

Excision of limbal dermoids. We reviewed the clinical files of 10 patients who had undergone excision of unilateral epibulbar limbal dermoids. Preoperatively, all of the affected eyes had worse visual acuity (P less than .02) and more astigmatism (P less than .01) than the contralateral eyes. Postoperatively, every patient was cosmetically improved. Of the eight patients for whom both preoperative and postoperative visual acuity measurements had been obtained, in six it had changed minimally (less than or equal to 1 line), and in two it had improved (less than or equal to 2 lines). Surgical complications included persistent epithelial defects (40%) and peripheral corneal vascularization and opacity (70%). These complications do not outweigh the cosmetic and visual benefits of dermoid excision in selected patients.

Bell's palsy. A diagnosis of exclusion. In cases of acute unilateral facial weakness, a careful and systematic evaluation is necessary to identify the cause. Idiopathic facial paralysis (Bell's palsy) is a diagnosis of exclusion. It is also the most common cause of unilateral facial weakness seen by primary care physicians. The most important aspect of initial treatment is eye protection. Administration of systemic oral corticosteroids may lessen severity and duration of symptoms.

Retained endobronchial foreign body removal facilitated by steroid therapy of an obstructing, inflammatory polyp. Oral and topical steroids were used to induce regression in an inflammatory, obstructing endobronchial polyp caused by a retained foreign body. The FB (a peanut half), which had been present for over six months, was then able to be easily and bloodlessly retrieved with fiberoptic bronchoscopy.

Recurrent buccal space abscesses: a complication of Crohn's disease. A patient is described with generalized gastrointestinal involvement by Crohn's disease. Symptoms of recurrent ulceration and mucosal tags are well-described oral manifestations of Crohn's disease; however, in our patient recurrent facial abscesses, which required extraoral drainage, also developed. This complication has not previously been reported.

Intracranial fibromatosis. Fibromatoses are uncommon infiltrative lesions affecting musculoaponeurotic structures, most often of the limbs and trunk. Lesions involving the cranial cavity are rare and require the same aggressive surgical management as elsewhere in the body. This case illustrates their clinical and neuroradiological features and underscores the necessity for aggressive resection to avoid recurrence. The literature is reviewed.

The effect of intrathecal morphine on somatosensory evoked potentials in awake humans. Although the effect of systemic opioids on somatosensory evoked potentials has been well described, little is known about the interaction between intrathecally administered opioid analgesics and somatosensory evoked potentials. Accordingly, the influence of intrathecally administered morphine on posterior tibial nerve somatosensory cortical evoked potentials (PTSCEPs) was investigated in 22 unpremedicated, awake, neurologically normal patients scheduled to undergo elective abdominal or pelvic procedures. Patients were randomly assigned to receive either preservation-free intrathecal morphine sulfate (ITMS) or placebo. After baseline PTSCEP, heart rate and, mean blood pressure were recorded, ITMS (15 micrograms.kg⁻¹) was injected via standard dural puncture with the patient in the lateral position. PTSCEPs, heart rate, and mean blood pressure were recorded again at 5, 10, 20, 30, 60, 90, and 120 min. Control patients were treated identically (including position, sterile preparation, and subcutaneous tissue infiltration with local anesthetic), except for lumbar puncture, and were unaware of their randomization. Before administration of ITMS, PTSCEP P1, N1, P2, N2, and P3 latencies were 39.4 \pm 3.2, 47.6 \pm 3.9, 59.2 \pm 3.2, 70.4 \pm 3.7, and 84.6 \pm 5.5 ms, (mean \pm standard deviation), respectively. The corresponding P1-N1, N1-P2, and P2-N2 amplitudes were 2.4 \pm 1.1, 2.4 \pm 1.1, and 2.3 \pm 0.9 microV, respectively. There were no significant changes over time

between the control and ITMS groups. PTSCEPs resulting from left-sided stimulation were not different from those elicited by right-sided stimulation. All ITMS patients had intense postoperative analgesia for at least 24 h. It is concluded that ITMS does not affect PTSCEP waveforms in the 35-90 ms latency range during the awake state.

The 29th Rovenstine lecture: clinical challenges for the anesthesiologist. In conclusion, I hope that my comments have reaffirmed your biases or, even more importantly, stimulated you to think in a different way about the information explosion in our specialty and medicine in general. I believe our specialty is in a golden era that will benefit from the past and be nourished by new discoveries and understanding. We as clinicians must accept the challenge of recognizing what new information deserves incorporation into our practice, what old information deserves to be sustained, and what merits new scrutiny and perhaps should be discarded. If I had one wish, it would be that anesthesiologists would never lose their zeal to be students--their thirst for new information--as the continuum of anesthesia education is indeed a life-long process. That wish, ladies and gentlemen, is my challenge to all anesthesiologists.

Mortality in patients treated with flecainide and encainide for supraventricular arrhythmias. In a recent clinical trial, the class Ic antiarrhythmic drugs encainide and flecainide were found to be associated with an increased mortality risk in patients with new myocardial infarction and ventricular arrhythmias. The purpose of this study was to assess whether an increased mortality risk also accompanied the use of these drugs to treat patients with supraventricular arrhythmias. Data were obtained from the respective pharmaceutical sponsors on the mortality observed with each drug in United States and foreign protocols enrolling patients with supraventricular arrhythmias. Mortality in the encainide population (343 patients) and the flecainide population (236 patients) was compared with that in a research arrhythmia clinic, the Duke population (154 patients). Nine deaths occurred in the combined encainide-flecainide population and 10 deaths occurred in the Duke population; the follow-up periods averaged 488 days and 1,285 days, respectively. The 6-year survival functions of these 2 populations, estimated by the Kaplan-Meier technique, did not differ significantly ($p = 0.62$). The hazard ratio for the combined encainide-flecainide population relative to the Duke population was estimated to be 0.6 with a 95% confidence interval of 0.2, 1.7. These descriptive comparisons did not demonstrate any excess mortality when flecainide and encainide were used in patients with supraventricular arrhythmias.

Approaches to immunotherapy of cancer: characterization of lymphokines as second signals for cytotoxic T-cell generation. Lymphokines, the soluble molecules produced by cells of the immune system, regulate cell-cell interactions and, consequently, the functional status of the immune system. Altering immunoregulatory pathways with lymphokines *in vivo* may provide a mechanism for controlling a variety of immunologic disorders. Although normally produced *in vivo* in very small quantities, the widespread availability of recombinant lymphokines has made it possible to study the molecular signals involved in production of lymphocyte effectors with activity against tumor. For example, interleukin-2-based cancer immunotherapy programs have, in certain clinical situations, suggested that immunologic intervention can influence the regression of metastatic cancer. Ultimately the successful application of these biologic agents requires an understanding of the interaction between the immune system and tumor on a molecular level. To induce a given biologic effect, it is necessary both to classify the required lymphokines and to identify the relevant effector cell populations. This review will examine the progress made in identifying the requirements for lymphokine-induced cytotoxic T-lymphocyte function.

Retinal artery obstruction and atheromas associated with non-Hodgkin's large cell lymphoma (reticulum cell sarcoma). A 71-year-old woman developed branch retinal artery obstruction as the

presenting manifestation of a large cell non-Hodgkin's lymphoma. Multifocal chorioretinal scars were present in the same eye. She experienced progressive visual loss accompanied by development of multiple yellow retinal arterial wall plaques, extension of retinal opacification into other quadrants, and increasing vitreous cellular infiltration. Clinical diagnoses included branch retinal arterial obstruction caused by toxoplasmosis retinitis, multifocal choroiditis and panuveitis simulating the presumed ocular histoplasmosis syndrome, vitiliginous chorioretinitis, and the acute retinal necrosis syndrome. Four months after onset, the right eye was blind and was enucleated. Histopathologic examination revealed extensive lymphomatous infiltration and necrosis of the retina and optic nerve. The retinal arteries were partly obstructed by lymphomatous infiltration and atheromas. Subsequently, the left eye and central nervous system were involved by lymphoma.

The 'tonic' pain-related behaviour seen in mononeuropathic rats is modulated by morphine and naloxone. This study investigated the sensitivity to pharmacological manipulations of a rating method, adapted from the formalin test, to measure the tonic component of the pain-related behaviour induced by creating a peripheral mononeuropathy with 4 loose ligatures around the common sciatic nerve. Although the adequacy of opioid substances in alleviating neuropathic pain is highly controversial, the effects of morphine (1 mg/kg i.v.) and naloxone (1 mg/and 3 micrograms/kg i.v.) were tested 1-2 weeks after the nerve ligatures were established, when pain-related behaviours were well developed. Morphine (1 mg/kg i.v.) induced a potent and prolonged decrease in the pain-rating score at week 2 after surgery. Either at week 1 or week 2, naloxone elicited a bidirectional dose-dependent action: a further increase in the pain-rating score with the high dose (1 mg/kg i.v.), and a paradoxical decrease in the score with the low dose of 3 micrograms/kg i.v. These effects are comparable to those already described in several rat models of inflammatory pain and, in the same model of neuropathy, using a phasic nociceptive test, the measure of the vocalization to paw pressure. A few differences in the effects of naloxone on tonic and phasic pain are noted and discussed.

Examination of cardiorespiratory changes during upper gastrointestinal endoscopy. Comparison of monitoring of arterial oxygen saturation, arterial pressure and the electrocardiogram. Critical events including hypoxaemia, arrhythmias and myocardial ischaemia may occur more frequently during endoscopic procedures than during anaesthesia. A study was undertaken to assess the cardiovascular changes and to evaluate suitable monitoring techniques to detect critical events during sedation and endoscopy. Twenty patients scheduled to undergo a prolonged endoscopic procedure which required deep sedation were studied. Continuous recordings of electrocardiogram, heart rate and arterial oxygen saturation were made and arterial pressure was recorded at one-minute intervals. The study commenced immediately before administration of sedatives, continued for the duration of the examination and for one hour following the examination. Oxygen saturation decreased in all patients during the examination to a mean of 82.9% (SD 11.9), and remained below baseline for the duration of the examination and into the recovery period. Statistically significant increases and reductions of systolic arterial pressure and rate-pressure product were found during the procedures compared with baseline values recorded before administration of sedatives. Sixteen of the 20 patients developed tachycardia during the examination. Ten patients developed ectopic foci which were supraventricular, ventricular or both in origin. Electrocardiogram changes resolved during the recovery period. Myocardial ischaemia was assessed by S-T segment depression and a significant correlation was found between S-T segment depression and hypoxaemia, although the magnitude of the S-T depression was small and may not have been detected clinically. No correlation was found between S-T segment depression and arterial pressure, heart rate or rate-pressure product.

