MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Concept of Early Diagnosis in Strokes. R. G. Siekert and C. H. Millikan. A.M.A. Arch. Int. Med. 101:872-880 (May) 1958 [Chicago].

Focal cerebral ischemia or infarction (commonly referred to as thrombosis) accounts for some 80% of all strokes. In the absence of specific measures for the prevention of cerebral atherosclerosis, attention need be drawn to means that can be utilized to anticipate and thereby possibly prevent the occurrence of selected varieties of strokes. Three syndromes are delineated: the syndrome of intermittent insufficiency of the vertebral-basilar arterial system; the syndrome of thrombosis within the basilar arterial system; and the syndrome of intermittent insufficiency of the internal carotid arterial system. Illustrating case histories are presented with each of these 3 syndromes. The syndrome of intermittent insufficiency of the vertebral-basilar arterial system consists of sharply episodic attacks of visual dimness, weakness of the limbs (monoparesis, hemiparesis, quadriparesis), dysarthria, dysphagia, diplopia, confusion, and vertigo in various combinations. Between attacks the patient is well. During an attack, neurological abnormalities are present. A single episode may suggest the diagnosis if it includes most or all of these symptoms. Usually, however, a single episode is a fragment of the whole, and one can only suspect the diagnosis. It is when a group of these episodes occurs over weeks or months with the inclusion of most of the above-mentioned symptoms that one can be more certain of the diagnosis. Careful study need be made to determine that intermittent vascular insufficiency is the fundamental factor involved, rather than some other cause, such as an expanding intracranial mass or epilepsy.

The neurological signs noted in the second syndrome when thrombosis with the basilar artery is in the process of occurring or has actually occurred include the following: weakness of the limbs, often with extensor spasms; pseudobulbar or bulbar weakness in the form of dysarthria and dysphagia with a weakened pharynx and palate and slowness and decreased protrusion of the tongue; ocular abnormalities, particularly in the pupils, where inequality, miosis, and nonreaction may be seen, or in the extraocular muscles, which are weakened in various combinations; homonymous hemianopsia, which may be bilateral; and facial weakness, either "central" or "peripheral" in type. The last, with contralateral hemiparesis, usually indicates involvement of the brain stem. Hyperpyrexia is common.

The syndrome of intermittent insufficiency of the internal carotid arterial system consists of attacks of unilateral impairment of motor or sensory function or both. With involvement of the artery to the dominant hemisphere, aphasic disorders may be seen. Decrease in vision or blindness in only 1 eye (amaurosis fugax), and that on the side of the involved artery, will be seen in some instances. While the degree of involvement will vary, the complexity is not as great as in vertebral-basilar insufficiency. Here, too, a single attack may in no way be diagnostic, but a group of attacks may permit one to make the diagnosis. With early recognition of these types of cerebrovascular disease, treatment may be instituted prior to the possible occurrence of extensive cerebral infarction. Treatment with anticoagulant drugs may prevent the continuation of these ischemic attacks and, therefore, also the possible occurrence of a catastrophic infarction.

The Fate of the Patients with Persistent Cavitation and Noninfectious Sputum ("Open-Negative") After Discharge from the Hospital. R. F. Corpe and F. A. Blalock. Am. Rev. Tuberc. 77:764-777 (May) 1958 [New York].

This report presents the preliminary experience of the authors with so-called "open healing" of tuberculosis cavities and with patients who have acquired a noninfectious status despite persistent cavitation under drug therapy. Between July 1, 1953, and Dec. 31, 1956, 159 patients with cavitary disease, sputum negative for tubercle bacilli, and pulmonary lesions stable on roentgenography were discharged from Battey State Hospital, Rome, Ga., and continued on drug therapy. On the basis of follow-up studies on these patients, the authors reached the following conclusions: It is safe to dis-

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charge patients with the "open-negative" syndrome to their home environment without creating a public health problem. The mortality rate in this group of patients was 3.8%, but these deaths occurred in patients who had not had bacteriological or roentgenologic relapse. They were not treatment failures. The reactivation rate was 8.8%. There were no additional reported bouts of suppuration or hemorrhage. There has been no discernible difference, up to the present time, in the reactivation rate between the Negro and the white race. The male sex has not fared as well as the female sex, 13 of the 14 reactivations occurring in men.

