venously; in both cases hypoglycæmia had been suspected. This led to rapid deterioration and to lactic acidosis.

In experiments on rabbits, lactic acidosis was developed at a high blood-sugar level maintained by intravenous glucose administration; large doses of insulin made the acidosis worse. These observations prompted us to record changes in blood standard-bicarbonate, ketone, and lactic-acid levels during treatment of diabetic coma. In 4 out of 9 patients the fall in blood-ketones was accompanied by no change in the lactic-acid level; but in the other 5 patients the decline in blood-ketone levels was accompanied by a rise of lactic-acid values, without obvious aggravation of clinical status. Thus, in the later period of coma treatment, the low standard-bicarbonate results primarily from the high lactic-acid level.

In cases where lactic acidosis developed, the blood-sugar was 800–1000 mg. per 100 ml. in the early period of coma. During insulin effect, the rise in blood-lactic-acid level was always accompanied by a substantial reduction of the blood-sugar. In our opinion, every case of non-ketotic coma presenting with acidosis is therefore suspicious of lactic acidosis.

These observations are to be published in detail in *Acta pædiatrica Academiæ scientiarum Hungaricæ*.

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SOLUTIONS FOR KIDNEY STORAGE

SIR,—You have published several letters on the preservation of kidneys by hypothermia after flushing with an electrolyte solution [1] having a composition resembling that of the intracellular fluid. Although the good results reported by Collins et al.[2] have been confirmed and extended to 48 hours by us [2] and by Liu et al.,[3] some workers have encountered difficulties with the solution.[4,5]

We have done some experiments in the dog in which we compared Collins' solution C_4 with the triple fluids of Brunius et al.[6] and a balanced-salt solution. In addition we have tried two solutions containing large amounts of potassium and magnesium. In all experiments the kidneys were flushed immediately with 200 ml. of cooled solution and then stored at 2°C. After 24 hours they were auto-transplanted; at the same time the other kidney was removed. Dogs developing vascular thrombosis were not included in the results.

The number of dogs surviving and the serum-creatinine level after 1, 2, and 4 weeks are shown in the table. Survival was lower and the postoperative rise in serum-creatinine was greater for Brunius' and the balanced-salt solutions than for C_4.

The use of a solution consisting only of buffered potassium chloride resulted in non-function in 3 out of 8 kidneys. The addition of magnesium chloride produced an improvement in so far as all the dogs survived, but the postoperative renal function was unsatisfactory.

In our hands Collins' solution has thus proved superior to the other compositions tried. We have had no problems with the stability of the solution. We regularly use this solution for human kidneys.

NUMBER OF DOGS SURVIVING AND MEAN SERUM-CREATININE FOR SURVIVORS

Solution	No. of dogs	Survivors	Serum-creatinine (mg./100 ml.), wk. postop.: 1	2	4
Collins	6	6	1·6	1·4	1·1
Brunius	6	5	3·9	2·2	1·3
Balanced-salt*	7	5	5·9	3·7	1·5
Potassium chloride (125 meq./l.)†	8	5	4·4	2·8	1·5
Potassium chloride, magnesium sulphate (100–50 meq./l.)†	4	4	5·7	4·6	2·6

* Dextran (M. wt. 40,000), heparin, lignocaine, and glucose added; buffered with sodium bicarbonate.
† Glucose added; buffered with THAM.

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AMYLOIDOSIS, ALZHEIMER'S DISEASE, AND AGEING

SIR,—Your editorial on the amyloidosis of ageing (Sept. 19, p. 598) refers to the possible role of "slow viruses" in supposedly "genetic" and "senile" conditions, notably Creutzfeldt-Jakob disease. Investigations of scrapie (in which the genetic soil certainly plays an important role [1,2]) and kuru show that several changes which are to be found in the old brain appear in young animals with these diseases. Apart from the astroglial hypertrophy of old mouse brain (which itself may make differentiation from early scrapie in a 5-month-old animal difficult) changes include "neurotubular arrays" in Purkinje axons, amyloid bodies and deposits in astrocyte processes and in axons, and spiral filaments within astrocytes.

Neurotubular arrays have been described in adult brain but without indication of the age of animals.[3,4] They are rare in the normal young adult rat (7–8 months) but common in rats of this age with scrapie and in 20-month-old animals.[5]

Amyloid bodies and deposits are found in young adult animals with scrapie but not in the normal, where they only occur in old age.[6] The characteristic plaques of kuru have the structure of amyloid (though they may also be associated with herring-bone or filagree formations [7]), and small accumulations of amyloid material may be found in the cerebellum, both in human and chimpanzee kuru at the electron-microscope level (unpublished).

Spiral filaments and intra-astrocyte "filagree formations" are common in both human and chimpanzee kuru but very rare indeed in normal New Guinea brain or in the single old chimpanzee which has so far been available for study.

A quantitative study of the intranuclear rods described by Chandler and Willis [8] in neurones both in normal and scrapie mice has shown that they are much more frequent in the aged than the young animal (unpublished).