Hepatic transmethylation and blood alcohol levels. Golden Syrian hamsters that have elevated hepatic alcohol dehydrogenase activity were divided into four groups and group-fed on four different liquid diets for five weeks. Group I was fed a control diet formulated for hamsters. Group II was fed the control diet containing 20 micrograms of 4-methylpyrazole per litre. Group III was fed the hamster ethanol liquid diet (ethanol amounting to 36% of total calories). Group IV was fed the ethanol diet to which 4-methylpyrazole (20 micrograms/litre) was added. Groups I, II and III were group-fed the amount consumed by Group IV on a daily basis. Upon killing the animals, blood alcohol levels were found to be elevated in Group IV but not in Group III. Hepatic methionine synthetase (MS) was inhibited in Group IV. Betaine-homocysteine methyltransferase was induced in this group to compensate for the MS inhibition and liver betaine was lowered reflecting this induction. None of these changes were seen in Group III. Since none of the animals showed an aversion to their respective diets and gained weight normally, these data indicate that it was the elevated blood levels of ethanol rather than nutritional factors that were related to the changes in methionine metabolism.

Memory T cells represent the predominant lymphocyte subset in acute and chronic liver inflammation. T cells can be divided into two main phenotypic subpopulations-i.e., the CD45RA-positive (2H4-positive) "naive" subset and the CD45RO-positive (UCHL1-positive) "memory" subset. In light of this recent functional reinterpretation of T-lymphocyte subpopulations, we reinvestigated the composition of the inflammatory infiltrate in liver biopsy specimens from patients with acute and chronic hepatitis. In normal liver, the few scattered mononuclear cells present in portal tracts and in the intralobular parenchyma consisted of both CD45RA-positive (2H4-positive) naive and CD45RO-positive (UCHL1-positive) memory T cells. In inflammatory liver diseases, portal tract and periportal and intralobular areas of inflammation consisted virtually only of CD45RO-positive (UCHL1-positive) memory T cells, which strongly expressed the CDw29 (4B4) antigen, and the adhesion molecules LFA-1, CD2, LFA-3, CD44 and VLA-4 and the activation marker human leukocyte antigen-DR. These results indicate that activated memory T cells represent the predominant subpopulation of lymphocytes in areas of liver inflammation. Memory T cells strongly express various homing receptors and adhesion molecules, which probably allow them to accumulate at inflammatory sites and to strengthen interaction with target cells. Furthermore, the increased number of memory T cells with enhanced interferon-gamma production in areas of liver inflammation may contribute to the maintenance and up-regulation of immune responses occurring in inflammatory liver diseases.

Inflammatory properties of neutrophil-activating protein-1/interleukin 8 (NAP-1/IL-8) in human skin: a light- and electronmicroscopic study. Neutrophil-activating protein-1/interleukin 8 (NAP-1/IL-8), purified to homogeneity from lipopolysaccharide-stimulated human peripheral blood monocytes, was injected intracutaneously into human skin. Sequential biopsy specimens were taken in order to investigate the sequence of ultrastructural changes induced by the cytokine. Whereas intracutaneous injection of 100 ng of NAP-1/IL-8 per site caused no macroscopic changes, by histology infiltration with polymorphonuclear leukocytes (PMN) and monocytes was present within 1 h and increased at 3 and 5 h. No lymphocyte infiltration was noted. The first ultrastructural changes (30 min) consisted of the presence of cytoplasmic 7-nm microfilament bundles, as well as numerous protrusions of the luminal plasma membrane of endothelial cells (EC). As a striking feature, multiple 100- to 160-nm electron lucent vesicles could be observed in the EC cytoplasm. These structures differed from plasmalemmal vesicles and suggest secretory activity. When PMN and monocytes appeared in the vascular lumen (1 h and later), the number of 100-160-nm electron-lucent vesicles had decreased significantly. In contrast to C5a-injected skin sites, mast cell degranulation was absent.

Bronchogenic carcinoma with chest wall invasion. Bronchogenic carcinoma with chest wall involvement continues to present a major clinical challenge. We have treated 52 patients since 1973, excluding those with superior sulcus tumors. There were 37 male and 15 female patients with an average age of 62.9 years. Chest pain was an initial symptom in 37%. All patients had negative mediastinoscopy results. Squamous cell carcinoma was present in 53% and adenocarcinoma in 35%. The median number of ribs resected was two (range, one to six), and only 2 patients required chest wall reconstruction. Pathologic staging was T3 N0 M0 in 83% and T3 N1 M0 in 17%. Operative mortality was 3.8%. Absolute 5-year survival was 26.3%. Patients who had N1 disease had a 5-year survival of only 11%. Radiation therapy was employed in 46% for positive nodes or close margins. Bronchogenic carcinoma with chest wall invasion remains potentially curable if N2 nodes are not involved. The role of radiation therapy has not been clearly defined. Morbidity and mortality should be minimal.

Electronic weaponry--a question of safety [published erratum appears in *Ann Emerg Med* 1991 Sep;20(9):1031] Electronic weapons represent a new class of weapon available to law enforcement and the lay public. Although these weapons have been available for several years, there is inadequate research to document their safety or efficacy. Two of the most common, the TASER and the stun gun, are reviewed. The electronic weapon was initially and still is approved by the US Consumer Product Safety Commission; its approval was based on theoretical calculations of the physical effects of damped sinusoidal pulses, not on the basis of animal or human studies. These devices are widely available and heavily promoted, despite limited research into their safety or efficiency and despite recent animal studies documenting their potential for lethality.

Operative management of acoustic neuromas: the priority of neurologic function over complete resection. The objective of surgical management of acoustic tumors is to remove them entirely and preserve facial nerve function and hearing when possible. A dilemma arises when it is not possible to remove the entire tumor without incurring additional neurologic deficits. Twenty patients who underwent intentional incomplete surgical removal of an acoustic neuroma to avoid further neurologic deficit were retrospectively reviewed. They were divided into a subtotal group (resection of less than 95% of tumor) and a near-total group (resection of 95% or more of tumor) and were followed yearly with either computed tomography or magnetic resonance imaging. The subtotal group was planned and consisted of elderly patients (mean age, 68.5 years) with large tumors (mean, 3.1 cm). The near-total group consisted of younger patients (mean age, 45.8 years) and smaller tumors (mean, 2.3 cm). The mean length of followup for all patients was 5.0 years. Ninety percent of patients had House grade I or II facial function post-operatively. Radiologically detectable tumor regrowth occurred in only one patient, who was in the subtotal resection group. Near-total resection of acoustic tumor was not associated with radiologic evidence of regrowth of tumor for the period of observation. Within the limits of the follow-up period of this study, subtotal resection of acoustic neuroma in elderly patients was not associated with clinically significant recurrence in most patients and produced highly satisfactory rates of facial preservation with low surgical morbidity.

Torsades de pointes occurring in association with terfenadine use. Torsades de pointes is a form of polymorphic ventricular tachycardia that is associated with prolongation of the QT interval. Although found in many clinical settings, torsades de pointes is most often drug induced. This report describes the first association (exclusive of drug overdose) of symptomatic torsades de pointes occurring with the use of terfenadine in a patient who was taking the recommended prescribed dose of this drug in addition to cefaclor, ketoconazole, and medroxyprogesterone. Measured serum concentrations of terfenadine and its main metabolite showed excessive levels of parent terfenadine and proportionately reduced concentrations of metabolite, suggesting inhibition of terfenadine

metabolism. We believe that a drug interaction between terfenadine and ketoconazole resulted in the elevated terfenadine levels in plasma and in the cardiotoxicity previously seen only in cases of terfenadine overdose.

Asymptomatic celiac and superior mesenteric artery stenoses are more prevalent among patients with unsuspected renal artery stenoses. The prevalence of unsuspected renal artery stenosis among patients with peripheral vascular disease has been reported to be as high as 40%, but the prevalence of asymptomatic celiac and superior mesenteric artery stenoses in these patients is not known. The biplane aortograms of 205 male patients who were military veterans and had aneurysms or occlusive disease were independently reviewed, and medical records were studied to determine associated coronary disease, risk factors, and patient outcome. Fifty-six patients (27%) had a 50% or greater stenosis in the celiac or superior mesenteric artery, and seven patients (3.4%) had significant stenoses in both mesenteric arteries. Patients with celiac or superior mesenteric artery stenoses were older ($p = 0.002$) and had a higher prevalence of hypertension ($p = 0.029$) than those without significant mesenteric stenoses. Fifty of the 205 patients had significant renal artery stenoses, and 20 had advanced (greater than 75% diameter loss) renal stenoses. Ten of the 20 patients (50%) with advanced renal stenoses had a concomitant celiac artery stenosis, compared to 40 of the 185 patients (22%) who did not have advanced renal stenoses ($p = 0.011$). In the present study asymptomatic celiac or superior mesenteric artery stenoses were common among male veterans evaluated for peripheral vascular disease, but the prevalence of significant stenoses in both the celiac and superior mesenteric arteries was low. The prevalence of significant celiac stenosis was higher in patients with advanced (greater than 75%) renal artery stenoses who might be considered for prophylactic renal revascularization. Lateral aortography with evaluation of the celiac artery is always appropriate in these patients.

Brain-stem auditory evoked responses in 56 patients with acoustic neurinoma. The brain-stem auditory evoked responses (BAER's) recorded from 56 patients with acoustic neurinomas were analyzed. Ten of the patients had intracanalicular tumors and 46 had extracanalicular tumors. It was possible to obtain BAER's following stimulation of the affected side in 28 patients and after stimulation of the unaffected side in all 56. Five patients (11%) had normal BAER's following stimulation of both sides; three of these patients had intracanalicular tumors. Among BAER's obtained following stimulation of the affected ear, the mean interpeak latency (IPL) for peaks I to III associated with extracanalicular tumors was significantly prolonged relative to controls (p less than 0.001), and linear regression analysis revealed a significant positive correlation between tumor size and IPL of peaks I to III (p less than 0.05). Analysis of the 56 BAER's recorded after stimulation of the unaffected side revealed a significant positive correlation between the IPL's of peaks III to V and tumor size (p less than 0.001). This correlation was not strengthened when accounting for the degree of brain-stem compression. Finally, evidence of preserved function within the auditory pathway, even in the presence of partial hearing loss, is presented. This finding suggests that more patients might benefit from surgical procedures that spare the eighth cranial nerve.

First heterotransplantation of a human carcinoid tumor into nude mice. The first successful heterotransplantation of a human carcinoid tumor into nude mice is reported. CSH, a voluminous hepatic metastasis of a primary bronchial carcinoid tumor (CSB) was resected and transplanted into three irradiated nude (Swiss-nu/nu) mice both by subcutaneous (SC) and intramuscular (IM) routes; the success rate was five of six. Heterotransplanted tumors took 4 to 5 months to appear in the mice and 1 month to attain a width of 0.5 cm. Both human and mouse tumors (named CSH-SC and CSH-IM) were studied by light and electron microscopy. They were Grimelius-positive, neuron-specific enolase-positive, and bombesin-negative by immunocytochemistry. Furthermore, CSH-SC cells

presented characteristic (pear-shaped, rod-shaped, or tadpole-shaped) neurosecretory granules. Although CSB and CSH were slightly serotonin positive by immunocytochemistry, only a few serotonin-positive cells were found in CSH-SC and none in CSH-IM, suggesting partial loss of differentiation or an increase in serotonin catabolism during transplantation.

