary dktc which developed a spontaneous cpe. characterization and serological studies of the virus indicated that the virus was a new member of the herpes virus group.

.I 912

.W

immunopathologic changes in rheumatoid arthritis synovium. synovial tissue from 8 children and 7 adults with rheumatoid arthritis was examined for localization of immunoglobulins and complement. three cases were found to have c' and immunoglobulins within the cytoplasm of synovial cells, four cases had discrete localization within the connective tissue stroma; the remaining 7 cases demonstrated larger, more weakly staining collections which were found more diffusely

throughout the synovium. no immunoglobulin or complement localization was present in 10 out of 11 additional patients with forms of joint disease other than rheumatoid arthritis. correlation of these results with the clinical findings and joint fluid c' assays was made.

.I 913

.W

electron microscopic studies of mycoplasma (pplo strain 880) in artificial medium and in tissue culture. mycoplasma strain 880, isolated from a leukemic patient, was studied in broth cultures and in several cell culture lines. this strain exhibited considerable pleomorphism in size, internal structure, and shape, including forms with filamentous projections. the most common form observed was 0.5 to 1 in diameter and had a nuclear area of fibrillar strands, probably dna. the cytoplasm of the organisms contained ribosome-like granules and a flattened vacuole which indented the nuclear area. there were various other forms, including 'elementary bodies' 100m in diameter that were very electron-dense. in the tissue culture lines in which

the cells grew as a monolayer, the mycoplasma were closely associated with the cell surface and were occasionally seen in membrane-lined cytoplasmic vacuoles. in cell lines that did not attach to the glass, the mycoplasma were fewer and not attached to the cell surface. although the ultrastructure of this strain is similar to that of previously described strains, there are differences in details of structure which may be related either to the growth conditions used or to characteristics of the strain. the various forms of the organism are consistent with the suggestion that mycoplasma may have several mechanisms of reproduction (growth). the intracellular mycoplasma may be protected from antibiotics. this would partly explain the difficulty of eradicating mycoplasma from infected cell cultures.

.I 914

.W

long-term prognosis and the response of schizophrenic children to drug therapy: a controlled study of trifluoperazine.

it is evident from this study that treatment and control groups must be matched for severity of illness, since this affects the responsiveness to pharmacological

as well as to other types of treatments. the use of the double-blind technique does not of itself guarantee a well-controlled study; the comparison of 2 or more treatment regimes may be misleading if the groups are not matched, or if the matching is not based on critical factors. in this study, both the response to the nonpharmacologic aspects of treatment and the type of response to the drug itself were related to the initial severity of language impairment. thus the major developmental defect which determines long-term outcome for schizophrenic children in this group also predicted the immediate responsiveness to treatment. within the 2 major prognostic subgroups of young schizophrenic children, those with speech and those without, are children with different profiles of disordered development and different patterns of assets and handicaps.

.I 915

.W

the long-term treatment of a psychotic child in a psychiatric hospital.

description of one phase of the long term psychotherapy of a 6 yr. old psychotic boy, within the framework of a mental hospital. the first part deals briefly with the lay-out and the structure of a new unit for emotionally disturbed children. underlining the well-known importance of the therapeutic milieu in the treatment and care of the mentally ill particularly important when the patients are children. the child presented was diagnosed,

when admitted, as a case of severe childhood psychosis, of the autistic type. the unusually rich data at disposal were obtained through non-verbal communication, because the child has no language. nevertheless, he can express himself clearly through play and gestures. the analysis of this precious clinical material focuses the discussion on the existence and the quality of an object-relationship preceding the psychosis, the importance of the 'early unusual sensitivities' in the formation of a premature and fragile ego and the method of choice in the treatment of childhood psychoses.

.I 916

.W

comments on a case of infantile psychosis. an account is given of a case of infantile mutism which depended not so much upon a true autism as on a withdrawing into himself as a defence against a dangerous and threatening environment. there was a spectacular and unusual improvement of the symptomatology with psychotherapy.

.I 917

.W

the problems of infantile autism and psychiatric nosology. in psychiatric literature the syndrome of early infantile autism has been divided into several subgroups (as, for instance,

the subgroup of kanner and the subgroup of asperger) and has been assigned to different mental conditions (schizophrenia, psychopathy, neurosis). these distinctions and classifications are thought to be controversial, so long as the etiology of early infantile autism is unknown. nor should any 'psychiatric school' claim to have the 'right' concept of schizophrenia, since the etiology of schizophrenia, too, has not yet been discovered. in this particular 'pre-scientific' situation of psychiatry it seems more promising to analyze the individual mental case and to concentrate on clinical symptomatology instead of discussing arbitrary 'nosological entities'.

.I 918

.W

families of children with early childhood schizophrenia.

emotionally disturbed children were divided

into 3 groups on the basis of their

diagnoses of: (1) autism or symbiosis,

(2) chronic undifferentiated schizophrenia,

and (3) other forms of emotional disturbance.

the 3 groups were compared statistically

on the following demographic measures:

(1) educational level of parents; (2)

occupational level of father; (3) prevalence of broken homes; (4) male-female ratio in each patient group; (5) ordinal position among siblings; (6) ordinal position among siblings of same sex; and (7) age of parents at birth of child. results indicated that families of children diagnosed as autistic or symbiotic show many similarities to those with the diagnosis of chronic undifferentiated schizophrenia. in general, the parents in these 2 groups were better educated and were employed in more highly rated occupations than parents of otherwise disturbed subjects. broken homes were prevalent in the group of disturbed nonschizophrenic children, but not in the autistic or chronic undifferentiated schizophrenic groups. the male-female ratio was not significantly different among the 3 groups; in the autistic group, specifically, it was 2.8:1. the data revealed no trend in ordinal position.

.I 919

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childhood psychosis.

a description is given of the diagnostic criteria put forward by creak and her associates

in 1961 for what they have called
'schizophrenic syndrome of childhood'.
psychotic reactions in childhood are grouped
into: (1) childhood schizophrenia, (2)
organic states with psychosis, (3) mental
subnormality with psychosis, (4) sensory
deprivation, (5) neurosis, and (6) manic-depressive
psychosis. it is suggested that
the generic term 'psychosis' is the best
available, and a classification is presented
and discussed.

.I 920

.W

psychotic reactions of childhood: experiences of a mental retardation
pilot project.

clinical team evaluations are presented of a group
of 32 psychotic children who were initially thought to be
mentally retarded. emphasis is placed on consideration
of as many aspects of the total picture as possible with
diagnosis resulting from a synthesis of the individual
pieces of information. caution is suggested regarding
interpretation of incomplete psychological test findings,
especially in regard to prognosis. the results of this
study offer guidelines for differential diagnosis between
psychosis resulting from primary emotional disorders
and psychosis superimposed on a chronic brain syndrome
in children. questions are raised about early infantile

autism as a unitary syndrome on the basis of etiology.

the need for a better and more comprehensive diagnostic classification of the psychotic reactions of infancy and early childhood is stressed. this must be developed before valid comparisons of treatment and prognostic considerations can be made among groups of clinicians working in the field.

.I 921

.W

modification of autistic behavior with lsd-25.

lsd-25 appears to offer a useful adjunct to the psychotherapy of autistic children because of its positive effect in areas which are closely related to the process of psychotherapy. a pair of identical male autistic twins was periodically administered 50 of lsd-25 and observed for behavior changes. control and drug observations were made while the subjects were placed in a series of standard test situations referred to as the socialization test, social isolation test, peek-a-boo, pat-a-cake, face-to-face, hand-holding and following tests.

diverse behaviors were recorded in the areas of self-stimulatory behavior, social interaction and affect.

recordings were made using an esterline angus multiple pen recorder. all behaviors were measured in total time appearance and plotted as percent time in appearance. consistent behavioral changes resulted after lsd in that the subjects demonstrated an increase in eye-to-face

contact, an increase in laughter and smiling behavior
and decrease in self-stimulatory behavior.

.I 922

.W

the influence of organic and emotional factors on the origins, nature
and outcome of childhood psychosis.

a group of 65 children diagnosed as 'child
psychosis' (or one of its synonyms)

was followed up for an average of 15 yr.

none of the parents were schizophrenic;

6 (10%) had a parent who had psychiatric

treatment for neurosis. only 2 children

had a sib with transient autistic episode.

none had sibs with the adult type of

schizophrenia. these findings are felt to

mitigate against the view that child

psychosis is part of the schizophrenic group.

among the 65 children: 40% had an

i.q. below 50, 40% between 50 and 80 and

only 20% above 80. the i.q. was found

in general to be a good predictor of later

performances. mental retardation is

regarded as a primary component of the

clinical picture. evidence of brain damage

was conclusive in 15 children (24%) who showed

epileptic attacks (developing in 10

of them during the follow-up). speech disorders

were the most outstanding manifestation.
five children had confirmed receptive
aphasia and 14 others show some
evidence of it. in 75% of the speaking children
echolalia was noted; 11% had abnormalities
of delivering spoken words. the
view that reduction of speech is due
to social withdrawal is rejected. psychogenic
factors and parental attitude were
not found to be relevant to the etiology. the
psychosis is not considered primarily
emotional in origin, although emotional
relationships as well as educational management
have considerable influence on the
outcome of the disease.

.I 923

.W

compliance and resistance in the conditioning of autistic children:
an exploratory study.

twelve autistic children between 4 and 9 yr
of age were asked to choose red objects
and square objects from a stimulus array.
ten subjects made correct choices
significantly less often than chance, that is,
they avoided emitting correct responses.
the subjects were given 60 conditioning
trials in which choices of either red or

square objects were reinforced. those who attained either concept subsequently performed perfectly when asked to produce both red and square concepts; the other subjects continued giving fewer-than-chance correct responses. thus, conditioning trials elicited in some subjects an increased tendency to comply with the experimenter's instructions. the results suggest that more attention should be paid to the distinction between responses that autistic children are unable to make and responses that they are unwilling to make.

.I 924

.W

the etiology of autistic syndromes of children. examination and treatment of 92 children and youths with the autistic syndromes of early childhood over a period of ten years led to the impression that these disorders are a primary organic syndrome of manifold etiology. this view is supported by many relevant clinical experiences and data, which are discussed in detail.

.I 925

.W

acquisition of imitative speech by schizophrenic children.

two mute schizophrenic children were taught

imitative speech within an operant

conditioning framework. the training

procedure consisted of a series of increasingly

fine verbal discriminations; the children

were rewarded for closer and closer

reproductions of the attending adults' speech.

it is found that reward delivered

contingent upon imitation was necessary for

development of imitation. furthermore,

the newly established imitation was shown

to have acquired rewarding properties

for the children.

.I 926

.W

hallucinations in children at a state hospital.

hallucinations in children at referral and upon admission

to a state hospital were studied by reviewing

randomly selected charts of current patients. there

were no significant differences in the incidence of

hallucinations in boys and girls, between racial groups,

and between schizophrenic children under 12 and over

12. the children diagnosed psychosis with convulsive

disorder had the highest incidence of hallucinations

(81%); those diagnosed childhood schizophrenia had an

incidence of 70%; and children diagnosed primary behavior

disorder had the lowest incidence (35%). specific auditory, visual, and olfactory hallucinations were described. the nature of hallucinations in boys and girls was similar. psychotic children tended to have more bizarre hallucinations than nonpsychotic children. there was no difference in the nature of hallucinations among the different groups of psychotic children. although this population consisted of severely disturbed and deprived children who had a high incidence of hallucinations, these hallucinations were of simple content and not organized into delusional systems.

.I 927

.W

treatment of childhood schizophrenia. a three-year comparison of day and residential treatment.

a carefully designed study of 13 day-treatment children matched individually with 13 residential children is presented. in each case the diagnosis of schizophrenia was carefully confirmed on the basis of impairment in human relationship, disturbance in personal identity, resistance to change, unusual preoccupations, perceptual and cognitive disorders, and panic reactions. the ages ranged between 6 and 11. the children were selected, as the result of matching, with regard to age of onset, culture, and family organization. intactness of the family structure was required. residential treatment implied round-the-clock therapeutic interaction

with the child for 7 days each week, 12 mth of the year.
day treatment consisted of 9 a.m. to 4:30 p.m. care
5 days a week for 9 mth of the year. staff distribution
was identical in the 2 groups, but in the day-care group
the teacher assumed a larger relative position in the
world established for the child. all children were matched
in ego status at the beginning of the experiment
by means of the wisc and psychiatric evaluation,
changes in this status being measured by the wisc and
the metropolitan achievement test series. the results
indicated no significant improvement in either day or
residence in those schizophrenic children who, on admission
had unscorable wisc tests and who were the
most severely impaired in ego structure. among the
children scorable on the wisc, the organic groups in
day and in residential treatment showed equivalent degrees
of progress, the non-organic children in residence
gave evidence of more improvement than did the
matched children in day treatment.