Considerably increased numbers of dense bodies and pleomorphic inclusions with laminated internal structure occur in scrapie neurones as compared with normal animals

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of the same age, and the appearances are quite like those in old animals.[9]

Taken together these and other findings, reviewed elsewhere,[10] suggest that in scrapie-kuru, changes which are associated with ageing in the brain are brought forward, as it were, to an earlier age. Other organs do not seem to be affected. It is as if the " abiotrophy " of Gowers had been produced experimentally by a " slow infection " of the nervous system. Studies of D.N.A. polysaccharide[11,12] and protein turnover in scrapie brain suggest they are all speeded up. Whilst this could be interpreted as in some way associated with production of the scrapie agent, an alternative explanation would be that the brain is coursing through its vital career at an accelerated pace.

We have found that explants from a biopsy specimen of Alzheimer's presenile dementia grow much more readily than those from comparable normal brain. Scrapie [13] and multiple sclerosis explants likewise have increased growth potential.[14] Electron microscopy of the presenile dementia explants has shown amyloid formation within cells which appear to be astrocytic in origin and that this amyloid (which has a fibrillar structure and is laid down commonly in concentric masses) is later extruded from the cells. The cells producing it grow unusually well so that their behaviour suggests a " programmed senescence ". Could this be associated with a " slow infection " ?

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CHANGING SCENE IN BRITISH PSYCHIATRY

SIR,—Fundamental changes are now taking place in the way psychiatry is practised in Britain, but little is being done to monitor these changes and analyse their effects. Yet since these changes are acts of faith rather than the fruits of rational analysis, and can be carried out in a variety of ways, careful examination of what is happening might show us which ways will best achieve desired ends, and how to avoid mistakes.

For example, many psychiatric hospitals are now being amalgamated with general hospitals under single managements with a single budget. Four years ago, in a survey of 108 British psychiatric hospitals, the Royal Medico-Psychological Association [15] found 14 already so amalgamated, and only 8 of them were satisfied with the results. They suggested the need for full evaluation of amalgamation methods and their effects before proceeding with wider plans, but this has not been done. Instead, we have rumours flying about that hospitals A and B, for instance, prefer amalgamation, but that hospitals of the X metropolitan region do not, that administration becomes unwieldy, and nursing standards deteriorate, and so on. What we need, I suggest, is: public exchange of experiences, good and bad; a new R.M.P.A. survey; research by university departments of social administration on communications and committee structure within the groups, and on the role of specialism; and some attempt to assess clinical as well as administrative efficiency of different psychiatric units.[16–18]

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PHENFORMIN AND BLOOD-UREA

SIR,—I was interested in the letter by Dr. Menon and Dr. Dewar (Aug. 1, p. 263) describing an increase in the blood-urea of two patients being treated with phenformin. I am sure they should indicate the method that was used and the precautions that were taken to ensure that the high values obtained were due to an actual increase in the concentration of urea in the blood rather than to an interference in the method by phenformin or its metabolites.

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*** This letter was shown to Dr. Menon and Dr. Dewar, who reply as follows: " It is, in our opinion, highly unlikely that the increase in blood-urea was caused by interference in the method by phenformin or its metabolites, since the increase was consistent and moreover did not occur in any of the other patients (approximately 50) so far treated by us with this drug, using in all cases the ' AutoAnalyzer ' method for blood-urea estimation. Blood-samples without stasis were collected from all patients by the same examiner, and transferred in an identical manner to the same laboratory for estimation."—ED. L.

RUBELLA AND RHEUMATOID ARTHRITIS

SIR,—Rubella infection often produces acute polyarthritis, especially in young women, and generally at the acute phase of the disease. Although the synovitis in rubella patients is self-limited and short-lasting, a possible association between rubella arthritis and the subsequent development of rheumatoid arthritis has been suggested.[1] However, the level of rubella hæmagglutination-inhibiting antibody in two matched groups of rheumatoid and non-rheumatoid subjects was found not to be significantly different.[2] We have now attempted to detect rheumatoid factor in the sera of 22 women patients with clinically and serologically confirmed rubella.

In each patient, both the acute-phase serum, collected 0–5 days after the onset of rubella rash, and the convalescent-phase serum, collected 10–21 days after onset, were tested. Rheumatoid factor was detected by slide test using a commercial kit (' Rheumaton ', Denver Laboratories, Australia) and also with formalinised sheep cells sensitised by human IgG prepared by ' Sephadex ' G-200 and diethylaminoethyl cellulose column chromatography. The slides were examined by naked eye and microscopically for agglutination of sensitised cells by rheumatoid factor. Positive and negative control sera were used each time for comparison.

Rheumatoid factor was identified in 2 of the 22 patients, in both the acute and convalescent sera. The frequency of rheumatoid factor in these rubella patients is not much greater than in other non-rheumatoid subjects.[3] It seems likely that rubella synovitis, at least at that early stage after infection, may be caused by factors other than a secondary immune response which may produce rheumatoid factor. Grayzel and Beck [4] have in fact suggested that this synovitis may be due to virus multiplication within synovial cells.

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