A prospective evaluation of the immediate reproducibility of the signal-averaged ECG. The purpose of this investigation was to prospectively evaluate the immediate reproducibility of the signal-averaged electrocardiogram (SAECG). A total of 114 patients undergoing evaluation for ventricular arrhythmias were enrolled in this protocol. Two consecutive SAECG's (40 Hz bidirectional high-pass filtering with a computer-automated system) were performed 10 minutes apart. Abnormal SAECG parameters were defined as (1) vector QRS duration more than 120 msec, (2) terminal root mean square (RMS) voltage less than 20 microV, and (3) low-amplitude signal (LAS) duration more than 40 msec. An SAECG was defined as abnormal if at least one vector parameter was abnormal. There was close correlation between vector parameters during the two SAECG observations: QRS duration had the highest reproducibility ($r^2 = 0.97$, p less than 0.001) followed by terminal RMS voltage ($r^2 = 0.92$, p less than 0.001), and LAS duration ($r^2 = 0.90$, p less than 0.001). The mean (\pm SD) percentage of change between the two recordings was 2% \pm 2% of the QRS duration, 13% \pm 22% for terminal RMS voltage, and 7% \pm 11% for LAS duration. The reproducibility of an initially normal SAECG was 92% and of an initially abnormal SAECG, 96%. Seventeen patients (15%) had a change in one of the three vector parameters between the two recordings. There were no clinically significant differences between the 17 patients in whom the SAECG was nonreproducible and the 97 patients in whom the SAECG was reproducible. However, reproducibility was significantly higher in patients with an initially normal versus an initially abnormal SAECG (92% vs 76%, $p = 0.03$).

Hypertension, lipoprotein(a), and apolipoprotein A-I as risk factors for stroke in the Chinese. We analyzed the serum concentrations of lipids and lipoproteins and the prevalence of other risk factors in a case-control study of 304 consecutive Chinese patients with acute stroke (classified as cerebral infarction, lacunar infarction, or intracerebral hemorrhage) and 304 age- and sex-matched controls. For all strokes we identified the following risk factors: a history of ischemic heart disease, diabetes mellitus, or hypertension; the presence of atrial fibrillation or left ventricular hypertrophy; a glycosylated hemoglobin A1 concentration of greater than 9.1%; a fasting plasma glucose concentration 3 months after stroke of greater than 6.0 mmol/l; a serum triglyceride concentration 3 months after stroke of greater than 2.1 mmol/l; and a serum lipoprotein(a) concentration of greater than 29.2 mg/dl. We found the following protective factors: a serum high density lipoprotein-cholesterol concentration of greater than 1.59 mmol/l and a serum apolipoprotein A-I concentration of greater than or equal to 106 mg/dl. The patterns of risk factors differed among the three stroke subtypes. When significant risk factors were entered into a multiple logistic regression model, we found a history of hypertension, a high serum lipoprotein(a) concentration, and a low apolipoprotein A-I concentration to be independent risk factors for all strokes. The attributable risk for hypertension was estimated to be 24% in patients aged greater than or equal to 60 years. In this population, in which cerebrovascular diseases are the third commonest cause of mortality, identification of risk factors will allow further studies in risk factor modification for the prevention of stroke.

Prevalence of air bronchograms in small peripheral carcinomas of the lung on thin-section CT: comparison with benign tumors. Despite improved techniques--such as bronchoscopy and percutaneous needle biopsy--to evaluate pulmonary nodules, there are still many cases in which surgical resection is necessary before carcinoma can be differentiated from benign lesions. The present study was undertaken to determine if the presence of an air bronchogram or air bronchiologram (patent visible bronchus or bronchiole) is useful in distinguishing small lung cancers

from benign nodules. Thin-section chest CT scans were obtained in patients with 20 peripheral lung cancers less than 2 cm in diameter (18 adenocarcinomas, one squamous cell carcinoma, and one large cell carcinoma) and 20 small benign nodules (eight hamartomas, seven tuberculomas, two foci of aspergillosis, one focus of cryptococcosis, one chronic focal interstitial pneumonitis, and one plasma cell granuloma). The images were compared with regard to the patency of any bronchus or bronchiole within the lesions. After surgical resection, the specimens were inflated with agar and sectioned transversely to correlate gross morphology and low-power histologic sections with the CT appearance. An air bronchogram or air bronchiologram was seen in the tumors on 65% of CT scans and 70% of histologic sections. Benign nodules had a patent bronchus or bronchiole on CT scans and histologic sections in only one case (5%). These findings suggest that the presence of an air bronchogram in a lung nodule is a useful finding to help differentiate adenocarcinomas from benign lesions.

Long-term spinal administration of morphine in cancer and non-cancer pain: a retrospective study. Records of 313 patients who had been treated with spinal morphine via an implanted Port-A-Cath were reviewed. In 284 cases the Port-A-Cath was implanted for epidural delivery of morphine in patients with cancer-related pain. These patients were treated for a mean of 96 (range 1-1215) days. There was a wide variation in dose requirements, minimum daily dose ranging from 0.5 to 200 mg and maximum daily dose from 1 to 3072 mg. However, there was no clear trend to increasing dose as period of epidural morphine administration increased. The most frequent complications were pain on injection (12.0% incidence), occlusion of the portal system (10.9%), infection (8.1%) and leakage of administered morphine such that it did not all reach the epidural space (2.1%). In all but 1 case infections were limited to the area around the portal or along the catheter track. All infections resolved without sequelae following removal of the portal and/or administration of antibiotics. In 17 patients Port-A-Caths were implanted for the intrathecal delivery of morphine to control cancer-related pain. These patients also exhibited wide variations in morphine dose requirements. Port-A-Caths were also implanted for delivery of spinal morphine in 12 patients with chronic pain which was not related to cancer and which failed to respond to other therapies. These patients were treated for a mean of 155 (range 2-575) days. Port-A-Caths were removed from 7 of these patients, primarily due to infection (2 cases) and inadequate pain relief and pain on injection (2 cases).

Real-time ultrasound for the detection of deep venous thrombosis. **PURPOSE:** Accurate diagnosis of deep venous thrombosis (DVT) is a clinical problem in emergency practice. A prospective trial was conducted comparing real-time ultrasound with contrast venography in the diagnosis of proximal DVT. **METHODS:** Seventy patients whose clinical presentations mandated diagnostic evaluation for DVT had real-time ultrasound of the involved leg followed by contrast venography. Initial readings of ultrasound and venography were compared with each other and with final readings to assess reliability of interpretation. **RESULTS:** Final ultrasound readings agreed with final venogram readings in all patients. Negative initial ultrasound readings agreed with final venogram readings in 56 of 56 patients (negative predictive value, 100%; 95% confidence interval, 94 to 100). Eighteen patients had positive initial ultrasound readings compared with 14 who had positive final venogram readings (positive predictive value, 78%; 95% confidence interval, 55 to 91). **CONCLUSION:** Negative real-time ultrasonography reliably excludes proximal DVT. Positive ultrasound reliably diagnoses proximal DVT only in experienced hands.

Single- versus dual-chamber sensor-driven pacing: comparison of cardiac outputs. Previous studies have shown that single-chamber sensor-driven pacing improves exercise tolerance for patients with chronotropic incompetence. However, long-term single-chamber pacing has a number of inherent problems that limit its usefulness. Although sensor-driven dual-chamber pacing largely obviates the

problems inherent with single-chamber sensor-driven pacing, the physiologic benefit of dual-chamber sensor-driven pacing has not yet been demonstrated. Accordingly, the purpose of this study was to compare exercise-induced cardiac output for patients with chronotropic incompetence, after programming their pacemakers to either a simulated sensor-driven single or simulated dual-chamber mode. Cardiac output was measured noninvasively at rest and peak exercise using standard Doppler-derived measurements, obtained in a blinded fashion. At rest the Doppler-derived resting VVI and DDD cardiac outputs were 4.49 ± 0.3 L/min and 4.68 ± 0.3 L/min, respectively. At peak exercise, the DDD cardiac output was 5.07 ± 0.5 L/min, whereas the simulated activity VVI and DDD cardiac outputs were 6.33 ± 0.6 L/min and 7.41 ± 0.70 L/min, respectively. Analysis of variance showed that there was an overall significant difference in cardiac output from rest to peak exercise (p less than 0.001). However, only the simulated activity DDD cardiac output was significantly different from its respective control value (p less than 0.05). Thus this study shows for the first time that the addition of rate responsiveness to dual-chamber pacing results in a significant improvement in cardiac output for patients with chronotropic incompetence.

FDP D-dimer induces the secretion of interleukin-1, urokinase-type plasminogen activator, and plasminogen activator inhibitor-2 in a human promonocytic leukemia cell line. We studied the effect of fibrinogen degradation products D, E, and D-dimer on a human promonocytic leukemia cell line, NOMO-1. After exposure to a 10^{-5} -mol/L fragment D or D-dimer, the cells displayed macrophage-like characteristics, such as adherence to plastic surfaces, and showed approximately a twofold increase in response to the nitroblue tetrazolium reduction test. The secretion of interleukin-1 alpha (IL-1 alpha) into the medium was markedly stimulated by a 10^{-5} -mol/L fragment D, E, and D-dimer, whereas a significant increase in IL-1 beta secretion was observed only in D-dimer-stimulated cells. In addition, D-dimer induced a rapid increase in urokinase-type plasminogen activator on day 1 (0.52 ± 0.02 ng/mL v 0.07 ± 0.01 ng/mL in the control culture) and a slow increase in plasminogen activator inhibitor-2 on day 5 (3.9 ± 1.6 ng/mL v 1.2 ± 0.2 ng/mL in the control culture). An increase in tissue factor (TF) was also demonstrated on the cell surface of NOMO-1 cells exposed to fragment D or D-dimer by indirect immunofluorescence using an anti-TF monoclonal antibody. Scatchard plot analysis showed that fragment D and D-dimer bound to the NOMO-1 cells with a K_d of 3.3 nmol/L and 2.7 nmol/L, respectively. These results suggest that fragment D-dimer specifically stimulates cells of monocyte-macrophage lineage to secrete key substances that regulate blood coagulation, fibrinolysis, and inflammation.