.I 928

.W

visual versus tactual receptor preference in normal and schizophrenic
children.

receptor preferences between visual or tactual
stimuli were measured in schizophrenic and normal
children; 4 pairs of standardized choice situations between
visual or tactual stimuli were used, with the time

of engagement with either stimulus constituting the preference measure. schizophrenic children between the ages of 7 and 9 were compared with same aged normal children. a group of retardates were used for ma control. schizophrenics were significantly lower in visual preference than the same aged normals, and an age trend for increased visual preference was found in the normal sample. retardates showed greater visual preference than schizophrenics of comparable ma. some implications for theory of schizophrenia were discussed.

.I 929

.W

the effect of folic acid on growth and deoxyribonucleic acid synthesis in the rat kidney.

the effect of a single injection of folic acid (250 mg/kg of body wt) on growth of the rat kidney was studied. the patterns of the response were found to be essentially similar in animals aged between 3 wk and 12 mth. maximum values of kidney weight and nucleic acid content, relative to body weight, were found at 4 days at folate administration. the increases in wet and dry weights at this time were approx. 80% and 30% resp. above the control weights, and the percentage dry matter of the kidney was significantly lower than normal during this period. at 4 days the rna content of the kidney was also maximal, being about 90% greater than the control value, and the dna content after 4 days was increased

by about 60%. whereas the dna values in 6-wk-old rats were slightly lower at 7 and 10 days than at 4 days, in 12-mth-old animals a further small increase was observed at 7 days, suggesting a prolongation of dna synthesis in the older animals. autoradiographic studies of dna synthesis with thymidine-h have shown a greatly increased labeling index in all zones of the kidney following folate injection. maximum values were observed at 48 hr in the cortical zone, but the patterns of the changes in the medulla were less well defined. the labelling indices in the kidneys of 12-mth-old rats remained above normal for a longer period than in 6-wk-old rats. these results concur with the evidence of an increased dna contents of the kidneys of older rats between 4 and 7 days after folate.

.I 930

.W

renal renin in unilaterally nephrectomized hypertensive rats. juxtaglomerular index, renal pressor activity and width of the zona glomerulosa were normal in unilaterally nephrectomized hypertensive rats maintained on a normal sodium intake, increased in those subjected to sodium depletion and decreased in those receiving 1% saline. this indicates that renin formation and secretion are most likely the result of the sodium state

of the animal rather than loss of a renin-stimulating agent in the contralateral or unclipped kidney. failure of sodium to influence the degree of hypertension in unilaterally nephrectomized hypertensive rats militates against a direct quantitative relationship between blood pressure and the renin-angiotensin-aldosterone system.

.I 931

.W

hypertensive vascular disease produced by homologous renin. administration of rat renin to uninephrectomized rats reproduced most, if not all, the changes (hypertension, vascular disease, hypertrophy of the zona glomerulosa of the adrenals) found after partial constriction of the renal artery. this is taken as evidence that the renal pressor system plays a major role in the pathogenesis of renal hypertension.

.I 932

.W

effects of hypophysectomy and growth hormone on renal compensatory hypertrophy in rats.

the effect of hypophysectomy on renal compensatory hypertrophy (rch) was observed in unilaterally nephrectomized rats receiving no therapy and those

receiving replacement therapy and was compared to the rch attained by non-hypophysectomized unilaterally nephrectomized rats at 2, 5, and 10 days. in the latter group there was an initial rapid rch seen at day 2 which continued, but at a slower rate, through day 10. in the hypophysectomized group without replacement therapy there was also an initial rch in the first 48 hrs. however, instead of the rch continuing there was a regression in kidney size at 5 days and with no subsequent change at 10 days. in the hypophysectomized group receiving hormone replacement there was an initial rch comparable to the other 2 groups, but the further renal enlargement at 10 days was much less than that of the non-hypophysectomized animals. the results of this experiment and of other reported studies imply existence of a renotropic factor which is not produced in the pituitary, but which requires an intact pituitary for full effectiveness.

.I 933

.W

extrarenal fibromuscular hyperplasia.

clinical, radiologic, and pathologic studies on 19 patients with lesions in the extrarenal arteries that resembled fibromuscular hyperplasia are described. in 11 patients fibromuscular hyperplasia was present in the renal arteries. patients with involvement of the celiac artery were the only ones who had symptoms of

visceral ischemia. fibromuscular hyperplasia of the internal carotid arteries was observed in 6 patients, 2 of whom had symptoms of cerebral ischemia. nine patients with fibromuscular hyperplasia of the carotid or renal arteries had intracranial aneurysms, and in 2 others intracranial hemorrhage developed in the absence of demonstrable aneurysms. the histologic similarities between intracranial aneurysms and other types of aneurysms that appear in patients with fibromuscular hyperplasia, the frequency of intracranial aneurysms in patients with extracranial fibromuscular hyperplasia, and the similar sex and age incidence suggest a common etiologic origin.

.I 934

.W

some speculations on the nature and significance of developmentally small kidneys (renal hypoplasia).

renal hypoplasia may take several forms. among these the best known is perhaps renal dysplasia in which the parenchyma is maldeveloped. other forms of hypoplasia in which the renal parenchyma is normally formed but merely diminished in amount, do exist and may have severe clinical consequences. the finding at postmortem examination of anatomically small kidneys in children who suffered excessive or

unexplained dehydration has prompted the thought that renal tubular insufficiency may result from renal hypoplasia.

.I 935

.W

a study of induced renal hyperplasia using autoradiography.

to establish a base line for future

autoradiographic investigations, compensatory

renal hyperplasia was studied using tritiated

thymidine. labelled cells were infrequent

in the tubular tissues of control kidneys.

in the kidneys remaining after unilateral

nephrectomy there was a 5- to 6-fold

increase in the cortex and a 12- to 13-fold

increase in the medulla of labelled tubular

cells over the numbers seen in control

tissues. the findings obtained here are in

agreement with the observations made in

earlier investigations with routine methods

of staining and mitotic observation.

.I 936

.W

compensatory structural and functional changes in the kidney.

the radiographic assessment of the renal

size and the factors influencing renal

hypertrophy are discussed. the importance

of compensatory hypertrophy and its

prognostic significance is emphasised.

the changes are correlated with renal function

as measured by the glomerular filtration

rate and renal plasma flow.

.I 937

.W

bilateral renal hypoplasia of the pig.

bilateral renal hypoplasia of the pig is described

and is compared with a previous

description. the defect was observed in 19

piglets out of a total of 73 born in 8

litters, sired by one large white boar.

twelve affected piglets died at or soon

after birth and 7 died between the ages of 11

and 69 days. inheritance by a simple

autosomal recessive factor is suggested by

the evidence. grossly the condition

was characterized by varying degrees of

hypoplasia and persistence of fetal lobulation.

microscopically, the dominant feature

was the poor development of the collecting

tubule system. it is concluded that

the basic defect is a failure of development

of mesonephric mesenchyme.

.I 938

.W

the effect of nortestosterone phenylpropionate on compensatory

hypertrophy of the remaining kidney after unilateral nephrectomy.

forty-eight hr. after unilateral nephrectomy,

both in non-castrated and in castrated

male mice the relative dry weight of the

remaining kidney increased significantly.

this compensatory hypertrophy was significantly

stimulated as early as 96 hr. after

operation by treatment with 19-nortestosterone

phenylpropionate (= npp) at the

time of operation. the percentual increase

of the kidney weight was approximately

the same in non-castrated as in castrated

mice. the absolute initial values as well

as the resulting values 96 hr. after operation

were higher in non-castrated male

mice than in castrated animals. the number

of cells and the dna concentration per

g. tissue decreased during the period of

non-stimulated compensatory hypertrophy

in both groups of animals. npp caused a still

further decrease. the concentration

of dna per cell did not change. following

non-stimulated compensatory hypertrophy,

there was no change in the rna concentration

per g. tissue or per cell in castrated

mice. in non-castrated mice the concentration

increased. npp caused approximately

the same percentual increase of rna concentration in non-castrated as in castrated animals during the period of compensatory hypertrophy. the difference between both groups of mice in the rna concentration in the remaining kidney following stimulation of the compensatory hypertrophy by npp was statistically significant.

.I 939

.W

thyroid and pituitary gland activity during compensatory renal hypertrophy.

autoradiographic studies with tritiated thymidine showed an increased synthesis of dna and cellular proliferation of the thyroid and pituitary during compensatory renal hypertrophy.

.I 940

.W

the influence of thyroid hormone on renal function during the course of compensatory hypertrophy.

during the course of compensatory hypertrophy of the kidney, glomerular filtration and renal plasma flow increased to a less extent in thyroidectomized animals than in control animals. the secretory capacity of the renal tubules of thyroidectomized

animals increased insignificantly during compensatory hypertrophy, but increased markedly after administration of thyroid hormone.

.I 941

.W

kidney cell proliferation after unilateral nephrectomy as related to age.

the effect of unilateral nephrectomy on the number of cortical kidney cells undergoing dna synthesis and mitosis was measured by tritiated thymidine autoradiography in both weanling and adult rats. among the unoperated control animals, the weanling rat group showed a base line labeling index of 0.59%, and the adult animals, one of 0.11%. the response to unilateral nephrectomy resulted in a peak value of 3.6% in the weanling animals and 1.2% in the adult animals, both occurring at 36 hr. mitotic indices were 0.056% in the weanling control animals and 0.0062% in the adults, with a peak of 0.30% and 0.088%, resp., at 36 hr. separate counts of tubule and stromal cells in the cortex revealed that the maximum increase in % labeled cells occurred later in the stromal cells than in the tubule cells; the stromal cells not reaching a maximum until 57 hr after nephrectomy. the findings indicate that, although the relative proliferative activity is much lower in adult animals, a similar

response, qualitatively, is obtained in both groups after unilateral nephrectomy.

.I 942

.W

influence of the adrenal glands on dna synthesis in normal and compensating kidneys.

the role of the adrenal glands in controlling

the synthesis of dna in normal and

compensating kidneys of rats given saline

drinking fluid was studied using tritiated-thymidine

and radioautography. adrenalectomy

alone increased significantly the

labeling of the renal cortex and medulla of

otherwise intact rats. two days following

unilateral nephrectomy of rats with intact

adrenal glands, the number of labeled

nuclei in the remaining kidney increased by

factors of about 4 and 2.5 in the cortex

and the medulla, respectively. adrenalectomy

moderately decreased the hyper-plastic

response of the cortex of the remaining

kidney, but increased still further

the labeling index of the medulla. by 5 days

after unilateral nephrectomy of rats

with intact adrenal glands, neither the cortex

nor the medulla of the remaining kidney

exhibited a marked hyperplastic response.

in adrenalectomized animals, also,
unilateral nephrectomy caused only slight
increases in the labeling indices of the
cortex and the medulla of the remaining kidney.

.I 943

.W

auto-radiographic studies of the protein metabolism of the single
kidney in the nephrectomized rat.

rats were subjected to unilateral nephrectomy,
following which the protein metabolism
of the other kidney, which exerted
a compensatory activity, was studied
with h-labelled l-phenylalanine, at different
intervals (3hr. to 7 wk.). two
phases of enhanced incorporation of amino-acids
into the cells of the convoluted
tubules were found, with one maximum
after 6 hr., at which time the uptake is
limited to the cytoplasm, and a 2nd maximum
on the 4th day, when the nucleus is
equally involved. in the course of the 2nd
phase of enhanced amino-acid uptake,
there is also an increased mitotic index
of the epithelia of the tubules. in the
collecting tubules, there was only one phase
of enhanced amino-acid uptake, with a
maximum on the 4th day, also coinciding

with an increased mitotic index. the increase of the number of cells of the kidney was determined by a study of the variations of the mitotic index. the mean multiplication factor in the beginning amounts to 1.6. the protein metabolism is increased 1.3 times. the increase of the volume (factor 1.3) and the increase of the protein metabolism per unit of volume (factor 1.3) of the hypertrophic kidney result in a total increase of the protein metabolism of 2.1 times, once the adaptation process is complete, so that the residual kidney has approximately the same protein metabolism as 2 normal kidneys.