Only 2% of the patients were confined to their homes because of their physical disabilities. If such people can be adequately cared for in a home situation, they are much happier, and it is cheaper to maintain them on drugs outside the hospital than as inpatients. A considerable number of these people, even with cavitary disease, if given the opportunity, with public health clearance as to noninfectiousness, can become self-supporting and again take their place in society. Forty-five per cent of the patients had unlimited activity, and more than 25% were found to be working full time. The authors feel that these observations somewhat counterbalance their earlier belief that these cavities should be removed surgically or collapsed by thoracoplasty prior to the time when the patients could hope to return to their families and earn a living. Long-term follow-up observations on patients in this category are of extreme importance, since there are many unanswered questions, such as: How long should a patient with the "open-negative" syndrome be continued on drug therapy? This must be individualized, but a considerable number of these people should be continued on drug therapy indefinitely. On the other hand, among the group of 38 patients whose drug therapy had been stopped, there have been no reactivations to date.

Heart Failure of the Hunchback. T. Hanley, M. M. Plattis, M. Clifton and T. L. Morris. Quart. J. Med. **27**:155-171 (April) 1958 [Oxford, England].

This paper deals with 24 persons with severe hunchback. Ten of these patients had severe kyphoscoliosis and heart failure. The clinical features, arterial blood-gas values, and pulmonary function of these 10 patients were compared with those obtained in the 14 persons who had severe spinal curvature but had not suffered from heart failure. It was found that severe kyphoscoliosis may reduce the total lung capacity and the vital capacity to as little as one-quarter of normal. The diminutive lungs are, however, ventilated with an efficiency only a little less than normal, and emphysema is usually slight. The diagnosis of kyphoscoliotic heart disease did not present great difficulty. In kyphoscoliotic heart failure peripheral vascular signs were predominant, and the clinical picture closely resembled that of anoxic cor pulmonale due to emphysema.

Reduced arterial oxygen saturation and retention of carbon dioxide were found in 8 of the 9 patients with true kyphoscoliotic heart disease, but these changes were present in only 2 of the 14 patients without heart failure. It was not possible to make such a clear distinction, simply by measuring either the volumes of the various compartments of the lungs or the efficiency of ventilation, between those with and those without a history of heart failure. Cardiac catheterization was done in 3 patients; it showed a moderate rise of the pulmonary artery blood pressure in 2 anoxic patients who had recovered from heart failure and a small rise in 1 patient who had not had heart failure.

Clinical and Microbiological Aspects of Salmonellosis. G. M. Eisenberg, L. Brodsky, W. Weiss and H. F. Flippin. Am. J. M. Sc. **235**:497-509 (May) 1958 [Philadelphia].

In a previous report on 95 patients with salmonellosis seen during 1947-1952 at the Philadelphia General Hospital, it was pointed out that diagnosis on clinical grounds alone was frequently hazardous in view of the protean nature of the clinical manifestations. The practical importance of employing diagnostic antigens capable of demonstrating serum antibodies resulting from infections induced by Salmonella organisms, other than the classical typhoid-paratyphoid strains, was illustrated. Information on an additional 75 cases of bacteriologically proved Salmonella infections during the period from January, 1953, to June, 1957, was obtained subsequently from a review of records at the same institution, and it is these data which form the subject matter of the present report. The current study includes results of antibiotic susceptibility tests on cultures of the various Salmonella serotypes. Of the 75 patients comprising the study group, 40 were adults and 35 were infants and children.

Fever and diarrhea were encountered most frequently in both pediatric and adult patients, diarrhea being more common in the former. The proportion of patients with fever and the occurrence of vomiting was about the same in both groups. The over-all mortality rate was 20%; however, if the estimation of mortality is based only on those cases in which death was unquestionably attributable to the salmonellosis, the fatality rate is reduced to 5.3%. Fatalities occurred among infants and older debilitated individuals. In contrast to the experience in the 1947-1952 series, in which most of the deaths were associated with infection by Salmonella organisms of serogroup C, mortality in the present study was associated with strains be-

longing to serogroup B. Evidence is presented to support the view that any of the several clinical syndromes may be produced by the same or different Salmonella serotypes. The length of time that these organisms continue to be shed in the stools after apparent clinical cure of the patient is variable. Where such information could be obtained, this interval has ranged from 10 to 604 days, with an average of 127 days. In vitro antibiotic susceptibility testing of the 62 salmonellas isolated from patients revealed them to be uniformly sensitive to chloramphenicol. About one-half of the strains were susceptible to the tetracyclines, streptomycin being quite ineffective. No relationship between serotype and antibiotic susceptibility could be detected. Despite the in vitro superiority of chloramphenicol, its clinical use, either alone or concomitantly with other agents, exerted little, if any, influence upon the fatality rate.