Stereotactic management of colloid cysts: factors predicting success. Stereotactic aspiration is a valuable surgical alternative for colloid cysts when used alone or in conjunction with microsurgical resection. Since 1981, the authors have performed computerized tomography (CT)-guided stereotactic aspiration as the initial procedure in 22 patients with colloid cysts; stereotactic aspiration alone was successful in 11 patients (50%). Of the 11 patients in whom aspiration failed, stereotactic endoscopic resection was attempted in three and was successful in one. Seven patients required a craniotomy and microsurgical removal of the cyst performed via a transcortical approach. The preoperative CT appearance in eight cases of a hypodense or isodense cyst correlated favorably with successful aspiration of the cyst in six patients. A hyperdense appearance on the preoperative CT scan in 14 cases was associated with subtotal aspiration in 13 patients; five required craniotomy for removal. Preoperative magnetic resonance (MR) imaging in eight patients provided excellent anatomical definition of the cyst and its relationship to other structures of the third ventricle, but it was not possible to correlate successful aspiration with cyst appearance on MR images with short or long relaxation time sequences. The authors' 9-year experience suggests that preoperative CT studies accurately determine size, predict viscosity, and help to define a group of colloid cyst patients for whom stereotactic cyst aspiration will likely be successful. Unsuccessful stereotactic aspiration was

related to two features: the high viscosity of the intracystic colloid material (nine patients), or deviation of the cyst away from the aspiration needle due to small cyst volume (two patients). Because of its simplicity and low risk, stereotactic surgery can be offered to selected patients as the initial procedure of choice. Craniotomy can be reserved for those whose imaging studies predict failure or for those whose cyst cannot be aspirated.

Cranial magnetic resonance imaging in chronic demyelinating polyneuropathy. Twenty one patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and five patients with chronic demyelinating polyneuropathy associated with benign monoclonal paraproteinaemia none of whom had signs or symptoms of central nervous system disease, had cranial magnetic resonance imaging (MRI) on a 1.5 Tesla unit. Areas of increased white matter signal intensity were seen in one of 10 patients aged less than 50 years and in five of 16 patients aged more than 50 years. In only two of the patients (8%), neither of whom had paraproteinaemia, did the appearance strongly suggest demyelination. The only clinical variable that predicted MRI changes was age (p less than 0.01).

Bleeding patterns during continuous combined estrogen-progestogen therapy. Bleeding and climacteric symptoms were recorded in two groups of postmenopausal women receiving either continuous combined estradiol and norethisterone acetate or estradiol and cyproterone acetate. Out of a sample of 99 postmenopausal women aged 45 to 54 years, 86 completed a 2-year, double-blind, placebo-controlled study. Comparison of the bleeding patterns in the two groups revealed a statistically significant difference: More women in the estradiol-cyproterone acetate group experienced bleeding and for a longer duration. Thirteen women in the estradiol-norethisterone acetate group were amenorrheic, compared with two in the other group. The Kupperman index score in both groups declined to about 30% to 40% of initial values (p less than 0.001). The hot flushes in both treatment groups decreased to a highly significant degree (p less than 0.001), to a value below 20% of baseline values. We conclude that a continuous combination of estrogen and progestogen can produce amenorrhea and symptomatic relief. However, the progestogen components seem to differ in their ability to control bleeding.

Impaired hepatic handling and processing of lysophosphatidylcholine in rats with liver cirrhosis. Lysophosphatidylcholine is a major metabolic product in the plasma and cellular turnover of phospholipids, with well-known membrane-toxic and proinflammatory properties. Because the liver plays a key role in plasma lysophosphatidylcholine removal and biotransformation and because virtually nothing is known of these processes in a diseased organ, the hepatobiliary metabolism of lysophosphatidylcholine was investigated in rats with carbon tetrachloride-induced liver cirrhosis. Twelve adult male Wistar rats with histologically confirmed cirrhosis and 8 control animals were fitted with jugular and biliary catheters and allowed to recover. The animals were kept under constant IV infusion of taurocholate (1 $\mu\text{mol}/\text{min}$). Two microcuries of sn-1-[^{14}C]palmitoyl-lysophosphatidylcholine was administered as a single bolus. The fate of the injected radioactivity, including removal from plasma, uptake, and subcellular location in the liver and molecular and aggregative forms, was studied by combined chromatographic and radiochemical methods. Major findings were (a) that lysophosphatidylcholine has a prolonged permanence in plasma of cirrhotic rats, due both to decreased hepatic clearance and to depressed conversion into phosphatidylcholine; (b) that the rate of lysophosphatidylcholine acylation is much slower in the cirrhotic than in the normal liver, both at the microsomal and at the cytosolic level; (c) that cytosolic lysophosphatidylcholine in the cirrhotic liver, but not in the normal liver, is predominantly non-protein bound; (d) that the strict molecular selectivity of lysophosphatidylcholine acylation observed in controls is partially lost in cirrhosis; and (e) that a consistent fraction of lysophosphatidylcholine is converted into triacylglycerols in cirrhotics but not in controls. These findings show a profound

derangement of lysophosphatidylcholine handling and processing in the cirrhotic liver, which is of potential pathogenetic significance.

The value of single versus multiple sections for detection of lymph node metastasis. This study was undertaken to determine the value of serial sectioning of lymph nodes as an aid in optimally examining cervical specimens for metastasis. The presence or absence of lymph node metastasis in 802 lymph nodes obtained from 51 consecutive neck dissection specimens were initially determined by the routine method, examination of one section from each node. This examination revealed 40 lymph nodes with metastatic involvement. Further study of the 716 lymph nodes that were initially interpreted as free of tumor by serial sectioning added only two positive nodes. Thus, serial sectioning did not contribute significantly to the detection of lymph node metastasis.

Cytotoxic activity in plasma from patients with amyotrophic lateral sclerosis. The present study evaluates an assay of cytotoxic effect of plasma from patients with amyotrophic lateral sclerosis. Plasma from 20 recently diagnosed ALS patients induced hemolysis of normal red blood cells with a significantly greater intensity than that of normal controls. After at least 1 month of treatment with prednisone and azathioprine, the hemolytic activity of ALS plasma was reduced but was still higher than that of control plasma.

Multiple giant cell tumors and Paget disease of bone: radiographic and clinical correlations. The clinical and radiographic findings of four patients with multicentric giant cell tumor (GCT) of bone and Paget disease were retrospectively reviewed. Three patients underwent magnetic resonance (MR) imaging evaluation; all patients underwent computed tomography (CT). The MR characteristics of the bone component in pagetic GCT appeared to reflect the pagetic phase; a sclerotic pattern was largely represented by hypointense marrow signal intensity on images obtained with both long and short repetition times (TRs) and echo times (TEs). Conversely, a tumor appearing in a mixed pagetic phase demonstrated more heterogeneous signal intensity with all pulse sequences. Extensive soft-tissue components, noted in all cases, showed largely intermediate signal intensity on short TR/TE images and foci of increased signal intensity on longer TR/TE images. In most cases, dramatic reduction in tumor bulk was noted with the use of steroids alone. An awareness of this entity is important because the appearance of lytic lesions with soft-tissue extension in patients with Paget disease does not necessarily imply a grave prognosis. Serial CT or MR imaging is helpful in monitoring the remissions and exacerbations that reflect response to therapy in Paget disease and GCT.

Magnetic resonance assessment of the postoperative spine. Degenerative disc disease. The magnetic resonance (MR) imaging findings in patients after surgery for degenerative disc disease in the lumbar and cervical spine are discussed. In the lumbar spine, changes seen in the immediate postoperative period, use of Gd-DTPA in distinguishing scar and disc and postoperative complications are reviewed. In the cervical spine, operative approaches and types, the appearance of bony stenosis, and disc herniations are demonstrated.

Urethroplasty using the pedicled island flap technique in complicated urethral strictures. Many techniques have been described for the repair of recurrent urethral strictures. Experience with 1-stage correction of hypospadias and epispadias, using a vascularized island flap technique, has led to its increased application for complicated adult urethral strictures. The advantage of the vascularized island flap technique is that reconstruction can be completed with only 1 operation, and it provides good subjective and objective results. Analysis of 50 consecutive cases treated by this approach has proved its validity. Of the 50 cases fistulas occurred in 20%, of which 12% required surgical correction, and stricture recurred in 32%. The largest proportion of recurrence was noted in patients

who were primarily treated with 3 or more urethrotomies within a short time. Therefore, we recommend open surgical repair when 1 or 2 internal urethrotomies fail to produce a good result.

Bullous pemphigoid autoantibodies, HIV-1 infection and pruritic papular eruption. Bullous pemphigoid (BP)-type autoantibodies were found by Western blot (WB) analysis of epidermal extracts in the serum of 38% of HIV-seropositive patients compared with 21% of HIV-seronegative patients with chronic pruritus and 76% of patients with BP. They were further identified as BP autoantibodies (BPAb) by immunoprecipitation and immunoelectron microscopy. Their incidence increased from 21% in HIV infection stage II to 37% and 43% in stages III and IV, respectively. Of the patients suffering from HIV-related chronic pruritic papulovesicular eruption, 75% showed circulating BPAb as compared with 29% in those without skin problems ($P = 0.0066$) and, among them, 30% met the diagnostic criteria for BP when histology, WB, immunofluorescence and immunoelectron microscopy techniques were used. In conclusion, this study identifies an autoimmune skin reaction that may account for, or be related to, the distressing pruritic eruptions occurring in HIV-infected patients.

Molecular characterization of a region of DNA associated with mutations at the agouti locus in the mouse. Molecular characterization of a radiation-induced agouti (a)-locus mutation has resulted in the isolation of a segment of DNA that maps at or near the a locus on chromosome 2 in the mouse. This region of DNA is deleted in several radiation- or chemical-induced homozygous-lethal a-locus mutations and is associated with specific DNA structural alterations in two viable a-locus mutations. We propose that DNA probes from this region of chromosome 2 will be useful for ultimately characterizing the individual gene or genes associated with a-locus function.

Fatty acids in human platelets and plasma. Fish oils decrease sensitivity toward N₂ microbubbles. Platelet aggregation induced by N₂ microbubbles (simulating microbubbles developed during deep diving) was measured in seven volunteers before and after intake of ethyl-eicosapentaenoate (-EPA, 3.5 g/day) and ethyl-docosahexaenoate (-DHA, 2.5 g/day) for 2 wk. The relative content of arachidonic acid (AA) decreased in platelets from all individuals, whereas the content of EPA and DHA increased. The decrease of AA was almost identical with the increase of EPA plus DHA. In plasma the AA content was unchanged, while EPA and DHA increased. The N₂ microbubble-induced aggregation showed a significant negative correlation with the DHA content both in platelets and in plasma. Less aggregation was also observed with high EPA content in platelets or plasma. A significant correlation between AA content in platelets and aggregation was seen. Intake of marine oils may be beneficial to divers under deep diving and to patients during extracorporeal circulation, because this may reduce the microbubble-induced aggregation.