.I 944

.W

two brothers with nephrogenic diabetes insipidus. the patients, a 5-year-old and a 13-year-old boy, had suffered from polydipsia and polyuria since the age of 1 yr. physical and mental retardation, hyperchloremia, and lowering of kidney concentrating power were observed. the patients were resistant to pitressin. they were considered to be suffering from nephrogenic diabetes insipidus caused by a recessive heredity factor.

.I 945

.W

studies on the sweat in renal diabetes insipidus during treatment with saluretics.

description of a 5-month-old boy suffering from familial diabetes insipidus. his sweat as well as that of his mother had an increased nacl content. chlorthalidone and furosemide had a different effect both on the quantity and on the nacl content of the sweat. a single dose of chlorthalidone decreased the nacl content for a short time, but increased the quantity of sweat during 3 days. furosemide given intermittently produced a decrease of the sweat nacl also during the intervals and an increase of the quantity of sweat; however, as a contraregulation during the intervals, the quantity of sweat decreased and at the same time the urea content increased. from the isotonic serum filtrate in the sweat glands H_2O and nacl were reabsorbed in the ducts and the urea concentration increased but the reabsorption of H_2O and nacl did not go parallel, therefore the sweat is hypotonic. this regulation is altered in diabetes insipidus, therefore the high values

of nacl. without changing the osmolarity,
na is exchanged with k. this mechanism
is accentuated if the na-concentration
is high.

.I 946

.W

diabetes insipidus treated with synthetic lysine vasopressin.

a case of diabetes insipidus was associated
with an eosinophilic granuloma in a
2.5-year-old child. partial control of symptoms
was achieved with pitressin tannate in
oil, 7.5 u. i.m. on alternate days. synthetic
lysine vasopressin i.m. controlled
the urine output at a dose of 5 u. 8-hourly,
but the preparation was not well tolerated.
it was therefore given by the nasal route,
and over a 6-month period the diabetes
was controlled with a dose of 14 u. t.d.s.

.I 947

.W

the action of vasopressin in renal diabetes insipidus.
as the water-retaining action of antidiuretic
hormone is eliminated in renal diabetes
insipidus, the steps in na transport can
be separately determined. vasopressin
induced a prompt increase in freewater
clearance and urinary volume, as well

as a delayed increase in sodium clearance.
it is suggested that vasopressin brings
about stimulation of sodium reabsorption in
the ascending limb of henle's loop. it
is supposed that both physiological actions
of antidiuretic hormone - the antidiuretic
and the sodium-active effect - become operative
in two different places in the nephron
and synergistically produce a maximum
concentration of urine.

.I 948

.W

pituitary diabetes insipidus associated with progressive urinary
tract dilatation.

a case of pituitary diabetes insipidus with
associated obstructive urinary tract
changes is described. the patient was treated
both by surgical correction of lower
tract obstruction as well as by control of
the diabetes. reversal of anatomic changes
over a 1-year followup period is demonstrated.

.I 949

.W

the antidiuretic effect of angiotensin in diabetes insipidus.

the effect of angiotensin (val-5-hypertensinii-asp- -amide)
was studied in 2 children with diabetes
insipidus (a 9 yr old boy with diabetes insipidus neuro-hormonalis

and a 4 yr old girl with diabetes insipidus renalis) in whom the clearances of inulin, pah, na and urea and the osmolar and free-water clearances were examined. angiotensin produces a prompt antidiuresis which is combined with a gross decrease of the na-clearance. the osmolality of the urine is increased only slightly and the free-water clearance does not become negative, both effects being contrary to those seen with vasopressin. the antidiuresis and antinatriuresis can be produced in salt-loaded and salt-deprived states. furosemide reverses the effects of angiotensin. the clearance of urea is not changed by angiotensin as long as the glomerular filtration rate remains normal.

.I 950

.W

polyuria in children.

twelve polyuric children have been investigated in the present report from their etiologico-clinical aspect and they have been classified into four broad groups. the first group of diabetes insipidus syndrome included 4 cases - 3 of idiopathic type and one of the acquired variety due to hand-schuller-christian-disease. the 4 cases in the second group of nephrogenic diabetes insipidus after further investigations were diagnosed as renal acidosis (1 case), other renal tubular syndromes with multiple defects (2 cases), and hypokalaemic nephropathy (1 case). the third group of polyuria due to chronic renal

failure has been exemplified by one case. the fourth group of 3 cases had compulsive water drinking as the probable etiology. in addition to the illustrative case histories, a practical diagnostic approach in the context of physiopathology of normal urine excretion has been recommended.

.I 951

.W

treatment of diabetes insipidus: synthetic lysine vasopressin nasal solution.

twenty patients with vasopressin-deficient diabetes insipidus were treated with a nasal solution of synthetic lysine vasopressin. use of the nasal spray 2 to 8 times daily controlled polyuria in all patients without recurrence of the side effects occasionally observed with posterior pituitary preparations of animal origin. one pregnant patient was well controlled to term without undesirable uterine stimulation. because of its ease of administration, the absence of significant water retention (if used judiciously) and the freedom from potentially serious allergic reactions to foreign protein, this synthetic preparation is recommended for clinical use.

.I 952

.W

synthetic lysine vasopressin nasal spray in the treatment of diabetes insipidus.

thirteen patients with diabetes insipidus

were satisfactorily and conveniently

treated with synthetic lysine vasopressin

nasal spray, the material being administered

3 to 5 times per day in a total daily

dosage ranging from 35 to 125 u. a

transient decrease in effectiveness was noted

during periods of upper respiratory

infection or allergic rhinitis. the only adverse

effects of the nasal spray consisted

of minor nasal irritation in 3 patients and

increased frequency of bowel movements

in one child after he increased the dose in

an effort to concentrate and restrict

urine volume. in hydrated normal subjects,

lysine vasopressin administered

s.c. is 7.4 times as effective as the nasal spray preparation.

.I 953

.W

diabetes insipidus treatment with 8-lysine vasopressin in a nasal spray.

synthetic 8-lysine vasopressin administered

as a nasal spray to 3 patients with diabetes

insipidus resulted in excellent control

in one. in the other 2 it was of some

value as therapy supplemental to pitressin

tannate in oil. the patient who was adequately controlled with 'spray therapy' alone required the sprays every 3 hr. during the day, but none during the night.

.I 954

.W

salt and water distribution in hereditary and in induced hypothalamic diabetes insipidus in the rat.

salt and water metabolism and the distribution of na, k, and water in gastrocnemius and in aorta were measured in spontaneous hereditary hypothalamic and in surgically induced diabetes insipidus in the rat.

the degree of severity in the 2 types of the disease was estimated in terms of salt and water handling. water turnover in 24 hr. was about equal to body weight in the hereditary disease and about 60% of body weight in the induced disease. skeletal muscle na increased more than 20% in the familial disease, and the gain involved both cells and environment. there was no corresponding loss of k. similar changes of lesser degree were noted in the induced disease. the degree of na accumulation appears to be partially dependent on the duration of the disease.

.I 955

.W

antidiuresis induced by saluretics in diabetes insipidus.

in hypothalamus-pituitary and less regularly

in nephrogenic diabetes insipidus some

diuretics cause a fall in diuresis mainly

due to reduced excretion of free water.

this adh-like action, not correlated with

the extent of the natriuretic action or with

salt depletion, depends on a direct effect

of the drug on water permeability in the

distal tubule and is suppressed by cortisone.

it is maximal for the thiazide

derivatives and diminishes progressively

with mercurial compounds, spiro lactones

and triamterene in that order and is absent

for acetazolamide. the reduction in

glomerular filtration and increased proximal

reabsorption of na following salt

depletion induced by the diuretics is of less

importance and irregular in appearance.

.I 956

.W

congenital hydronephrosis.

histological study of the renal parenchyma

in cases of hydronephrosis is a guide for

surgical treatment. if the renal parenchyma

is reduced in thickness to 3 mm. or less
it leads to complete atrophy. but if the
thickness is more than 3 mm. conservative
procedures are justified.

.I 957

.W

neurohypophysial principles in rats with familial hypothalamic
diabetes insipidus (brattleboro strain).

antidiuretic and oxytocic assays were
performed on tissues from 3 female rats with
familial hypothalamic diabetes insipidus (di)
and on 3 normal females. oxytocic
activity was only slightly lower in the pituitaries
from the di rats. antidiuretic activity
in the pituitaries from 2 di rats was
no more than that expected from their
content of oxytocin. thus, these pituitaries
appeared to contain oxytocin but not
arginine vasopressin. the hypothalami from
these 2 rats showed minimal antidiuretic
activity, which might have been due to
oxytocin or vasopressin. the pituitary
from the third di rat contained more antidiuretic
activity than could be due to oxytocin.
antidiuretic responses to extracts of
pituitary and hypothalamus from this
rat resembled those produced by arginine

vasopressin. this pituitary appeared to contain about 1/100 the normal amount of vasopressin. since vasopressin can inhibit diuresis in these di rats, it would appear that they have a specific deficiency of endogenous arginine vasopressin.

.I 958

.W

familial renal diabetes insipidus.

renal diabetes insipidus has been known for 20 yr. only. the first german report on such a case appeared in 1957. nevertheless this disease appears to be more frequent, also in germany. a report is given on 4 infants from 2 families with a verified diagnosis. in the one family there were 3 other cases with the features of the disease (polydipsia, polyuria, low sg of the urine). in the other family anamnestic studies revealed 5 such cases.

.I 959

.W

evaluation of 20 years' experience with the treatment of hydrocephalus in infants.

a total of 394 infants were examined between 1943 and 1962. till 1961, 369 infants were examined and 246 were operated on (66.7%);

this group is analyzed. laurence's opinion on the favorable spontaneous evolution is not agreed to and the merits of surgical treatment are proved. a dynamic form of hydrocephalus in operated infants is shown; the patients who were not operated on suffered from other diseases combined with macrocephaly which must be distinguished from hydrocephalus. a spontaneous arrest of the process was observed in only 14 children, e.g. 3.8%, as compared with laurence's 42.6%. the cause and pathological findings are analyzed in 102 infants operated on between 1957 and 1962. a great discrepancy between the time of the onset of first symptoms and the time of operation was found. this disease manifests itself in 50% of infants in the first month of life, but the average age of infants at the time of operation is 6.1 mth. only 3% of infants are operated on in the first month. thirteen operating procedures were used in the 20 yr. under review. until the introduction of deviation of the csf into the jugular vein or into the cardiac atrium, 15.33% of the infants survived 1 yr. after operation. since the

introduction of this procedure the survival rate of infants was 67.8%. in spite of the late operation about 27% of surviving children showed an average mental development. surgical treatment of dynamic hydrocephalus is advocated. they consider this method as the only means of helping the infant at present.

.I 960

.W

cerebrospinal fluid dynamics in the arnold-chiari malformation. a method using radio-iodinated serum albumin to measure the volume of the ventricular system, and the rate of disappearance of csf from the lateral ventricles, has been described. newborn infants with a rate of flow less than 70 ml. /24 hr. after surgical repair of the myelomeningocele will develop progressive hydrocephalus requiring a ventriculo-atrial shunt. the test can be used to detect the patency of a ventriculo-atrial shunt, and may allow safe removal of the shunt in selected patients.

.I 961

.W

coexistent cranial and spinal defects with hydrocephalus in five infants. the etiology and significance of craniolacunia in these

defects.

the clinical, roentgenographic and etiologic factors in 5 infants with varying cranial defects (craniolacunia and craniofenestra or cranial meningocele), hydrocephalus, and spinal defects (meningocele or myelomeningocele) are described. all of the infants expired of bacterial complications.

the etiologic factors and significance of cranial defects in these coexistent malformations of the central nervous system are reviewed.