Midventricular obstruction associated with chronic systemic hypertension and severe left ventricular hypertrophy. Midventricular obstruction is an uncommon finding previously defined by catheterization and angiographic techniques in patients with hypertrophic cardiomyopathy. This study describes the clinical and echocardiographic findings of 10 consecutive patients (mean age 73 years) with severe concentric left ventricular (LV) hypertrophy and the unusual finding of a dynamic systolic obstruction located in the midportion of the left ventricle. All patients were known to have chronic hypertension, and none had a history or family history of hypertrophic cardiomyopathy. In each case, a well-defined, high velocity, turbulent jet was identified by Doppler color flow imaging and subsequently confirmed with conventional Doppler techniques. Septal and posterior wall thickness averaged 1.67 and 1.57 cm, respectively. Mean LV mass index was 199 g/m² and ejection fraction averaged 78%. Peak systolic velocity obtained by continuous-wave Doppler averaged 2.7 m/s and appeared as either a "late-peaking" or a "spike and dome" configuration. Seven of 10 patients gave a history of syncope or severe presyncope at the time of echocardiographic examination. At a

mean follow-up of 1 year, syncope or presyncope had resolved in 5 patients in whom medication was adjusted based on the ultrasound study, but persisted in 2 patients in whom diuretic therapy was continued. It is concluded that obstruction to systolic flow can occur at the mid-LV level in some patients with severe concentric LV hypertrophy and avoidance of medication known to lower LV volume may relieve symptoms of transient inadequate cardiac output.

The impact of nonidentical ABO cadaveric renal transplantation on waiting times and graft survival. Blood type O recipients of cadaveric renal transplants have longer pretransplant waiting periods than blood type A, B, and AB recipients. To evaluate reasons for and consequences of this discrepancy, we studied both the frequency of various donor and recipient blood type combinations and their outcomes. Among 37,659 cadaveric renal transplants performed during 1983 through 1989, there were 2,625 transplants (7%) received by patients of compatible but nonidentical blood types. Of 18,575 type O donor organs, 16,784 were received by type O patients for a recipient to donor ratio of 0.9. The corresponding ratios were greater than 1.0 for all other blood types (1.02 for blood type A, 1.14 for type B, and 2.18 for type AB). This causes blood type O patients to have a lower access to transplantation and to have significantly longer waiting times than patients of all other blood types. This inequality of access diminished significantly (P less than 0.001) over the years, but did not resolve by 1989. Analysis of relative risk for first graft loss by multiple regression (Cox) showed that transplantation across compatible blood types had a 9.1% higher risk (P less than 0.1) than that of transplantation among identical blood types. Cadaveric renal transplantation within identical blood types optimizes access to transplantation and avoids further aggravating past disadvantages for blood type O recipients.

Results of a recently instituted programme of thrombolytic therapy in acute lower limb ischaemia. Twenty-eight patients with acute lower limb ischaemia received low dose intra-arterial thrombolytic therapy over a 2-year period. Eighteen patients received streptokinase and ten patients received recombinant tissue plasminogen activator (rTPA). Indications included arterial thromboemboli and graft failures. Mean ischaemic times were similar in both groups. Treatment time to achieve lysis was significantly less with rTPA (P less than 0.01). Subsequent vascular procedures, including angioplasty or reconstruction, were undertaken in 36 per cent of patients. Arterial puncture site bleeding occurred in eight (29 per cent) patients. Three (11 per cent) patients suffered rethrombosis after initial successful lysis. All rethromboses were successfully lysed with rTPA. There were two major amputations. Five (18 per cent) patients died, all lytic failures in the streptokinase treatment group. There were no cerebral haemorrhagic events and no patient died as a result of thrombolytic therapy. Good clinical outcome was obtained in nine of 18 patients treated with streptokinase and in nine of ten patients treated with rTPA. Intra-arterial thrombolysis provides effective therapy with high rates of limb salvage and a low mortality rate. This study suggests that rTPA may be a more effective agent, causing less morbidity, than streptokinase.

Metastatic melanoma to the heart presenting with ventricular tachycardia. Intraventricular tumors in adults are uncommon, and the association of these with ventricular tachycardia is even more rare. We report a case of an intracardiac metastatic melanoma in a woman who presented with syncope due to ventricular tachycardia.

Risk stratification after myocardial infarction. Clinical overview. Many patients with an acute myocardial infarction can be stratified into subgroups that are at high risk for morbidity and mortality on the basis of clinical characteristics that indicate recurrent myocardial ischemia, persistent left ventricular dysfunction, and/or recurrent cardiac arrhythmias. In patients with uncomplicated myocardial infarction the assessment of symptoms, physical findings, and ECG changes during predischARGE exercise testing often identifies patients at increased risk for further cardiac events.

Because of the suboptimum sensitivity and specificity of the exercise ECG for detecting myocardial ischemia, myocardial perfusion imaging with ^{201}Tl and/or assessment of global and segmental ventricular function by two-dimensional echocardiography or radionuclide cineangiography during or immediately after exercise are often added to the predischarge risk stratification.

Recurrent pericarditis and cardiac tamponade in a patient with hypocomplementemic urticarial vasculitis syndrome. We describe a patient with hypocomplementemic urticarial vasculitis syndrome complicated by recurrent pericarditis and cardiac tamponade. The episodes of pericarditis were associated with urticarial vasculitis, hypocomplementemia, and circulating IgG antibodies to the collagen-like region of C1q. Histopathologic examination of the skin and pericardium demonstrated vasculitis associated with immunoglobulin and complement deposition suggesting an immune complex mediated etiology. Recurrent pericarditis should be included in the clinical spectrum of hypocomplementemic urticarial vasculitis syndrome.

Symptomatic benefit of supplemental oxygen in hypoxemic patients with chronic lung disease. We have compared the symptomatic benefit of air and oxygen at rest in hypoxemic patients with chronic obstructive airway disease (COAD) or interstitial lung disease (ILD). A total of 12 severely disabled patients with COAD (mean \pm SEM, PaO_2 , 50.3 \pm 3.7 mm Hg) and 10 with ILD (PaO_2 , 48.0 \pm 3.1 mm Hg) received 28% oxygen and air by Venturi face mask, each gas on two occasions, in a double-blind randomized fashion. SaO_2 increased (p less than 0.01) in both groups during oxygen breathing: COAD, 85.1 \pm 2.3% versus 93.1 \pm 1.4%; ILD, 85.5 \pm 1.7% versus 94.7 \pm 0.9%. The patients with COAD stated that air helped their breathing on 15 of 24 occasions and that oxygen helped on 22 of 24 occasions (p less than 0.05). In the patients with ILD the values were 6 of 20 and 13 of 20 occasions, respectively (p less than 0.05). In both groups of patients the severity of breathlessness recorded on a 100-mm visual analog scale was significantly (p less than 0.05) lower during oxygen breathing: COAD, 29.6 \pm 4.5 versus 45.6 \pm 6.0; ILD, 30.2 \pm 5.1 versus 48.1 \pm 4.4. Ventilation measured by magnetometers was significantly lower during oxygen breathing in the patients with COAD (8.2 \pm 1.0 versus 9.3 \pm 1.1 L/min; p less than 0.05), but the difference between oxygen and air in patients with ILD was not statistically significant (9.3 \pm 1.3 versus 11.2 \pm 1.6 L/min; p greater than 0.05).

Mitomycin C as an adjuvant treatment to resected gastric cancer. A 10-year follow-up. Seventy consecutive patients were entered in a two-arm randomized trial after surgical resection for locally advanced gastric cancer. In the first arm, 37 patients were included as a control group, receiving no further treatment after surgery. In the second arm, 33 patients were treated with adjuvant chemotherapy consisting of mitomycin C (MMC), 20 mg/m² administered intravenously once every 6 weeks for four consecutive cycles. All patients in both arms were followed in the same way for 5 years. At 5 years 23 of 37 patients in the control arm and 7 of 33 patients in the treatment arm were dead because of relapse. Actuarial survival curve was statistically significant in favor of patients given adjuvant MMC (p less than 0.001). After 10 years follow-up, 31 of 37 patients in the control arm and 16 out of 33 patients in the treatment arm were dead because of relapse, the statistical differences continuing in the actuarial survival curve in favor of treated patients (p less than 0.01). The best advantages of adjuvant treatment were observed in the T3N0M0 stage. The most frequent relapse site was the peritoneal cavity and the relapse pattern shows special decrease in liver metastases in treated patients. Toxicity was acute and mild. No delayed toxicity or second malignancies were observed. These data suggest that adjuvant MMC after resected surgery of gastric cancer is a successful treatment and its effects are still evident after 10 years of follow-up.

Mucin-producing tumor of the pancreas. A new pancreatic tumor, called mucin-producing tumor, has received great attention in Japan. These tumors are found inside the pancreatic duct and produce

large quantities of copious mucus. The authors examined 22 cases of these tumors histologically and histochemically. In 12 malignant cases, the tumors inside the ducts consisted of cancerous lesions over small areas along with papillary or atypical hyperplasia. Tumors in ten benign cases mainly consisted of papillary hyperplasia. Except for three patients with carcinoma in situ, cancerous tumors infiltrated the pancreatic parenchyma and, in some cases, were observed invading the bile duct or duodenum. A mucous histochemical study showed evidence of sialomucin in malignant cases; neutral mucin was dominant in benign cases. Characteristics of this disease were also compared with 13 cases of mucinous cystic neoplasm. From the results, it was concluded that these two diseases can be classified into the same conceptual category.

A rat model of acute liver necrosis induced by a monoclonal antibody to liver-specific antigen and complement. Acute massive hepatic injury was induced in rats by a monoclonal antibody against a rat liver-specific membrane antigen, and its histological characteristics were investigated. A single intravenous injection of murine ascites containing a monoclonal antibody produced numerous hemorrhagic foci of degenerated and necrotic liver cells predominantly in zones 1 (the periportal area) and 2 (the area of transition between the periportal zone and the perivenular zone) of the liver lobule within 10 min. Massive hepatocellular necroses were observed 1 hr later, but no inflammatory cell infiltration occurred in and around the necrotic foci. Immunohistological study demonstrated marked deposition of the third component of the complement system in the necrotic area. Serum complement activity was sharply decreased immediately after the injection of the antibody, suggesting that the hepatic necrosis is ascribable to a complement-mediated immune attack on the liver cell membrane induced by the antigen-antibody reaction. The hepatic necrosis in response to monoclonal-antibody injection did not progress to a chronic disease and healed almost completely, changing to scar tissues within 2 wk. Although it is not clear whether this hepatic injury has any clinical relevance, this antibody/complement model may be useful for investigating the cause and therapy of hepatic diseases such as fulminant hepatitis.

Preserved action of a rectus muscle after transection by an encircling solid silicone band. We present a case of anterior migration of a solid silicone band through a lateral rectus muscle. In this patient the action of the lateral rectus was preserved, and this is demonstrated photographically. The possible reasons for this rare complication and the possible mechanism by which lateral rectus activity remained intact are explained.

Clinical features of Behcet's disease. Report of four cases. Behcet's disease is a multisystem inflammatory disorder of unknown etiology. The unifying histologic reaction pattern is a leukocytoclastic vasculitis that affects predominantly the skin, oral mucosa, and eyes. Many other sites of involvement have been reported but are inconsistently found in individual patients. Early recognition and treatment of Behcet's disease may help prevent devastating permanent sequelae such as blindness. Because oral involvement is often the first manifestation of this disorder, dental practitioners are in a unique position to help these patients. We report four cases of Behcet's disease in North American patients. Diagnostic criteria and treatment options are reviewed.