.I 962

.W

hydrocephalus and myelomeningocele. central nervous system infection.

a series of 38 incidents of cns infection in 34 patients with hydrocephalus, myelomeningocele, or both have been summarized.

gram-positive organisms occurred more frequently and caused infections resulting in a mortality of 33%. the gram-negative organism induced infections resulted in a mortality of 60%. nearly 50% of the infections occurred in patients before any shunting procedure was done. the staphylococcus caused two-thirds of the infections in patients with a shunt in situ.

no obvious portal of entry could be demonstrated in a majority of patients. of 5 patients who received nonspecific prophylactic therapy because of an oozing myelomeningocele 4 survived. of the 5 given no prophylactic therapy, one survived. a combination of kanamycin, sodium methicillin, and chloramphenicol appeared in vitro to be effective against most of the gram-positive cocci. the combination of chloramphenicol, kanamycin, and polymixin b appeared in vitro to be an effective combination against most of the gram-negative bacilli.

.I 963

.W

myelomeningocele and hydrocephalus. the first year of 50 patients. fifty infants with hydrocephalus and myelomeningocele were treated comprehensively by a team of specialists. patients were evaluated at death or the first birthday, whichever occurred first. twenty patients died, 13 from bacterial infection. thirteen of the survivors were classified as noncompetitive, that is, were thought to have a poor prognosis based on a developmental quotient of less than 80. seventeen patients were judged competitive; in

each case the latest developmental quotient was more than 79 and the urinary tract was not irreversibly decompensated. developmental quotient was based on motor development, adaptive behavior, language development, and personal-social development. this report is a progress report in a longitudinal study. in comparison with a previously surveyed group the results seem encouraging: current data from 39 older patients followed 6 to 13 yr. show 2 competitive survivors, 11 noncompetitive survivors, and 26 deaths.

.I 964

.W

pneumoencephalographic changes in the cavum septi pellucidi and their clinical significance.

the pneumoencephalographic appearances and clinical problems associated with communicating and non-communicating cavum septi pellucidi are discussed on the basis of 11 cases. non-communicating csp may lead to intermittent headaches due to variations of intracranial pressure and obstruction to the flow of csf. in rare cases, representing a special etiological group, the foramina of monro and the

aqueduct may be narrowed. a communicating csp is generally associated with mild to moderate symmetrical internal hydrocephalus. in the author's opinion this is in most cases a direct result of the cavum, since fluid continues to be formed in the cavum after communication with the rest of the ventricular system has been established. the conditions resemble those in hypersecretory hydrocephalus. for these reasons the author rejects the view that a communicating csp is of no clinical significance. in some cases the possibility of a combination of a cavum with a cerebral malformation must be considered.

.I 965

.W

posterior scalloping of vertebral bodies in uncontrolled hydrocephalus. two cases of extensive posterior scalloping of the vertebral bodies are presented in men aged 17 and 23 years, having long-standing hydrocephalus. two additional cases with scalloping of only one lumbar vertebra when partially controlled hydrocephalus has been present for a shorter time are also noted. no previous association between these entities has been

recorded. it is supposed that the increased intraspinal pressure which must have been present in the first 2 patients for many years, was present near the time of closure of the epiphysis at the junction of the arch and the bodies and caused not only widening of the spinal canal but also excavation of the vertebral bodies. scalloping of vertebral bodies has been described in: (1) neoplasms (neurofibromas, meningiomas, gliomas, hemangio-endotheliomas, hemangiomas, lipomas): (2) intraspinal cysts (intradural arachnoid cysts, tarlov's perineural cysts, thoracic extradural cysts in kyphosis dorsalis juvenilis): (3) congenital anomalies of the spine and cord (fusion defects, myelodysplasia, hydromyelia, absence of a single vertebral pedicle, meningoceles): and (4) neurofibromatosis (with or without a thoracic meningocele).

.I 966

.W

electroencephalographic picture of the infantile hydrocephalus.

in 50% of 33 cases of congenital hydrocephalus

the eeg examinations were normal.

asymmetry of the eeg recording was the

most common abnormality encountered

both in congenital and in acquired hydrocephalus.

none of the children examined

revealed any focal neurological symptoms.

it is concluded that eeg examinations could

be useful in differentiating congenital from

acquired hydrocephalus, because a normal

eeg recording suggested the congenital

nature of the condition.

.I 967

.W

consecutive hydrocephalus. report of 2 cases.

two patients, each with 3 consecutive hydrocephalic

newborns, are reported. consanguinity

was present in both families. a

genetic basis for the hydrocephalus is suggested.

.I 968

.W

fanconi's anaemia with hydrocephalus and thyroid abnormality.

a case is described in a girl who suffered

from dwarfism due to congenital hypoplasia

of the pituitary and from other congenital

malformations. the pancytopenia

manifested itself at the age of 2 yr. and was

resistant to a combined corticosteroid-testosterone

treatment. unusual findings in

this case were congenital hydrocephalus,

hypoplastic spleen, and hypoplasia of thyroid

together with persistently high pbi
serum levels but without apparent changes
in thyroid function.

.I 969

.W

dandy-walker-taggart 'syndrome' (a case report).

dandy-walker-taggart 'syndrome' in a
6-month-old girl has been substantiated by a
correlation of clinical and pathological
features. all 3 exit foramina of the 4th
ventricle have failed to open, resulting in
severe cystic dilatation of the ventricle and
hypoplastic distortion of posterior midline
cerebellar structures.

.I 970

.W

hydrocephalus due to smallpox occurring in the fetal period.

out of 450 cases of hydrocephalus in the years
1959-1962, 15 were found whose mothers
had contracted variola after the 3rd
month of pregnancy. based on these personal
cases and the sparse data in the literature,
the clinical, epidemiological,
radiographical (skull), biological and histopathological
aspects are presented (2 fatal
cases were histopathologically examined).
it could be demonstrated that the hydrocephalus

occurred as a manifestation of a disease involving the fetus and was caused by a variola infection during gestation; inferences are given from the eeg and examination of the liquor.

.I 971

.W

air-pantopaque ventriculography in congenital hydrocephalus and myelomeningocele.

a study of the csf pathways by combined pantopaque-air ventriculography in infants

with congenital hydrocephalus and myelomeningocele

is presented. the advantages

of this method are discussed. combined pantopaque

and air ventriculography provides

not only a demonstration of the extent of

the hydrocephalus but also the exact

location and cause of the obstruction. in infants

with myelomeningocele it permits

the disclosure of unmanifested hydrocephalus

and coexistent intracranial malformations.

the early detection of the latter is very

important for the complete evaluation,

management and prognosis. the introduction

of pantopaque into the ventricular

system of infants did not produce an immediate

reaction and did not precipitate

deterioration of the clinical status. retention of small amounts of pantopaque in the lateral ventricles did not interfere with the function of bypassing procedures.

.I 972

.W

two cases of dandy walker's syndrome.

dandy walker's syndrome refers to a particular kind of malformative hydrocephaly characterized anatomically by association with a more or less considerable agenesis of the cerebellar vermis and with an imperfection of the foramina of luschka and magendie.

the dysgenetic nature of this picture is obvious, but the pathogenesis of the hydrocephaly is not simple and the etiology remains obscure. the malformation is compensated more or less quickly in the life of the subject. the clinical picture is that of a hydrocephaly by a tumor of the posterior fossa. the diagnosis can and must be carried out by x-ray examination, the ventriculographic images being pathognomonic.

the extreme ease of surgical restoration of the passage of flow and the effectiveness of timely operation emphasize the interest of this syndrome, which turns out to

be a rare kind of curable malformative hydrocephaly.

the authors report 2 unpublished cases in respect of 3-yr.-old children. the first, already going back several years (1945) had unfavorable postoperational results. the second (1962) recovered completely, without sequelae, after resection of the posterior wall of the cyst.

.I 973

.W

incidence and treatment of post-meningitic hydrocephalus in the newborn.

the incidence of meningitis in the first few weeks of life is higher than in any comparable period of life, even if cases associated with spina bifida cystica are excluded. the gravity of the prognosis even since the introduction of many powerful antibiotic drugs has been frequently emphasized.

among the 7 cases which occurred in a maternity unit, 5 eventually made a complete recovery. in a group of 19 infants who developed postmeningitic hydrocephalus and were referred either with still active meningitis or the postmeningitic state, only 1 infant could not be treated by a ventriculocaval shunt. this infant and 4 others died later. of the 14 survivors, 7 recovered

without sequelae, in spite of extreme hydrocephalus

which was demonstrated by air

studies before operation. the degree of

hydrocephalus, no matter how severe, is no

contraindication to operation.

.I 974

.W

comparative values of thick drop and concentration methods detection
of filaria infection.

blood was drawn from the finger and vein

in 246 students from 11 p.m. to 2

a.m. to compare the diagnostic efficacy of thick

drop method vis-a-vis concentration

method. infection rate was found to be the

same (2.5%) by both methods, and 5

students harbouring infection were found to

be positive by both methods. infestation

rate in the concentration method was

higher being 14 per slide against 4 per

slide in the thick drop method.

.I 975

.W

filariasis in its relation to a a bo, mn, kell, duffy and rhesus blood
groups and secretor factor.

603 filariasis patients have been studied for

a a bo blood groups; 281 for duffy,

kell and rhesus blood groups; 178 for secretor

factor; and 503 for mn blood groups,
to find out if there is any association between
filariasis and these blood groups.
no association, whatsoever, has been found
between the blood groups studied and
filariasis.

.I 976

.W

a polyethylene tube culture method for the diagnosis of parasitic
infections by hookworms and related nematodes.
studies were made in amami island and in
bangkok to compare the diagnostic efficiency
of direct microscopical examination,
test tube culture and the newly devised
polyethylene tube culture method for the detection
of filariform larvae. the results
show that the new technique has a number of
advantages over the other methods. it
is more sensitive than the others for the detection
of cases of slight infection and
greatly reduces the risk of overlooking small
numbers of larvae. polyethylene tubes
are extremely cheap, compact and light, and
can be very easily disposed of after
use.

.I 977

.W

some observations on the effects in vivo of varying ambient temperatures on filarial worms of snakes.

new information was obtained on the biology

of filarial worms from experiments

using constrictor constrictor mexicanus

boas, infected with macdonaldius oschei

worms. the microfilariae of m. oschei are

aperiodic with respect to the light cycle,

but fluctuate sharply in density from day

to day. maximum minimum levels occur

approx. 2 days apart. the microfilariae

are larger and more variable in size on

the days of maximum density than on the

days of minimum density. it is suggested

that the smaller microfilariae on the days

of low parasitemia are those that have

been born recently and that they enlarge

during the following 48 hr. before they enter

the peripheral capillaries. low ambient

temperatures have little effect upon

m. oschei. exposure of the host to ambient temperatures

above 36 c for a period of

24-48 hr. appears sufficient to kill adult

m. oschei. all microfilariae apparently die

within 144 hr. at this temperature, and in

slight infections. they disappeared from

the blood altogether within that period. microfilariae

from an infection 20 times more severe, however, were not eliminated from the circulation prior to the death of the host after 288 hr., although all those observed were either decomposed or distorted and apparently dead. the indication that the temperature serves as a limiting factor for the parasite at a point several degrees lower than that postulated for the host species, is probably correlated with the nocturnal habits of the host.

.I 978

.W

preliminary report on the leucoconcentration technique applied to the study of microfilaraemia.

in a case of filariasis due to wuchereria bancrofti the routine leucoconcentration technique used in the demonstration of steinberg's neoplastic cells in circulating blood was applied. this method makes it possible to obtain considerable enrichment. demonstration of filaria can be performed during daylight. from the material obtained, preparation of specific antigens, that make possible an immunological diagnosis, may be carried out.

.I 979

.W

concentration techniques of sanguicolous microfilariae.

a technique is described for concentration

of sanguicolous microfilariae, a modified

harris and summers method.