Recombinant granulocyte-macrophage colony-stimulating factor after autologous bone marrow transplantation for lymphoid cancer. BACKGROUND. The period of neutropenia after autologous bone marrow transplantation results in substantial morbidity and mortality. The results of previous phase I-II clinical trials suggest that recombinant human granulocyte-macrophage colony-stimulating factor (rhGM-CSF) may accelerate neutrophil recovery and thereby reduce complications in patients after autologous bone marrow transplantation. METHODS. We conducted a randomized, double-blind, placebo-controlled trial at three institutions. The study design and treatment schedules were identical, and the results were pooled for analysis. One hundred twenty-eight patients were enrolled.

Sixty-five patients received rhGM-CSF in a two-hour intravenous infusion daily for 21 days, starting within four hours of the marrow infusion, and 63 patients received placebo. RESULTS. No toxic effects specifically ascribed to rhGM-CSF were observed. The patients given rhGM-CSF had a recovery of the neutrophil count to 500×10^6 per liter 7 days earlier than the patients who received placebo (19 vs. 26 days, P less than 0.001), had fewer infections, required 3 fewer days of antibiotic administration (24 vs. 27 days, $P = 0.009$), and required 6 fewer days of initial hospitalization (median, 27 vs. 33 days; $P = 0.01$). There was no difference in the survival rate at day 100. CONCLUSIONS. In patients undergoing autologous bone marrow transplantation for lymphoid neoplasia, rhGM-CSF significantly lessens morbidity. Further studies will be required to establish its optimal dosage and schedule of administration.

Candida tropicalis and *Candida albicans* fungemia in children with leukemia. The records were reviewed for all patients hospitalized at a pediatric oncology center for complications of leukemia ($n = 822$) or lymphoma ($n = 290$) during an 8-year period. The results of surveillance cultures (throat, rectal, and urine) and blood cultures were analyzed to identify cases of *Candida tropicalis* and *C. albicans* colonization and/or fungemia. None of the patients with lymphoma who had positive surveillance cultures for *C. albicans* ($n = 89$) or *C. tropicalis* ($n = 23$) had fungemia. Among patients with leukemia, significant fungal infection was documented in 12 of 107 colonized with *C. tropicalis* (11.2%) versus 14 of 700 (2%) colonized with *C. albicans* (P less than 0.001). The two groups of children with fungemia were similar in primary diagnoses (predominantly acute lymphoblastic leukemia) and in the frequency of several known risk factors for infection, including the duration of neutropenia (absolute neutrophil counts, less than 500/microliters). Patients with *C. tropicalis* fungemia all had disseminated disease compared with nine of 14 patients with *C. albicans* fungemia. Also, subcutaneous abscesses were unique to patients with *C. tropicalis* in this series. Two patients in each group died of their infection; central nervous system involvement was present in both fatal cases of *C. tropicalis* fungemia. A high index of suspicion and the early institution of appropriate antifungal therapy are critical to the successful management of these infections in patients with leukemia.

Prognostic importance of collateral flow and residual coronary stenosis of the myocardial infarct artery after anterior wall Q-wave acute myocardial infarction. Residual high-grade coronary stenosis and collateral flow are frequent findings in the chronic phase after a Q-wave acute myocardial infarction (AMI). The prognostic importance of a residual stenosis of the infarct artery and of collateral flow to the infarct area was analyzed in a group of 102 young patients (mean age 35 years, range 22 to 39) who had survived an anterior wall Q-wave AMI. Patients whose only significant lesion (greater than 50% luminal diameter reduction) was in the proximal portion of the left anterior descending artery were enrolled in the study. A 50 to 74% diameter stenosis was present in 33 of 102 patients (32%), 43 (42%) had a 75 to 99% stenosis and 26% had a total occlusion of the infarct vessel. Collateral vessels, which were evaluated by a scoring system, were present in 52 of 102 patients (51%). Four percent had only faint (score 1), 17 of 102 patients (17%) had moderate and 32 patients (31%) had good collateral flow (score greater than 4). The 8-year cumulative mortality was 15.2%—an eightfold increase compared with the age-matched general population. No patient with less than 75% stenosis died during follow-up, whereas the cumulative 8-year mortality was 23 and 17% in patients with a 75 to 99% stenosis or total occlusion, respectively (p less than 0.01). Patients with at least moderate collateral flow had a mortality rate of 21%, versus 8% for patients without or with faint collateral flow (p less than 0.05).

Late bleeding after rhytidectomy from injury to the superficial temporal vessels. Five healthy, normotensive women, whose mean age was 49.8 years, developed expanding hematomas between

8 and 10 days (average 9 days) after rhytidectomy. In each patient, the bleeding vessel could be identified: In two, it was the parietal branch of the superficial temporal artery; in two, it was the parietal branch of the superficial temporal vein; and in one, it was the superficial temporal artery immediately before its branching. Contributing factors may have been sudden physical exertion in four of the five patients and in another salicylate ingestion. Several measures can help avoid late bleeding from the superficial temporal vessels or their branches; not using a too potent vasoconstrictive agent (epinephrine) in the local anesthetic so that the vessels will be easier to visualize; not injecting the local anesthetic too deeply or incising too deeply; dividing and ligating the superficial temporal vessel and its major branches if injured; using bipolar coagulation on small branches; and instructing patients repeatedly not to engage in strenuous activity or to ingest salicylates for at least 2 weeks after operation.

Dietary fiber and bowel function in tube-fed patients. In tube-fed patients, dietary fiber is often used to manage constipation/diarrhea. Dietary fiber consists of water-soluble and insoluble plant compounds that are resistant to digestion by small-bowel enzymes but are fermented to varying degrees by colonic bacteria. Many physiologic effects of fiber may be related to the degree of fermentation. Few controlled studies of fiber-containing tube feedings have been performed. These studies have limitations and are nondefinitive as to whether fiber prevents or controls constipation/diarrhea. Constipation in tube-fed patients has not been shown to respond to mixed soluble/insoluble fiber in the few studies performed to date. Likewise, fiber may be of only limited benefit in controlling diarrhea in acute illness because of such factors as stress or medication. Fiber does play a role in maintaining gut integrity in all patients, whether they have diarrhea or not. Fiber may be recommended as part of a standard tube-feeding regimen to help assure gut mucosal integrity but not specifically to treat constipation/diarrhea. Further studies are necessary before the role of fiber in the management of constipation/diarrhea in tube-fed patients is determined.

Hepatosplenic candidiasis: successful treatment with fluconazole. **PURPOSE:** To determine if fluconazole is effective treatment for hepatosplenic candidiasis that has not resolved with amphotericin B and flucytosine treatment. **PATIENTS AND METHODS:** Six patients (ages 3 to 44) with acute leukemia and hepatosplenic candidiasis who did not respond to prior antifungal therapy were treated with fluconazole. **RESULTS:** All six patients had fever and three had nausea and vomiting; computed tomographic (CT) scan showed lucencies in the liver in six, lucencies in the spleen in five, and lucencies in the kidneys in three. Prior therapy with 1.6 to 4 g of amphotericin B in the five adults and 526 mg of amphotericin B in the child (with the addition of flucytosine in four) failed to improve clinical symptoms or lucencies in the liver, spleen, and kidneys seen on CT scan. Fluconazole was given at a dose of 200 to 400 mg daily (70 to 100 mg in the child) for 2 to 14 months. All patients had resolution of fever and other symptoms in 2 to 8 weeks. Improvement of the lesions noted on CT scan was seen in 4 to 8 weeks in all patients. Total resolution of lesions noted on CT scan occurred by 4 weeks in two patients, but took 4 to 5 months for three patients and 13 months for one patient. Three patients had relapse of their acute leukemia and two died, presumably cured of their candidiasis. Two patients underwent successful bone marrow transplantation without relapse of their candidiasis. **CONCLUSION:** Fluconazole appears to be useful in the treatment of hepatosplenic candidiasis that has not resolved with amphotericin B and flucytosine therapy.

Abnormal vascular responses to supine exercise in hypertrophic cardiomyopathy. **BACKGROUND.** Exercise hypotension has been documented in hypertrophic cardiomyopathy. It is not the result of an inability to augment cardiac output but instead relates to an inappropriate and exaggerated decrease in systemic vascular resistance at high work loads. **METHODS AND RESULTS.** To enable us to examine the behavior of the peripheral vasculature during exercise, 103 consecutive patients underwent

maximal symptom-limited supine bicycle exercise with measurement of forearm blood flow. A minimum reduction of 12% from the basal value was defined as a normal response based on the study of 25 normal controls. In the patients, two patterns of forearm blood flow were observed. Sixty-four patients had an appropriate reduction in forearm blood flow of $40 \pm 16\%$ from resting flow. In 39 patients, the forearm blood flow either failed to decrease or increased with exercise by $45 \pm 105\%$ of the resting value. Patients with an abnormal forearm vasodilator response were younger (31 ± 13 versus 46 ± 14 years), and more of them had a family history of hypertrophic cardiomyopathy and sudden death than did those with a normal vasoconstrictor response (16 of 39 versus eight of 64). Left ventricular end-diastolic cavity dimensions were smaller in those with an abnormal forearm blood flow response, but other clinical, echocardiographic, and arrhythmic variables were similar. To assess the relation of abnormal peripheral vascular responses to erect exercise blood pressure response, patients underwent treadmill exercise testing with careful monitoring of systolic blood pressure response. Thirty-eight patients had significant exercise hypotension with failure of the systolic blood pressure to increase during progressive exercise ($n = 6$) or an abrupt decrease in systolic blood pressure (20-60 mm Hg) from the peak value ($n = 32$); 65 patients had a normal exercise blood pressure response, but 18 of these patients had an oscillation in systolic blood pressure of 10 mm Hg or more early in the recovery phase. Thirty-one of 39 patients with an abnormal forearm blood flow response demonstrated exercise hypotension during the erect exercise testing, and the remaining eight patients had a normal exercise blood pressure response; however, five of these eight had abnormal oscillations in blood pressure during recovery ($r = 0.61$, p less than 0.001). CONCLUSIONS. The relation of abnormal peripheral vascular responses to exercise hypotension confirms the observation of hemodynamic instability in patients with hypertrophic cardiomyopathy. The finding of abnormal vascular responses in patients known to be at increased risk (young age and a family history of hypertrophic cardiomyopathy and sudden death) suggests that hemodynamic mechanisms may be important in the occurrence of sudden death in hypertrophic cardiomyopathy.

Surgical intensive care unit resource use in a specialty referral hospital: I. Predictors of early death and cost implications. The rationing of medical care prioritizes the need for early predictors of death in the surgical intensive care unit (SICU). We prospectively studied 100 consecutive SICU admissions, looking for predictors of early death in the SICU and the cost implications of these findings. Serial APACHE II scores on days 1, 3, and 5 were subjected to multinomial logistic regression analysis to determine significant predictors of death in the SICU on day 1. Survivors had significantly lower (p less than 0.05) mean day-1 APACHE II scores than had nonsurvivors (13.6 vs 22.1). Half of the patients with scores greater than 18 died, and all patients with scores on day 1 of 25 or greater died. Significant predictors of death on SICU day 1 were APACHE II scores, Acute Physiology Score, Glasgow Coma Score, creatinine level, and Chronic Health Evaluation Score. Forty-one patients had been transferred from community hospitals as a results of acute illness; this population accounted for two thirds of the deaths in the SICU. Ten of 18 nonsurvivors were predicted on day 1, with these patients incurring a total cost of approximately \$1 million. If therapy had been modified on days 5, 10, or 15, the potential cost savings would have been \$340,000, \$240,000, or \$140,000, respectively. Integration of the results of this study into the management decision-making process and treatment guidelines may reduce the cost of care in the SICU.

Aortoiliac dissection after percutaneous insertion of an intra-aortic balloon pump. Aortic or aortoiliac dissection may complicate percutaneous intra-aortic balloon pump insertion in various ways. Thrombosis can escape clinical recognition if no major obstruction develops. Death due to perforation after dissection is not uncommon. In this case study, aortoiliac dissection led to bilateral

iliac artery stenosis, an unusual complication of percutaneous femoral cannulation for insertion of a balloon pump.

Effects of heart rate and pulmonary artery pressure on Doppler pulmonary artery acceleration time in experimental acute pulmonary hypertension. Chronic pulmonary hypertension in humans is characterized by shortening of the pulmonary artery acceleration time as measured by Doppler echocardiography, such that the higher the pulmonary artery pressure, the shorter the pulmonary artery acceleration time. Increases in heart rate are also known to produce decreases in the pulmonary artery acceleration time. To explore the relationship between mean pulmonary artery pressure, heart rate, and Doppler pulmonary artery acceleration time, experimental acute pulmonary hypertension was created in nine Duroc swine, either by infusion of Sephadex beads with embolization of the pulmonary arterial circulation or by partially occluding the main pulmonary artery 8 to 10 cm distal to the pulmonic valve. Pulmonary artery Doppler flow velocity recordings and invasive pressure measurements were made at baseline and at paced atrial rates ranging from 60 to 160 beats per minute, in 20-beat increments. The results in this acute animal model reveal that increases in heart rate produced significant decreases in Doppler pulmonary artery acceleration time at mean pressures below 25 mm Hg. However, with mean pulmonary artery pressures greater than 25 mm Hg, both heart rate and increases in pulmonary artery pressure had no significant effect on acceleration time.

Hypo-fibrinolysis in patients with hypertension and elevated cholesterol. To test the hypothesis that increased blood pressure and hyperlipidaemia result in changes in the fibrinolytic system, 84 subjects with both hypertension and elevated serum cholesterol levels (the high risk group) were compared with 55 controls matched with respect to age, sex and body mass index (BMI). Plasminogen activator inhibitor (PAI-1), and tissue plasminogen activator (tPA) antigen and activity were measured before and after venous occlusion. In the high risk group, tPA activity was significantly lower both before and after venous occlusion and PAI-1 levels were significantly higher. In a multivariate analysis the triglyceride levels, diastolic blood pressure and cholesterol levels were independently associated with the PAI-1 levels. Diastolic blood pressure was independently and inversely associated with resting tPA activity. We conclude that patients with hypertension and hyperlipidaemia have a reduced activity of the fibrinolytic system, an effect which is unrelated to differences in age, sex, smoking or BMI.

Doppler ultrasound and the silent ductus arteriosus. A clinically undetectable, small ductus arteriosus was identified by Doppler ultrasonography in 21 individuals. Infants were excluded from the study and no patient had pulmonary hypertension. Persistence of the ductus arteriosus is likely to be more common than shown by less sensitive diagnostic methods. Some patients considered to have infective endocarditis with a normal heart may have a silent ductus arteriosus. Evidence of such an association would justify ligation or antibiotic cover as prophylactic measures.

Tears of the retinal pigment epithelium: occurrence in association with choroidal effusion. Two patients developed large tears of the retinal pigment epithelium associated with choroidal effusion. One tear occurred after combined cataract/filtration surgery complicated by postoperative choroidal detachment; the second developed in a patient with idiopathic uveal effusion syndrome. Weakness of the junctions of the pigment epithelial cells secondary to the accumulation of fluid in the subretinal or suprachoroidal space may result in tearing of the retinal pigment epithelium as it is stretched.

Cell kinetics of gastrointestinal tumors after different nutritional regimens. A preliminary report. Forty-four cases of different untreated gastrointestinal tumors were studied with regard to cell

kinetic activity. As a pilot experiment, we also determined the 3H-TdR Labeling Index (LI) in 28 patients in basal conditions and after 15 days of nutritional manipulation with prevalently lipid-based or glucose-based feeding to ascertain whether selective nutritional regimens could affect tumor proliferation. Preliminary results from this study indicate that a kinetic perturbation is induced in tumor cells by nutritional manipulation. Lipid-based feeding seems to produce effects similar to those of chemical or physical anticancer agents, thus suggesting a possible supporting role of nutritional manipulation in cancer treatment strategy.

HBV-DNA-related hepatocellular carcinoma occurring in childhood. Report of three cases. In a series of 325 HBV chronically infected children observed over an 18-year period, three developed HCC. These three children were born in southern Italy, a region characterized by a high endemic HBV infection rate; each had been infected perinatally, developed an acute hepatitis, and became a chronic carrier. Two of the three with cirrhosis were HBsAg positive at the time their HCC was detected. The remaining case had seroconverted to HBsAb but HBV-DNA integration could be demonstrated in the absence of cirrhosis; moreover HBV antigens were not expressed in the tissue of this case. The interval between HBV infection and HCC appearance in these three cases ranged from six to 11 years. A similarity between these three Italian cases and the majority of HCC arising in chronically infected children in the Far East is noted.

Localized recurrent postoperative pernio associated with leukocytoclastic vasculitis. A patient with recurrent pernio of the right ankle for 21 years after surgery had a leukocytoclastic vasculitis localized in the area. We suggest that the various histologic descriptions of pernio in the literature and in this case represent different levels of severity of the disease.

Intraoral reconstruction with a microvascular peritoneal flap. The microvascular peritoneal flap offers a new reconstructive option for closure of intraoral defects. The flap is easy to raise, and donor-site morbidity is low. Unlike fascial flaps, in which the raw surface may take weeks to "mucosalize," the peritoneal surface heals primarily. Finally, the rectus muscle effectively covers all forms of mandibular reconstruction, and the reliable skin paddle makes possible the closure of substantial cutaneous defects.

Interrelation of analgesia and uterine activity in women with primary dysmenorrhea. A preliminary report. The interrelation between uterine activity and pain from primary dysmenorrhea has been of interest for many years. Objective studies of uterine activity during non-steroidal antiinflammatory drug therapy have supported the assertion that uterine activity causes pain and that reducing that activity leads to pain reduction. Unfortunately, those studies could not refute the counter-assertion that reductions in uterine activity come about because of reduced pain through central analgesia and not by direct pharmacologic action. In an effort to clarify this question, a small number of women were studied using intrauterine pressure recording and analysis to evaluate objective changes in uterine physiology during transcutaneous electrical nerve stimulation (TENS) therapy for dysmenorrhea. The preliminary studies indicated that despite successful subjective therapy with TENS, intrauterine pressure parameters remained steady or showed signs of worsening. These findings indicate that TENS provides pure analgesia by an alteration of the body's ability to receive or perceive the pain signal rather than by a direct uterine effect. It appears that the reduction in uterine activity seen in objective drug studies represents direct drug action rather than a change from reduced pain through central analgesic effects.

Flow characteristics of enteral feeding with psyllium hydrophilic mucilloid added. One therapy for managing diarrhea in patients in intensive care units who are receiving enteral nutrition is administration of psyllium hydrophilic mucilloid (PHM). This laboratory study was conducted to

determine whether the addition of PHM (Metamucil) to enteral feeding formula (Entriton) adversely affected the flow characteristics of the feeding formula through a small-bore feeding tube. Descriptive data were obtained from 72 trials of feeding formula with varied infusion rates, formula osmolality and temperature, and PHM concentrations. Two thirds (n = 48) of the trials were successful (PHM did not clog the tubing and obstruct flow). The remaining one third of the trials (n = 24) were unsuccessful. Successful formula infusion was influenced by formula temperature and osmolality but not by infusion rate, PHM concentration, or flow interruption. If formula with PHM was followed by formula without PHM, the infusion was successful regardless of infusion rate or formula osmolality. Thus, the data from this laboratory study indicate that when therapeutic doses of PHM are prescribed, it is feasible for PHM to be mixed in room-temperature feeding formula and infused without clogging the feeding tube.

The role of growth hormone and insulin-like growth factor-I in experimental renal growth and scarring. Recent evidence suggests a causal link between early renal/glomerular hypertrophy and late kidney scarring and glomerular sclerosis. Insulin-like growth factor-I (IGF-I) is a growth-promoting peptide likely to play a role in the development of kidney growth. We observed an increased renal IGF-I content in two experimental models of accelerated kidney growth in the rat. By contrast, diabetic renal hypertrophy is abolished in the absence of growth hormone (GH). Dietary protein manipulations affect the expression of compensatory renal growth (CRG), as well as renal IGF-I content. The renotrophic effect of a high-protein diet on CRG seems GH-dependent and IGF-I-mediated. GH also appears to have a permissive role on the development of progressive renal scarring following extensive renal ablation in rats, as dwarf rats seem somewhat resistant to the development of accelerated scarring and renal failure.

Prognosis in T2N0M0 stage I breast carcinoma: a 20-year follow-up study. In a study of prognosis in node-negative breast carcinoma, we investigated 293 T2N0M0 patients treated by mastectomy and axillary dissection with a median follow-up of 19.8 years. The probability of surviving 20 years considering all causes of death was 41.3% +/- 3.0%. Recurrence-free survival (Kaplan-Meier estimate) was 68.6% +/- 3% at 10 years and 63.2% +/- 3.1% at 20 years. The estimated probability of cure determined by the method of Brinkley and Haybittle was 63% (95% confidence interval [CI], 55% to 72%). Prognosis was related to primary tumor size with the best separation (P = .06) when tumors from 2.1 to 3.0 cm (33% chance of recurrence at 20 years) and from 3.1 to 5.0 cm (44% chance of recurrence at 20 years) were compared. The histologic tumor type was prognostically important. Recurrence at 20 years was not significantly different for patients with invasive duct (34%) and lobular (42%) carcinoma. Women with special types (medullary, mucinous, papillary, etc) of carcinoma had a 25% chance of recurrence. Subsequent contralateral breast carcinoma was diagnosed in 29 patients, and four of these were fatal, accounting for only 4.6% of breast carcinoma deaths. Thirty-two patients (10.9%) developed a nonmammary malignant neoplasm (NMMN) after the ipsilateral breast carcinoma, and 69% of these lesions were fatal. Although the chances of recurrence at 20 years related to tumor size and type did not differ statistically in the series, there were trends that suggest that T2N0M0 patients can be stratified into recurrence risk groups based on tumor size and histologic type. These factors should be taken into consideration in the design and analysis of clinical adjuvant therapy trials. Measures for the early detection of common NMMNs should be included in the routine follow-up of T2N0M0 breast carcinoma patients.