.I 980

.W

pathology of schistosoma japonicum in the taiwanese monkey

(macaca cyclopis). i. comparison of formosan and japanese strains.

ii. effect of passing the formosan strain through japanese snails.

i. nearly equal recovery rates of adult worms

from taiwanese monkeys (macaca

cyclopis) infected with formosan or japanese

strains of sch. japonicum were recorded.

worm recovery rates from the monkeys

were low when comparison was

made with the highly susceptible laboratory

rabbit, signifying only partial susceptibility.

formosan strain granulomas in

the liver contained fewer eggs but

were considerably more severe and extensive

than japanese strain granulomas.

the possibility that the large, atypical granulomas

could be reactions to young,

degenerating formosan worms is discussed.

an alternative hypothesis to explain

the dissimilar reactions, that formosan strain

eggs are stronger tissue irritants than those of the japanese strain, is proposed.

ii. the formosan strain of sch. japonicum was passed through the japanese snail intermediate host (oncomelania nosophora) for 4 consecutive generations. progressively rising rates of snail infection and mortality were recorded. the resultant laboratory strain of formosan schistosoma was used to infect taiwanese monkeys. monkeys infected with the natural formosan strain and natural japanese strain served as controls. worm recovery rates were similar in the 3 groups. granulomatous responses in the liver produced by the laboratory strain were compared with the large atypical granulomas of the natural formosan strain and the conventional granulomas of the natural japanese strain. the new formosan strain appeared altered toward characteristics possessed by the japanese strain.

.I 981

.W

a review of immunologic methods for the diagnosis of filariasis. the author reviews the historical application of the skin test, cft, precipitin test,

haemagglutination and bentonite flocculation,
and prausnitz-kuestner test to the
diagnosis of various filarial infections in
man and animals, with a discussion of
areas requiring further study. he is of the
opinion that with standardization of techniques,
immunologic methods can be made
to furnish a reliable means of diagnosis,
notwithstanding the past unreliability of such
methods. a bibliography arranged in
chronological order lists 125 papers covering
the period from 1916 to 1962, and a
supplementary list of references includes
22 recent papers on general aspects of
the subject.

.I 982

.W

schultz-dale reaction with sera of eosinophilic lung patients - a
preliminary report.

schultz-dale tests have indicated that specific
antibodies to metabolite products
of microfilariae are present in the serum
of an e. l. patient and that diethylcarbamazine
in concentrations of 1:2000 - 1:1000
were required to cause perceptible
cessation of contraction in intestinal strips
used. sufficient tests have not yet been

completed to indicate a consistent relationship between any particular filarial species and eosinophilic lung disease.

.I 983

.W

an evaluation of the bentonite flocculation and indirect hemagglutination tests for the diagnosis of filariasis.

the indirect haemagglutination test and the bentonite flocculation test utilizing a

saline extract of *dirofilaria immitis* have been

evaluated. the test was reactive

with sera from individuals with infections of

acanthocheilonema perstans and showed

higher titres for symptomatic patients with

microfilariae in the blood. in a group

of 42 symptomatic patients, 92% of 13 microfilariae-positive

patients and 62% of 29

microfilariae-negative patients showed positive

serologic tests. in a group of 15

asymptomatic individuals with microfilariae

in the blood, 67% were positive. from

a group of 295 asymptomatic microfilariae-negative

individuals, 21 sera (7%) were

positive. testing 632 sera from 295 normal

missionaries, 84 normal americans,

and 253 individuals with various other parasitic

and bacterial infections, an overall

non-specific response of 10% was obtained, utilizing the following criteria for a positive serologic test: (1) haemagglutination titre of 1:200 or higher with a positive flocculation of 1:5 or higher, or (2) a haemagglutination titre of 1:400 with a negative flocculation reaction. sera from 141 patients with helminth diseases showed a non-specific rate of 21%. this high rate was due to cross-reactions with trichinosis sera (35%), schistosomiasis (20%) and ascariasis (27%). since the schistosomiasis and ascariasis sera were from individuals born in an area endemic for filariasis, the reactions may represent a serologic response to past experience with filariasis. only 5% of 112 sera from individuals with non-helminthic diseases and 5% of 84 sera from normal individuals were positive.

.I 984

.W

filariasis in mountain province, luzon, republic of the philippines. an endemic focus of *w. bancrofti* in mountain province, luzon (calaccad valley), is discussed. an 11% microfilaremia rate was found. the parasites were probably brought into this area in the original human

migration, as recent immigrants came from non-infected areas. no infection was found in children under 12 yr. of age, which correlates with spraying of the area since 1953. however, some people live in unsprayed houses, and children may become infected. with coming road development and urbanization, *Culex p. fatigans* will move in and undoubtedly increase transmission. currently *Anopheles minimus* *flavirostris* is the most important local vector. *Aedes (finlaya) niveus* was probably also a vector.

.I 985

.W

immunological studies on filariasis. iii. isolation and purification of antigen for intradermal skin tests.

an antigen for intradermal skin tests was extracted from the homogenate of *Dirofilaria immitis* with a phosphate buffer at pH 7.2 and purified by sephadex g-100 gel filtration, cm-cellulose chromatography and deae sephadex a-50 column chromatography.

the finally purified antigen, fscd1, was a protein with a small amount of carbohydrate (2.5%) and gave a relatively broad band by electrophoresis on cellophane

film. the aminoacids detected by high-voltage paper-electrophoresis of the acid hydrolyzate of the antigen were lysine, arginine, glycine, alanine, glutamic and aspartic acids, and valine. wheals and an erythema appeared within 15 min. of the injection of the antigen 0.05 , on proved filariasis patients. cross reactions were examined in patients with *p. westermani*, *s. japonicum*, hookworm, *a. lubricoides* or *e. vermicularis*, but only weak skin reactions were noticed in all cases. the protein nature of the antigen was further proved by the fact that proteolytic enzymes destroyed the antigenic activity to a considerable extent.

.I 986

.W

human filariasis. identification of species on the basis of staining and other morphologic characteristics of microfilariae. new staining procedures for human microfilariae are described. the morphologic details characteristic of each species are illustrated with apparent greater clarity than previously obtainable. a simple key to the human microfilariae is outlined, based on criteria clearly demonstrated with

these stains.

.I 987

.W

immunological studies on filariasis. iii. fractionation and purification of antigen for intradermal skin reaction in filariasis.

it had been reported that the antigen tca

obtained from adult worms of *dirofilaria*

immitis produced noticeable reactions in

filariasis patients in whose blood microfilariae

could be demonstrated. further fractionation

and purification of this antigen

was attempted in order to study the

substance responsible for the skin

reaction and to obtain a more reliable

antigen with high sensitivity and specificity.

the fraction fs obtained by treatment

similar to that described in

the previous report was used as parent material.

by gel-filtration and sephadex

g-100 column chromatography of antigen fs,

antigen fsi, which produced noticeable

reactions in the filariasis patients,

was obtained. this highly reactive antigen

fsi was separated into 6 fractions, viz.fsc-1,

fsc-2, fsc-3, fsc-4, fsc-5 and

fsc-6, by cm cellulose chromatography.

the 6 antigens were tested at the 1

(protein component) level on patients infected with wuchereria bancrofti. antigen fsc-4, containing 1,500 of protein and 40 of carbohydrate per ml., was most active. next, the further fractionation of antigen fsc-4 by deae-sephadex a50 column chromatography was carried out to yield 4 antigens, viz. fscd-1, fscd-2, fscd-3 and fscd-4. the 4 antigens were tested at the 0.05 (protein component) level on filariasis patients. antigen fscd-1 produced the most noticeable skin reaction in the patients. the elimination of protein components from antigen fscd-1 was attempted with nagase (a proteolytic enzyme) and pronase to obtain antigens fscdn and fscdp. each of these 2 antigens was tested on the patients proved to have filariasis, but the reaction produced by the injection of each antigen was weaker than that produced by antigen fscd-1. it may be inferred from these studies that the substance responsible for the skin reaction is proteinic.

.I 988

.W

identification of canine microfilariae.

the importance of microfilarial identifications in diagnosing canine filariasis was emphasized by comparing the significance of infections due to different species. personal experiences and an analysis of published reports found the modified knott method to be the simplest and most practical of the reliable methods. its usefulness was improved by new morphologic criteria for differentiating microfilariae. microfilarial concentrations in peripheral blood from a number of naturally infected dogs were determined. the average count for 44 dogs infected with *dirofilaria immitis* was only 24,430 (range: < 50 to 168,350) per ml. of blood compared with an average of 235 (range: < 50 to 2,450) per ml. for 100 dogs infected with *dipetalonema reconditum* only. of 38 dogs with inapparent infections of *d. immitis*, 17 had microfilarial concentrations within the range found for infections of *d. reconditum* only. male and female dogs with *d. reconditum* had similar concentrations of microfilariae.

.I 989

.W

chemotherapy of metastatic gastro-intestinal cancer.

cancer of the digestive tract is the commonest cause of death from neoplastic disease in the united states. a large number of patients with these forms of incurable cancer may be candidates for specific anti-tumor drug therapy. the criteria employed for the selection of patients for systemic or regional chemotherapy are reviewed and methods of treatment are outlined. systemic chemotherapy, using fluorinated pyrimidines, the antifol, methotrexate, and the alkylating agent, cytoxan, has been found to be of significant practical value in 10 to 30% of the patients receiving these anticancer drugs. protracted hepatic artery infusion chemotherapy in patients with primary and secondary hepatic neoplasms and tumors of the biliary system has resulted in objective tumor response and associated clinical benefit in 60% of the patients treated. length of survival has been prolonged in patients with advanced metastatic liver cancer from primary tumors of the colorectum. it is concluded that systemic and regional cancer chemotherapy, in selected cases, has contributed to the practical management of patients with incurable cancer of the gastrointestinal tract.

.I 990

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palliative treatment of osseous metastases from carcinoma of the breast and carcinoma of the prostate with radio-active phosphorus and testosterone.

fifty-three patients suffering from pain arising
in bony metastases from carcinoma
of the breast and prostate are discussed.
a method of palliative treatment is outlined
and the results reported.

.I 991

.W

regional chemotherapy by prolonged arterial infusions in head and neck
tumors.

methotrexate was injected into the superficial
temporal or superior thyroid artery
by perfusion: 100 mg./1. (20drops/min.)
every day for 8 days. the area to be irrigated
was decided on by preliminary perfusion
of patent blue violet 11%. results
in 54 inoperable patients were: deaths 7,
failures 19, improvements 28, total regressions 3.
pain was relieved in 3/4 of the patients.

.I 992

.W

intra-arterial infusion emphasizing treatment of malignant neoplasms.
this review of the english medical literature
summarizes most of the significant
papers concerned with intra-arterial infusion.
this technique of cancer therapy is
effective for palliation of many advanced primary
and recurrent cancer patients.

head and neck cancer patients form the largest group of patients that have been treated because of the easily accessible arteries. however, almost any involved organ can be infused by external approaches to the femoral, brachial and common carotids. most oncolytic chemotherapeutic agents can be given via the intra-arterial route at notably increased dosages with the exception of 5fudr. partial and complete regression of many tumors can be obtained with present day chemotherapeutic agents for 1 or 2 mth. the best therapeutic results have been in patients with head and neck and pelvic tumors. currently infusion techniques using small mobile pumping units permit the patient to be ambulatory during course of anti-tumor therapy. complications from intra-arterial infusion are usually minor but serious complications do occur such as embolic phenomena to the CNS with internal carotid infusion; aplastic bone marrow from drug toxicity, hemorrhage from tumor degeneration. technical complications of the infusion may not be life threatening but frequently prematurely terminate the therapy. continued interest in

this form of therapy appears inevitable.

.I 993

.W

prolonged intra-arterial chemotherapeutic infusion in cancer therapy;

its indications and limits.

in this review article (48 references) the principles

of cancer treatment using continuous

intra-arterial chemotherapy are described.

selection of patients, operative

technique and complications are dealt with.

two cases are presented which have

been infused with methotrexate (1050 and 1600 mg.)

with partial or complete objective

remission: a woman of 72 with a carcinoma

of the amygdaloid fossa, and a man

aged 27 with a reticulosarcoma of the rhinopharynx.

.I 994

.W

intra-arterial chemotherapy for cancer metastatic to liver.

twenty-two patients with cancer metastatic

to the liver were treated by the intra-arterial

infusion of cancer chemotherapeutic

agents. the drugs were introduced

directly into the hepatic artery in 10 patients

and into the aorta to the level of the

celiac axis in 12 patients. no significant differences

in results were observed in the

2 groups. of the 10 patients who received cancer chemotherapy via the hepatic artery, one remains alive 2 mth. after treatment; 3 died in the immediate posttreatment period; 7 survived from 1-17 mths after treatment, an average survival of 6.1 mth. all 12 patients who were treated by the intra-aortic administration of cancer chemotherapy have died; 3 patients died in the immediate posttreatment period; the survival time of the remaining 9 averaged 3.7 mth. an objective significant shrinkage of the metastases in the liver was observed in 6 patients (3 treated by the intra-hepatic artery route and 3 via the aorta); this lasted from 1-10 mth. subjective palliation was observed in 12 patients (5 treated by the intrahepatic artery route and 7 by the intra-aortic route). the major complication noted was leukopenia; to a lesser degree, hepatic failure. in those patients with poor metabolic reserve and in those who had received chemotherapy, irradiation or both in the immediate past, the complications were severe. the need for critical screening for the proper selection of patients as candidates for cancer

chemotherapy is discussed.

.I 995

.W

cancer chemotherapy by continuous intra-arterial infusion. experience of the veterans administration surgical adjuvant cancer chemotherapy infusion study group.

two hundred fifty-one patients with advanced cancer have been treated with 365 courses of intra-arterial cancer chemotherapy.

this technique and its complications and results are analyzed and discussed.

objective response was obtained in

57% of the patients treated. the best results

were obtained in epidermoid carcinoma

of the head and neck and the poorest

in primary brain tumors and intra-abdominal

adenocarcinomas. ten per cent

of all patients receiving at least 1 course

of therapy and available for evaluation obtained

worthwhile palliation for 6 or more

months. ten patients have had satisfactory

results for periods of 12 to 28 months.

it is concluded that arterial infusion

chemotherapy may be of benefit in

the palliation of patients in whom other more

conventional methods have failed or

are contraindicated. the frequency of serious

complications suggests that at present this form of therapy should be used only by individuals and groups with special interest and experience in chemotherapy. much further study of this type of cancer treatment is needed and various areas of investigation are suggested.

.I 996

.W

treatment of cancer by bacterial toxins. the initial experience with toxin therapy for sarcoma and melanoma is reported in 3 groups of patients: toxins used as an adjunct to operation in potentially curable patients, palliative treatment for metastatic tumor and toxin therapy supplemented by radiotherapy for localized symptomatic tumor masses. the experience has not been encouraging in the first 2 groups. in 6 of 8 patients in the 3rd group there was marked objective remission of tumor subsequent to irradiation. further study is indicated in the use of radiotherapy following 'priming' with bacterial toxin injections.

.I 997

.W

radiotherapy of malignant rectal and anal tumors. methods and results

in 271 cases.

the results are given of the treatment of

271 patients (9 cases of anal and 262 of

rectal carcinoma) with conventional deep

therapy and ultrahigh kilovoltage irradiation.

the total 5-year survival rate

was 14%. with surgical treatment it is,

according to a survey of the literature made

by reifferscheid, 19.9%, according to

guleke 20-25%, and according to ottenheimer

21.3%. a total of 39 patients

received irradiation after questionable radical

surgery, and 11 patients received

palliative irradiation after palliative surgery

(in most of these cases an anus praeter

was performed). altogether 48 patients

received palliative irradiation without

surgery, and 45 patients received irradiation

because of recurrence after apparent

radical surgery; 11 patients received irradiation

because of metastases after apparent

radical surgery and 6 patients because

of metastases after palliative surgery.

ultrahigh kilovoltage radiation treatment

showed better results than conventional

deep therapy. irradiation with 1,200-1,600

r. on the site before surgery in stage

cases gives higher 5-year survival rates,
according to dukes (henschke;stearns et al.).

.I 998

.W

the management of advanced cancer.
patients with incurable cancer may receive
substantial relief of disabling mental
and physical symptoms by constant and continuous
medical management. while usually
of limited value, certain measures of
both specific anticancer therapy and
nonspecific supportive therapy may relieve
the symptoms and sustain the patient's
morale. general supportive measures
of value and the various cancer chemotherapeutic
compounds and techniques of
administration of these drugs are reviewed
from the standpoint of patient selection,
practical application to various
forms of cancer, and limitations of these agents
in patients with advanced cancer.

.I 999

.W

evaluation of ileal conduit as a palliative procedure.
during the 6.5 yr. period ending july 1963,
107 ileal conduit operations were performed
at the city of hope medical center in

the treatment of carcinoma of the bladder and other pelvic organs. the character and extent of the lesions are described in detail. the details of the surgical procedure are discussed. complications including pyelonephritis, uremia, enteric and urinary fistulas, wound infections, and thrombophlebitis were common. twenty-eight of the 107 patients died during the postoperative period. fifty-nine of the 79 surviving patients are known to have died, mostly as a result of recurrent, uncontrollable carcinoma. the procedure was considered palliative in 39 patients. in 12 of these patients the lesion was removed and the conduit established in one stage; 2 patients died. in only 1 of the surviving 10 patients was the tumor under control. the average term of survival was 8.5 mth. the procedure was carried out in 2 stages in 4 cases; 2 patients died after the 2nd stage. the 2 surviving patients lived 1.5 and 4 3/4 mth., respectively. an ileal conduit alone was established in 23 patients, 8 of whom died after the operation. the average time of survival was 4.5 mth.; 1 patient was alive after 11 mth. it is concluded

that an ileal conduit in conjunction with total cystectomy in 1 stage is indicated as a palliative procedure but only when severe intractable symptoms exist and only when patients are carefully selected. the procedure is poorly tolerated in older persons.

.I 1000

.W

cancer chemotherapy by continuous intra-arterial infusion of methotrexate.

continuous intra-arterial infusions of methotrexate were used in the treatment of

45 patients with malignant disease of the

head and neck, 16 patients with advanced

cancer of pelvic organs, and 7 with malignant

lesions of the lower limb. in 4 patients

with epidermoid lesions of the head

and neck there was complete regression

of the local tumor. thirty-three other patients

benefited from treatment for varying

periods of time, but the remaining 30

showed no response. eight patients died

during or immediately after treatment; all

had advanced cancers of the head-and-neck

region. the mean total dose of methotrexate

given in the patients with no response

was significantly less than in those

with partial regression of the tumor.

this suggests that the greater the total dose of methotrexate tolerated, the greater the chance of beneficial response. the role of continuous intra-arterial chemotherapy in the management of malignant disease is discussed.

.I 1001

.W

management of advanced ovarian carcinoma. the life graph is presented for the purpose of illustrating the results of treatment for patients with ovarian carcinoma who eventually died from their disease. it includes all patients regardless of initial stage of disease, histology of the tumor, or therapy employed. the series is a selected one because of the type of patient referred to the medical oncology service, and it demonstrates that almost 2/3 of the patients died within 2 yr. of diagnosis. all patients received active, aggressive anti-tumor as well as supportive therapy, although there was no formal protocol for patient management. it might be possible, employing a standardized therapeutic approach-irradiation when indicated to the entire

abdomen in the dose range of 3,500 rads, followed by judicious use of currently available anticancer drugs when the disease recurs-to produce a modest increase in the 2-year survival figures. since most series show that approximately 75% of patients with ovarian carcinoma are in stage iii of iv when first diagnosed, more attention might be directed to earlier diagnosis. while it is an important field for investigation, methods of facilitating early diagnosis are not apparent at the moment. controlled trials of adjuvant therapy for stage i and ii disease in which approximately 40% of recurrences are seen should be expanded. this might consist of instillation of radioactive or chemical agents into the abdominal cavity, the use of systemic chemotherapy during or immediately after operation, or infusion of drugs into the abdominal aorta. for stages iii and iv controlled trials of drugs alone, sequentially, or in combination with or subsequent to irradiation seem indicated. finally, efforts to find more effective anticancer drugs must continue.

.W

liver resections for embolic metastases from cancer of the colon and rectum.

two patients, who underwent resections of the left lobe of the liver for embolic metastases from primary cancers of the colon and rectum, are reported.

the internal anatomy of the liver, as it relates to the technic and terminology of resections, is reviewed.

cases of liver resection performed for embolic metastases from cancer of the colon and rectum, found in an extensive review of medical literature, are classified and the results are analyzed. resection of either half of the liver (hemihepatectomy) for embolic metastasis from cancer of the colon or rectum, so rarely cures the patient and carried such a high operative mortality rate, that it is seldom, if ever, justifiable. the lesser operations (left lobectomy or right-lobe metastasectomy) often can be performed simultaneously with the primary operation and are occasionally followed by freedom from recurrence for periods of 5 yr or more. they are justifiable if the metastasis is situated favorably in the liver for complete removal, and if the primary lesion appears to be curable.

.I 1003

.W

palliative treatment of nonresectable lung cancer by upper hemibody perfusion of chlorimine (short-acting alkylating agent). experience

with five cases.

a method is discussed for providing palliative treatment for patients with nonresectable lung cancer by means of administering a short-acting alkylating agent to the upper half of the body while temporarily occluding the circulation to the lower half of the body. with proper selection of patients and an awareness of the potential complications, the procedure appears to be safe and effective.

.I 1004

.W

congenital extrahepatic biliary atresia. a successful operated case on ductus hepaticus obstruction.

the author briefly reviews the history and the anatomical manifestations and the genesis of congenital extrahepatic biliary atresia, and its associations with other abnormalities. he collected 957 cases in the literature from ladd's first successful operated case up to the end of the year 1961. in publications he found 177 theoretically correctable cases and 124 which were recovered. in 1 of 2 personal cases he performed successfully a hepatico-duodenostomy in a 7-week-old girl. four years later the girl had developed normally and she was absolutely without symptoms and signs. the author, discussing the

differential diagnostic problems, stresses the diagnostic value of the gradually increasing direct serum bilirubin, proposing the term 'ex juvantibus differentiation' alluding to the differential diagnostic evaluation of the time which passes until the surgical exploration; he also emphasizes the need of early-latest up to the age of 8 weeks performed-surgical exploration. according to him the administration of vit. k is advantageous. he supposes the cause of the postoperative dehiscence of the operative wound lies in the metabolic changes as a result of icterus. the author in his own case, the relieved drainage of the bilio-digestive anastomosis solved by the help of a polyethylene nasal tube and which could be most safely removed by the surgeon. with statistical data of other authors and personal cases, the author points out that the correctable cases occur in 19.8% of all the cases. one may hope for successful operations on an average in 10.2% of all the cases and 50.8% of the correctable ones. fatal complications, the author believes, can be reduced by early surgery.

.W

icterus neonatorum simplex.

studies in 50 guinea-pigs demonstrate that at birth there is no activity of glucuronyltransferase. after birth activity gradually increases and reaches its highest level on the 3rd day of life. hereafter a gradual decrease can be shown. the suggestion is made that glucuronyltransferase is an adaptive enzyme. the results support the hypothesis that neonatal jaundice is caused by an inability of the liver of the newborn to excrete bilirubin.

.I 1006

.W

the importance of steroid hormones in hyperbilirubinemia, and icterus of the newborn.

administration of naturally occurring steroids (estriol, pregnanediol, cortisone) between the 7th and the 11th day of life increases the bilirubin level of these newborns. administration of the same steroids or of progesterone to nursing mothers results in hyperbilirubinemia of their infants. these facts explain the pathogenesis of neonatal jaundice. interpretation of the experimental and clinical findings leads

to the conclusion that the high amount of steroid hormones which must be excreted during the neonatal period in conjunction with the relative insufficiency of the neonatal liver is responsible for the inability to conjugate bilirubin with glucuronic acid. the steroid hormones probably compete with bilirubin for the enzyme and substrate necessary for conjugation. the functional capacity of the neonatal liver is not high enough to conjugate both bilirubin and steroids. only after excretion of the placental steroids does sufficient conjugation of bilirubin become possible. furthermore, pregnanediol appears to inhibit the enzyme glucuronyl transferase. these mechanisms show the importance of steroid hormones in the pathogenesis of neonatal jaundice and their importance as an aggravating factor in the development of jaundice due to erythroblastosis. these newly developed concepts may have therapeutic implications on which the author will report at a later date.

.I 1007

.W

problems in neonatal obstructive jaundice.

a critical analysis of 57 cases of neonatal obstructive jaundice led to the conclusion that proper diagnosis can be determined by study of liver biopsy. the very low percentage of surgically correctable lesions among patients with neonatal obstructive jaundice and the seriousness and high mortality of the cases of hepatitis treated with a hazardous operation are stressed. conservative management is recommended until 3 mth. of age and even later if a serial fall in bilirubin is noted.