Serum endothelin-1 concentrations and cold provocation in primary Raynaud's phenomenon To determine whether the vasoconstriction in Raynaud's phenomenon is associated with raised concentrations of the endothelium-derived vasoconstrictor endothelin (ET-1), responses to cold pressor testing were examined in 7 subjects with primary Raynaud's phenomenon and in 7 control

subjects. Baseline serum ET-1 levels (pg/ml), as measured by radioimmunoassay, were three times higher in Raynaud's subjects (5.3 [SEM 1.7] pg/ml) than in controls (1.7 [0.3]). With progressive local cooling digital arterial pulsatility, as measured by plethysmography, fell earlier and to a greater extent in Raynaud's subjects than in controls, with a half-maximum decrement in pulsatility occurring at 27 [2.6] degrees C and 18 [0.5] degrees C, respectively. Temperature reduction sufficient to cause loss of pulsatility in the Raynaud's subjects produced increases in ET-1 concentrations in both groups that were greater in Raynaud's (10.3 [4.4] pg/ml) than in control subjects (2.7 [0.9] pg/ml). Serum ET-1 in the contralateral arm rose in parallel to but to a lesser extent than that in the cold-challenged arm. Increases in ET-1 concentrations were temporally related to loss of pulsatility but followed the onset of symptoms. Thus the increased basal and stimulated serum endothelin concentrations in Raynaud's disease are associated with the enhanced, prolonged vasospasm of this disorder.

Embolization of arteriovenous malformations with peripheral aneurysms using ethylene vinyl alcohol copolymer. Report of three cases. The authors report three cases of arteriovenous malformations (AVM's) with aneurysms arising from the feeding artery; all were successfully treated with a new nonadhesive liquid embolic material, ethylene vinyl alcohol copolymer (EVAL). In two patients the AVM's were totally removed without difficulty, and in one the AVM was managed conservatively after embolization. No new neurological deficits appeared during or after embolization. After road-mapping techniques, EVAL was injected slowly until the feeding artery and aneurysm were completely obliterated. This embolic agent is easy to handle and is considered safe compared with other adhesive liquid embolic agents, such as isobutyl-2-cyanoacrylate or n-butyl cyanoacrylate. It is concluded that EVAL is an excellent agent for embolizing an AVM with a peripheral aneurysm on the feeding artery.

Duodenal obstruction by a nondeflating Foley catheter gastrostomy tube. We report the case of a 36-year-old mentally retarded man who presented to our emergency department after one day of vomiting and one episode of coffee-ground emesis. The Foley catheter used as his gastrostomy tube was found to be obstructing the duodenum, and the balloon could not be deflated. Removal was accomplished by rupturing the balloon by endoscopy. Our case illustrates one of many possible complications of feeding gastrostomy tubes.

Soft tissue sarcomas of the chest wall. Results of surgical resection. Primary soft tissue sarcomas of the chest wall are uncommon, and data concerning treatment and results are sparse. Most studies have categorized these tumors as truncal sarcomas and inferred a poor prognosis. To assess the results of surgical treatment, we reviewed our 40-year experience. Methods: Records of 189 patients admitted to our institution from 1948 to 1988 were reviewed. Pathologic material was available for review in the 149 cases (79%) that comprise this report. Survival was calculated by the Kaplan-Meier method, with comparisons by log-rank analysis and significance defined as p less than 0.05. Results: Ages ranged from 3 weeks to 86 years (median, 38 years); the ratio of male to female patients was 2:1. The initial complaint was mass or pain in 97% of the cases. Ninety sarcomas (60%) were high grade and 59 (40%) were low grade. Histologic types were as follows: desmoid tumor (n = 32, 21%); liposarcoma (n = 23, 15%); rhabdomyosarcoma (n = 18, 12%); fibrosarcoma (n = 17, 11%); embryonal rhabdomyosarcoma (n = 14, 9%); malignant peripheral nerve tumor (n = 13, 9%); malignant fibrous histiocytoma (n = 11, 7%); spindle cell sarcoma (n = 4, 3%); tenosynovial sarcoma (n = 3, 3%); hemangiopericytoma (n = 3, 3%); alveolar soft part sarcoma (n = 3, 3%); and other types (n = 12, 9%). Resection was the primary treatment in 140 cases (94%). Local recurrence developed in 27%. Metastases occurred in 52 (35%) of the cases (metachronous in 42, synchronous in 10) and were more common in patients with high-grade disease (46/90, 51%) than in those with low-grade disease (6/59, 10%). Overall 5-year survival was 66%. Five-year survival rate for those with high-grade

sarcomas (49%) was significantly lower than that for low-grade sarcomas (90%, p less than 0.0001). Tumor size and age of patient were not prognostic. Conclusions: Survival of patients with primary soft tissue sarcomas of the chest wall after resection is similar to that of patients with sarcomas of the extremities. Resection alone provides acceptable survival (90% at 5 years) for those with low-grade sarcomas, but adjuvant treatment should be considered for those with high-grade sarcomas.

Cephalometric measurements in snorers, non-snorers, and patients with sleep apnoea. Cephalometry is often used to assess patients with sleep apnoea but whether these measurements differ from those in non-apnoeic snorers and how they are influenced by age is not clear. Cephalometric radiographs of patients with sleep apnoea were compared with those of snorers without sleep apnoea and those of non-snorers. Fifty two snorers with suspected sleep apnoea had a conventional sleep study and were divided into two groups: those with an apnoea-hypopnoea index greater than 10/h ($n = 40$, sleep apnoea group) and those whose apnoea-hypopnoea index was 10/h or less ($n = 12$, snorer group). The cephalometric measurements in these patients were compared with those of 34 non-snoring control subjects. Controls were subdivided into two groups: control group 1 included 17 subjects similar in age to the sleep apnoea and snorer groups (mean (SD) age 50.0 (10.9), 50.7 (9.4), and 50.6 (9.7) years); control group 2 included 15 young men (25.4 (2.6) years). The distance from the mandibular plane to the hyoid bone (MP-H) and the length of the soft palate were greater in the patients with sleep apnoea (28.7 (7.8) and 43.6 (5.0) mm) than in the snorers (23.7 (4.2) and 40.3 (4.9) mm). The MP-H was similar in snorers and age matched control subjects, but was significantly greater in the older than in the younger control subjects (22.1 (6.1) vs 17.0 (6.8)). The soft palate was longer in subjects who snored (both sleep apnoea patients and snorers) than in control subjects. The MP-H distance significantly correlated with age for all subjects (snorers and controls) and for the control subjects alone. This study shows that non-apnoeic snorers have cephalometric abnormalities that differ from those of patients with sleep apnoea and that cephalometric values are influenced by the subject's age.

Intravascular stents in the management of superior vena cava syndrome. Superior vena cava syndrome can be effectively palliated with the use of intravascular stents. Adjunctive modalities which may be utilized prior to stent placement are thrombolytic therapy and balloon angioplasty. Six patients with an underlying malignancy were treated with these modalities. Complete resolution of symptoms occurred in five patients, and partial resolution occurred in the sixth. Two of the patients who had initial, complete resolution of symptoms had recurrences. One involved rethrombosis of the superior vena cava which occurred twice and required percutaneous thrombectomy, and the second involved restenosis requiring a percutaneous transluminal angioplasty of the SVC just distal to the stent. Both of these patients with second procedures, again, had complete resolution of symptoms. Intravascular stents are a valuable additional treatment of superior vena cava syndrome.

Chemicals and environmentally caused diseases in developing countries. This chapter discusses international aspects of diseases resulting from exposure to chemical pollutants in the environment, with an emphasis on developing countries. These countries share many of the same problems of air, water, and pesticide pollution that face the more industrialized countries. In developing countries, however, the problems are compounded by a number of unique situations, viz., economic priorities, high burden of infectious diseases, impoverishment, and absence of a regulatory framework for the disposal of toxic chemicals. This discussion emphasizes the importance of interactions among toxicants, malnutrition, and infectious diseases for both urban and rural populations insofar as these interactions contribute to disease. Toxicants not only produce disease directly but also exacerbate diseases with other causes. Specific examples from developing countries demonstrate how human health effects from exposures to environmental chemicals can be assessed. While they do not strictly

fall under the rubric of "developing countries," the public health consequences of inadequate control of environmental pollution in the East European countries should demonstrate the magnitude of the problem, except that in developing countries the public health consequence of environmental chemicals will be aggravated by the widespread malnutrition and high prevalence of infectious diseases. Much needs to be done before we can adequately quantify the contribution of environmental chemicals to morbidity and mortality in developing countries with the level of sophistication now evident in the charting of infectious diseases in these countries.

Acute spinal cord injury: magnetic resonance imaging correlated with myelopathy. Thirty-one patients (29 males and two females, 13-87 years of age (mean, 46.7 years) with acute spinal cord injury were studied by MR (magnetic resonance) imaging and the results were correlated with neurological findings. Magnetic resonance images were obtained with a 0.5 T superconductive MR scanner (Phillips Gyroscan S5). Initial imaging was performed within 24 hours after trauma in 13 patients, 1-7 days in 13 patients and 7-14 days in five patients. Twenty-six patients underwent follow-up examinations with MR imaging. Cord abnormalities including cord compression (23 patients), cord swelling (seven patients), and abnormal signal intensities on either T1 or T2-weighted images (26 patients) were observed on initial examination. Multivariate analysis showed that cord compression and abnormal intensities on T1-weighted images were important prognostic indicators. Hyperintensity on T2-weighted images was non-specific but correlated well with clinical recovery. Magnetic resonance imaging is useful in predicting the prognosis and for planning treatment following spinal cord injuries.

Can vitamin D deficiency produce an unusual pain syndrome? An unusual pain occurred in five patients in the presence of compromised vitamin D status and resolved 5 to 7 days after supplementation with vitamin D in the form of ergocalciferol. The pain had a hyperesthetic quality and did not respond to the use of analgesics, including opiate derivatives. Treatment with therapeutic levels of a tricyclic antidepressant did not bring relief of symptoms. In one case, months after treatment and subsequent improvement of vitamin D status and pain, the vitamin D status again declined and the pain recurred. The pain again resolved with vitamin D replacement and improvement of levels. There may be a pain syndrome associated with vitamin D depletion that appears as hyperesthesia worsened by light, superficial pressure or even small increments of movement. This pain restricts mobility and function and may lead to further complications, such as pressure sores.

Operations for Wolff-Parkinson-White syndrome. Forty-six patients with symptomatic tachycardia underwent operations to divide 55 atrioventricular accessory pathways. Mean age was 29 years (range 11 to 63). Ten patients (22%) had associated cardiac disease, including two with a congenital diverticulum of the coronary sinus and six (13%) who had concomitant surgical procedures. A bipolar hand-held electrode