.I 1008

.W

clinical study and histological study of the liver in hepatitis in infants. i. classification and findings of clinical study and histological study of the liver in hepatitis in infants (japanese).

clinical observations and histological studies

by liver biopsy on hepatitis in infancy,

i. e. obstructive jaundice of unknown cause in infants, were made. histologically,

hepatitis in infancy was divisible into 3 types:

(1) no giant cell formation was observed.

in general, slight degeneration of liver

cells, necrosis and inflammatory

changes with stasis of bile were characteristic.

(2) the so-called giant cell hepatitis

was characteristic. (3) specific type, presenting the picture of cholangiolitis.

histological changes in the liver other than biliary stasis were scanty. no specific changes which could clinically differentiate the 3 types were found. in each type, serum bilirubin, sgot and sgpt activities had slight characteristic points in clinical and laboratory studies. in type 1, the values were relatively low, while in type 2 they were markedly high. in type 3, sgot activity was within normal range. histological characteristics of the liver of type 1 were necrosis of liver cells, formation of acidophilic granules and balloon cells, cellular infiltration in glisson's capsule, and biliary stasis in the liver cells and fine bile ducts. morphologically, findings of viral hepatitis were observed. in type 2 liver tissue was replaced by many multinuclear giant cells. extreme distortion of cords of liver cells and cellular infiltration in glisson's capsule and lobules were noted. there was marked biliary stasis in the capillary bile ducts and liver cells. it was characteristic that proliferation of bile ducts and bile plugs were not found,

which was consistent with giant cell hepatitis of Craig-Lanning. In type 3, degeneration of liver cells, necrosis and inflammatory changes were slight. Biliary stasis in the hepatic lobules was conspicuous. Histological findings similar to cholangiolitic hepatitis due to drug poisoning were observed.

.I 1009

.W

the pathology of 'giant cell hepatitis' in early infancy. A 1-month-old male infant was admitted to hospital because of acute cardiac and circulatory failure. Autopsy revealed macronodular liver cirrhosis with splenomegaly, left ventricular dilatation of the heart, hydrothorax, and ascites. Histology of the liver showed a giant cell hepatitis. The portal areas were widened, with foci of erythropoiesis and histiocytic infiltrations. The liver cells showed vacuolar and degenerative changes. The giant cells, present in the margin of the regeneration areas, as well as in the degenerated lobules, had irregular borders and varied in size from 45-60 μ m. Their nuclei were large, sometimes bizarre. Their basophile

cytoplasm showed granules of iron pigment which was also found in some normal hepatic cells, in the prominent kupffer cells and in the connective tissue. in the spleen there were proliferation of connective tissue and scattered areas of erythropoiesis, as well as pigment deposits in the pulpa. iron pigment was also found in the pancreas and salivary glands. the islets of langerhans were hyperplastic. the etiology of giant cell hepatitis is still unknown. its pathogenesis may be due to a malformation, immunologic response to some type of antibody, inborn errors of iron metabolism and viral infection. it is suggested that the giant cell transformation is a response of the immature liver cell to a variety of stimuli. this case is of interest for the predominance of giant cells with 1 or 2 nuclei, presumably it is an intermediate stage or a variant of hepatitis.

.I 1010

.W

the surgery of infantile obstructive jaundice. the results of suruga-yamazaki's procedure in 14 cases of congenital biliary duct atresia are reported. postoperative anorexia,

diarrhea, or edema due to circulatory disturbance in the upper extremity have not been found after this operation. the operation is technically difficult. postoperative fat, protein, and electrolyte metabolism is a problem. in order to obtain better results this disease should be differentiated at an early period. a long-term follow-up and continued study of this problem is required.

.I 1011

.W

transient familial neonatal hyperbilirubinemia. a syndrome of transient familial neonatal unconjugated hyperbilirubinemia not due to known causes has been described in 24 infants of 8 unrelated, healthy caucasian mothers. four of the infants developed kernicterus. beginning in the 2nd trimester of pregnancy, sera from the 8 mothers and their newborn infants inhibited direct-reacting bilirubin and o-aminophenol glucuronide formation by rat liver slices and homogenates, respectively, 4 to 10 times more than was observed with sera from a control group of pregnant women and their infants. the serum inhibitory factor

in these women is unidentified. the fact that the inhibitor occurs in pregnancy serum suggests that it is probably a progestational steroid that inhibits glucuronyl transferase activity in the liver of neonates. the mechanism responsible for increased serum inhibitor factor activity in these women is unknown and requires further study.

.I 1012

.W

hepatitis virus in neonatal liver disease. liver-biopsy specimens from 3 babies with neonatal hepatitis, and 3 with extrahepatic biliary atresia, were studied for the presence of hepatitis virus. culture yielded positive results in all 3 babies with neonatal hepatitis and in 1 of the infants with biliary atresia.

.I 1013

.W

neonatal hepatitis: liver biopsy findings and clinical features. on 22 infants with a clinical diagnosis of neonatal hepatitis, histologic examination of the liver was made by needle biopsy and its relation to the clinical course was investigated. histologic findings were classified

provisionally into 3 types: type i showed no giant cells but only slight damage to hepatic cells with prominent intracellular cholestasis; type ii was characterized by occurrence of numerous giant cells; the specific type was characterized by centrilobular cholestasis without inflammatory reaction. laboratory examinations revealed that increases in serum transaminases and bilirubin were greater in type ii than in type i, and in the specific type there was no increase in serum transaminase but there was a direct hyperbilirubinemia. as to histologic sequelae, the results of serial biopsy revealed that in type i hepatic damage healed almost completely, and that in type ii giant cells disappeared within 1 yr and, in some cases, hepatic cirrhosis resulted. the prognosis of neonatal hepatitis may be said to be good in type i, poor in type ii, and undetermined in the specific type.

.I 1014

.W

spherocytic anemia with early deglobulisation crisis and avitaminosis a. from birth, 2 homozygous male twins had had a series of hemolytic crises. these

caused a low erythrocyte count and jaundice on the one hand, and xerophthalmia, probably owing to the existence, proven by liver biopsy, of a complicating obstructive biliary syndrome, on the other.

.I 1015

.W

neonatal hepatitis or familial neonatal obstructive jaundice?.

four siblings all of whom were boys with chronic obstructive jaundice are described. the onset of the jaundice varied from 1 day to 4 weeks after birth. two other boys and 2 girls in the same family are healthy. although in one of the 4 cases pathological findings were the same as in neonatal hepatitis ('giant cell hepatitis'), other possibilities could not be excluded. what has been described hitherto as giant cell hepatitis appears to be only a morphological picture, for which there must be several causes. it is concluded from the findings in the 4 patients that one of the possible causes of so-called giant cell hepatitis is an inborn error of metabolism.

.I 1016

.W

hypoplasia of the intrahepatic bile ducts.

a description of 2 cases: (1) a boy of 13 days old had atresia of the small intestine and pneumonia, and a slightly enlarged liver with faint green coloration. histological examination revealed numerous collapsed bile ducts which had solid ductular cell sprouts reaching the liver cells; the minor and smallest bile ducts were empty. (2) a girl of 1 yr and 4 mth had increasing jaundice since birth. autopsy revealed a hypoplastic common bile duct, which was, however, open to probing, and marked green coloration of the liver. also in this case, the bile ducts were very narrow and had solid ductular cell sprouts reaching the liver cells. this type of bile duct corresponds to a stage in ontogenesis and does not show signs of proliferation. it may be considered a form of hypoplasia, as the size and number of the primordial bile ducts is reduced. when present the anlage shows a regular connection with the liver cells. this hypoplasia is to be distinguished from an atresia. the long survival of the second case can be explained by the great compensatory capacity of the liver.

.I 1017

.W

fetal and neonatal hepatitis and its consequences.

the author reports on 18 fatal cases observed

in infants from 3 weeks to 1 year old.

in all cases, jaundice appeared just after birth

or during the first days of life, and

was persistent. the stools were sometimes

discolored. there was no blood incompatibility.

the picture was similar to that

of congenital biliary atresia. pathological

study revealed 2 groups: (1) with pathological

changes of hepatitis (11 cases).

the liver is enlarged, flabby and icteric. microscopy

shows dissociation of the cell

cords and polymorphism of the hepatic cells

(necrotic cells, balloon cells, giant cell

transformation). some of the giant cells show

vacuoles, erythrocytes, lipids and

acidophilic material in their cytoplasm. there

are signs of regeneration, collapse

of the stromal framework, proliferation of the

mesenchymal cells and bile retention.

cells of the erythrocytic series are scattered

in the periportal spaces with eosinophilic

leucocytes, lymphocytes and histiocytes.

(2) with fibrosis and cirrhosis (7

cases). the liver is green, firm, with a nodular or granular surface. the extra-hepatic biliary tree is normal. the spleen is enlarged. microscopy shows bile stasis, pericholangiolitic fibrosis, and proliferation of bile ductules. the periportal, interlobular and intralobular fibrous tissue is increased, and shows cellular infiltrations.

the architecture of the liver is disturbed by the presence of pseudolobuli in the regeneration areas. it is suggested that these cases are due to a congenital viral hepatitis, which is not only the result of an intrauterine infection, but also a feature of fetal hepatitis, with secondary pericholangiolitic or post-necrotic liver cirrhosis.

the neonatal giant cell hepatitis is to be considered as the result of a cytotoxic action of the virus. the author considers also the possibility of a viral etiology in cases of biliary atresia on the basis of their morphological similarity with congenital viral hepatitis.

.I 1018

.W

metabolism and excretion of bilirubin c in experimental obstructive jaundice.

bile duct ligation was carried out in a series of rhesus monkeys. the time required for the serum bilirubin to stop rising and achieve a relatively stable level, and the average serum bilirubin reached, paralleled closely that seen clinically. after the serum bilirubin levels had stopped rising and a 'steady state' had been reached, radioactive bilirubin was injected i.v. the radioisotope was distributed principally extravascularly and not in the same ratio as albumin, as in other forms of jaundice. daily turnover of bilirubin was found to be double that anticipated from normal hb breakdown, suggesting increased bilirubin production in obstructive jaundice. in animals followed for 2 wk nearly 80% of injected radioactivity was excreted in the urine, indicating that in obstructive jaundice the kidney takes over entirely from the liver the function of bilirubin excretion.

.I 1019

.W

major surgery on the severe hemophiliac, lessons in management. three cases of pseudotumor of the thigh which required surgical amputation and one case of open pericardial drainage for cardiac tamponade are briefly reported in severe hemophiliacs. in the first case hemostasis, following amputation, was produced, but the patient died of septicemia secondary to proximally infected tissues; the level of amputation

should, therefore, be proximal to all grossly infected tissues. in the second case, with infected massive pseudotumor of the left thigh, 5 separate operative procedures were performed. the last procedure was elective revision of skin flaps at the hip disarticulation site. here application of the knowledge gained from previous experience resulted in a completely uncomplicated postoperative course by dint of timing of the surgical procedure in relation to control of infection, loss of plasma fastness, and the judicious use of antibiotic and direct-current electrocoagulation therapy.

a plea is made to avoid the use of plasma and ahg therapy in hemophilias for trivial reasons and to consider patients for surgical procedures early in the course of their complications, which demand surgery, at a time when the patient is still responsive to hematologic therapy and prior to the onset of infection in areas of hematoma. it is felt that a second significant hemorrhage in any particular site constitutes a bona fide indication for surgical intervention, long before the time when surgery is considered as the last resort by the physician, patient and family. although the authors believe that surgery

in the hemophiliac is not to be taken lightly, they do not endorse the prevailing nihilistic attitude that has resulted in temporizing delays which can only guarantee a fatal outcome.

.I 1020

.W

immunological demonstration of factor viii protein in the plasma of hemophiliacs and its value for an insight into hemophilia a.

by immunization of rabbits one obtains antisera

against human factor viii, the action

of the immunsera has been determined using

a modification of the thromboplastin generations

test (the factor viii neutralization

test). the antibodies against factor viii

are equally absorbed by either normal or hemophilia

a plasma. this observation shows

that hemophilia a plasma contains as much factor

viii protein as normal plasma does.

in normal and hemophilia a serum one finds

at a lower level similar concentrations of

factor viii. in analogy with cross-reacting substances

(crm) in bacteria mutants an

hypothesis has been made according to which

the authors are dealing with the product

of a genetically altered synthesis of factor

viii. this product is functionally less active

but possesses the same antigenic determinants

as the normal factor viii. some inhibitor properties of the hemophilia plasma can be explained by competitive inhibition made possible by the similarity of structure. the fact that the inhibitor discovered by mammen and factor viii have similar properties support the hypothesis. the theory of some authors according to which the plasma of an hemophiliac a contains normal amounts of a normal factor viii blocked by a specific inhibitor, the pathogenetic agent of hemophilia a is rejected because of genetic considerations and because the accelerator appearing after ether treatment of hemophilia a plasma is not identical with factor viii.

.I 1021

.W

haemophilic pseudotumours (3 cases). the 2 first cases of haemophilic pseudo-tumours in 2 adults affected with haemophilia a reported are remarkable on account of their clinical latency and their intertrochanteric localization. the third, in a haemophiliac b, is very extensive and is accompanied by very marked clinical symptoms of tumour. there is an extensive femoral gap with a subjacent image of osseous infarction and a progressive

turgid tumour of the iliac wing of the same side. the literature data stress the discrepancy between the progressive character of this veritable tumour and the absence of any sign of histological malignancy.

.I 1022

.W

protein-losing enteropathy complicating prolonged bleeding in hemophilia.

gastrointestinal bleeding in a severe hemophiliac

continued for 110 days, and 263

pints of fresh blood were replaced. treatment

with eaca, steroids, and factor

viii, rich fibrinogen did not control bleeding.

marked hypoproteinemia developed

by the 94th day of bleeding. a protein-losing

enteropathy was suspected on the basis

of x-ray findings of mucosal thickening and

altered motility. discontinuance of

steroids and protein replacement resulted

in the appearance of a more normal

small bowel mucosal pattern and coincided

with the cessation of bleeding.

.I 1023

.W

bilateral hemophilic pseudotumors of the calcaneus and cuboid treated

by irradiation. case report.

a case is presented in which bilateral pseudotumors of the calcaneus and cuboid in an 11-year-old boy with apparent classic hemophilia responded promptly to deep x-ray therapy with relief of pain and subsequent disappearance of the tumors without recurrence for 2 yr. and 8 mth. after treatment. although previous reports on the effects of radiotherapy for pseudotumors have been conflicting, the results in this case were dramatic.

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some bone lesions in the course of blood diseases with special reference to the formation of bony callus and to the treatment of fractures in patients suffering from blood diseases. after some preliminary remarks on the embryology and physiology of the bone marrow and on the mechanism of coagulation of the blood, the authors pass on to a consideration of the genesis of bony callus, and the treatment of fractures in patients suffering from blood diseases. an account is given on the basis of some examples of pathological fractures, and also of some traumatic fractures in subjects affected by various kinds of blood diseases

such as solitary myeloma, polyosteotic plasmacytoma, waldenstroem's syndrome, the coagulopathic syndrome from a structural defect of the fibrin coagulum, and hemophilia. fractures in patients with blood diseases are characterized by an abnormal course, and, for an efficient cure, it is necessary to make an accurate diagnosis with regard to the pre-existing blood diseases and to re-establish hemostasis when this has been changed, to prevent hemorrhages, and to correct any plasma defect that may be present and which are reflected in the formation of the bony callus.

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studies of the antihemophilic factor (ahf, factor viii) produced in von willebrand's disease.

it has been confirmed that persons with autosomal ahf deficiency (von willebrand's disease) produce large quantities of ahf when transfused with ahf-deficient plasma from persons with hemophilia

a. this occurs despite the fact that 'complementation' does not occur in vitro. one prediction from a model suggesting

that the x-locus for ahf is structural while the autosomal locus is regulatory is that the ahf which appears in von willebrand's disease after transfusion will be structurally normal. the ahf obtained under these conditions has been tested by methods and the results fulfil the prediction. this may imply that the model is correct. on the other hand, the prediction may have been fulfilled for other reasons. perhaps the wrong parameters were examined, or the large standard errors of the tests masked a real difference. further tests are obviously needed before one can feel reasonably certain that mutation of a regulatory gene is the basis of von willebrand's disease. an examination of persons with sex-linked and autosomal ahf deficiency using an antibody prepared against wild type ahf might be very illuminating. also, transfusion studies should be carried out on persons homozygous for von willebrand's disease if such persons can be found. failure to obtain 'new synthesis' in a homozygote would throw great doubt on a model which implies that the reduced ahf levels in von

willebrand's disease heterozygotes is
due entirely to reduction in an effector substance
which neutralizes the repressor
of an x-chromosome operon directly coding
the ahf molecule.

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tumor-like bone lesions in hemophilia.
this report deals with the clinical and radiologic
findings in a hemophilic pseudotumor
of the femur observed over a period
of 10 yr. the pathogenesis, treatment
and radiologic differential diagnosis are
discussed.

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concurrent hemophilia and christmas' disease in one family.
a study is presented of a number of generations
of a family in whom two members had
christmas' disease and three hemophilia
a. it is suspected that the preceding generations
must have been afflicted with hemophilia
ab, or a mutation in x-chromosome genes
which are responsible for both types of hemophilia
must have occurred in the grandmother's
family. in her daughters the genes
responsible for hemophilia ab segregated

so that their children and grandchildren inherited

only one type of hemophilia i.e. hemophilia

a or christmas' disease. relevant genetic

considerations are briefly reviewed.

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albinism associated with angiohemophilia. report of a case.

a case is presented of a rare association of albinism

and angiohemophilia, occurring in a man of 25.

the bone marrow contained cells resembling proper

reticulum cells and containing large basophilic granules.

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major surgery in classic hemophilia using fraction i. experience in
twelve operations and review of the literature.

a therapeutic regimen that provides hemostasis in

hemophiliacs during and after major surgery without requiring

laboratory control has been established with a

factor viii concentrate. the effectiveness of this regimen

of fraction i therapy was evaluated in major surgery

of 6 severely deficient and 4 moderately deficient hemophiliacs.

an analysis of clinical results was made, combining

the 12 operations of the series with the 116 major

operative procedures on hemophiliacs recorded in the

english literature, in which fraction i was the sole or

major source of factor viii therapy. dental and nondental

surgery were analyzed separately, as was the

special problem of blood cysts. although the over-all mortality rate following major surgery in hemophiliacs is presently only 5 to 10% using factor viii concentrates, problems still remain. these include the continued high incidence of abnormal postoperative hemorrhage, the variation in factor viii potency of different lots of fraction i, the late development of serum hepatitis, hemolytic anemia due to contaminating isoantibodies and the high cost of adequate amounts of the product. more efficient methods of preparing purer and more potent factor viii concentrates could eliminate most of these difficulties.

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lengthening of the thrombin time by an anti-equine antithrombin in a hyperthrombocyte myelosis.

a report is given on a patient treated with numerous i.m. injections of thrombase (equine thrombin) for chronic gingivorrhagia caused by a hyperthrombocytic myelosis. these were ineffective and an antithrombin specific against equine thrombin had developed. this did not cause any specific disturbance of the intrinsic coagulation. the observation can be compared with two cases of haemophilia where such an antithrombin had also developed after repeated injections of equine thrombin.

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epsilon-aminocaproic acid (e-aca) as a therapeutic agent based on 5

years clinical experience.

experience in the treatment of 744 patients with e-aca suggested that the use of the preparation is indicated in the following situations: (1) fibrinolytic haemorrhage in association with delivery. (2) acute systemic fibrinolysis in association with surgery. it is mainly major operations on the thorax, pancreas, prostate, liver and genital organs that are complicated by fibrinolysis, but fibrinolytic bleedings can occur after any operation. (3) acute systemic fibrinolysis in patients with cancer, particularly cancer of the prostate and pancreas. (4) systemic fibrinolytic states complicating various disorders, especially leukaemia, liver cirrhosis and boeck's sarcoid. (5) as an antidote in thrombolytic therapy. (6) local fibrinolytic activity in the urinary tract in the following situations: (a) after prostatectomy. e-aca will substantially reduce blood losses following prostatectomy, especially if the treatment is continued until the urine has become macroscopically clear. (b) haematuria in prostatic cancer, prostatic hyperplasia, prolonged haematuria after traumatic injury of the kidney, haematuria in haemophilia and other coagulation defects, and so-called essential haematuria. (7) ulcerative colitis. the drug is equally effective whether given orally or intravenously. in states with increased systemic fibrinolytic activity a dose of 0.1 g per kg body weight every 4-5 hours is recommended.

for inhibition of local fibrinolytic activity in the urinary tract, a dose of 3 g three times a day has proved sufficient. the side-effects consisted of dizziness, nausea and diarrhoea. no toxic effects of the drug on e.c.g., blood picture, n.p.n. and liver function tests were observed, not even in cases receiving more than 1000 g of e-aca. nor did postmortem examination in 46 cases reveal any signs of a toxic effect. no signs of intravascular coagulation in connection with e-aca therapy were observed. the incidence of thromboembolic complications after prostatectomy in patients treated with e-aca and a series of controls was identical. judging from the authors' experience in this material e-aca did not act as an agent inducing thrombosis.

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femoral neuropathy in hemophilia.

six new cases of femoral neuropathy in hemophilic patients are described. the syndrome begins with severe pain in the groin, in the inferior aspect of the thigh, and deep in the hip region. this is followed by a pronounced contracture of the hip in flexion and external rotation. a tender swelling appears in the iliac fossa and groin with a depression in the center corresponding to the inguinal ligament. finally, a flaccid paralysis of the quadriceps femoris and diminution or absence of sensation in the anteromedial aspect of the thigh and proximal

portion of the leg, with a depressed or absent patellar reflex, is discovered. the authors propose that this syndrome is the result of hemorrhage in the iliopsoas muscle at the musculotendinous junction beneath the iliacus fascia and that the femoral nerve becomes compressed beneath the unyielding inguinal ligament superiorly and the iliopectineal ligament medially. treatment consists in bed rest, analgesics, and freshfrozen plasma during the acute phase. during the convalescent phase, a hessing long brace is used to protect the knee from hemarthrosis until functional return of the quadriceps femoris has occurred. to date, the validity of the theory that the femoral-nerve palsy is the result of iliopsoas hemorrhage at the musculotendinous junction and compression of the femoral nerve beneath the inguinal ligament has not been verified. the authors anticipate some day seeing a non-hemophilic patient with a traumatic iliacus hemorrhage and femoral neuropathy. should such an opportunity present itself, exploration beneath poupart's ligament may show the femoral nerve to be compressed and thus confirm the proposed cause of the clinical picture.

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hemorrhagic episodes in hemophilia: a 5-year prospective study.

medicosocial studies of hemophilia are of particular clinical importance in allowing an assessment

of the likely course of the disease at different ages and for differing grades of severity, and in providing knowledge of which complications cause the most disability, loss of education, and earning capacity. they also overcome the distorted clinical impression of the disease which arises from the recurrent admission of the same few severely affected hemophiliacs. owing to the considerable individual variation in the number and severity of complications in different hemophiliacs an accurate individual prognosis can never be given. in general, however, the number of spontaneous episodes per year decreases with age, while the severity of individual episodes tends to increase, at least until the age of 21 yr. there is general agreement that the bulk of hospital hemophilic admissions are due to hemarthroses and that hemophilic arthropathy involves the knee more than it does any other joint. the increased time spent in hospital per episode in later life is in part at least due to the development of relatively unstable weight-bearing joints due to hemophilic arthropathy and associated muscle atrophy. thus the correct management of individual hemarthroses in childhood is of considerable importance, and at the present time too little is known of the best possible treatment for these episodes. little is known of the pathological mechanisms of

hemophilic arthropathy and whether it is the presence of blood or its presence under tension which leads to joint destruction. thus opinions differ concerning the routine admission of all hemarthroses to hospital regardless of severity and also about the advisability of joint aspiration in an attempt to avoid the development of destructive arthropathy. because of the individual variation between patients, the changes in the pattern of the disease with age, and the difficulty of obtaining suitable control patients these questions can be answered only by further longterm prospective medicosocial studies.