The Treatment of Eosinophilic Lung (Tropical Eosinophilia) with Diethylcarbamazine. T. J. Danaraj. Quart. J. Med. **27**:243-263 (April) 1958 [Oxford, England].

Earlier the author had demonstrated the efficacy of organic arsenicals in eosinophilic lung. The use of organic arsenicals, however, is associated with definite risks, so that a search was made for some form of treatment as effective but not toxic. Groups of patients were treated with various drugs—sulfathiazole, bismuth, penicillin, Achromycin, cortisone, piperazine citrate, and diethylcarbamazine—but only diethylcarbamazine was found to be of value. As diethylcarbamazine is known to be effective in the treatment of filariasis, it was important to exclude this disease. There was no evidence suggestive of past or present filarial infection in any of the 110 patients analyzed in this report. The duration of illness when they were first seen was variable, the shortest period being 1 week, and the longest 4 years; in the majority of the patients (97) it was under 6 months. The initial complaint was cough, which was most frequent and severe at night, occurring in paroxysms of a few minutes and productive of slight mucoid or mucopurulent sputum, which was sometimes streaked with blood; sleep was badly disturbed. A feeling of suffocation and breathlessness was usually present after each bout of coughing, and at times was severe enough to resembled bronchial asthma. The severity of symptoms was considered to be slight (cough only) in 9 patients, moderately severe (cough with breathlessness) in 75, severe (bronchial spasm) in 25, and very severe (status asthmaticus) in 1 patient. Occasional bouts of low fever, lasting for a few days, were noted in 24 cases. No history of allergy was obtainable, except in 1 patient, who suffered from attacks of urticaria. A family history of bronchial asthma was given by 6 patients. Abnormal physical signs, which were confined to the chest, were present in 88 patients and consisted of coarse crepitations and rhonchi heard over the bases of the lungs, together with bronchial spasm in 26 patients. In nearly all the patients radiologic examination of the chest revealed increased striations, with varying degrees of mottling.

The dosage of diethylcarbamazine given initially to 46 patients was that generally recommended in the treatment of ascariasis: 4 mg. per kilogram of body weight given 3 times daily for 4 days. Later, 2 larger dosages were tried: 6 mg. and 10 mg. per kilogram of body weight given thrice daily for 5 days to groups of 57 and 7 patients respectively. The average total adult dose for each of the 3 dosage schedules was 3,200 mg., 6,000 mg., and 10,000 mg. respectively. The drug was given after meals in the form of 50-mg. tablets, the sirup being used for children. Except for 11 patients who exhibited severe bronchial spasm and were treated with antispasmodics as well, the patients were given only diethylcarbamazine. The drug proved to be safe and effective in the 110 patients with eosinophilic lung. It had no effect on patients suffering from other diseases with eosinophilia. The results obtained compared favorably with those obtained with organic arsenicals. Diethylcarbamazine should replace the organic arsenicals, because the latter sometimes result in encephalopathy and death in a disease which, although incapacitating, has no mortality in itself.

Hypogammaglobulinaemia and Tuberculosis: Implications of Their Association, and Other Observations. R. Parkes. Brit. M. J. **1**:973-976 (April 26) 1958 [London].

The author reports on a 22-year-old unmarried woman who from the age of 4 years had recurrent colds and from the age of 5 years had typical grand mal epilepsy. Pulmonary tuberculosis occurred at the age of 19 years, for which the patient was treated with streptomycin and isoniazid. The tuberculous upper-lobe consolidation in the right lung, which was present on admission to hospital, resolved over a period of 6 months. Bronchograms obtained 2 years after the institution of the antimicrobial therapy showed moderately severe "saccular" bronchiectasis of the anterior and apical segment of the upper lobe of the right lung. Otherwise the bronchial tree appeared entirely normal. Two years after tuberculosis was detected, acquired hypogammaglobulinemia was diagnosed on the basis of the history of continued bacterial infection, gamma-globulin deficiency on paper electrophoresis, zinc sulfate turbidity test, fractional precipitation, and absence of isohemagglutinins. Gamma-globulin replacement therapy was instituted with 0.5 Gm. per kilogram of body weight in 1 week as a loading dose, followed by 0.025 Gm.

per kilogram of body weight per week for 4 months. The patient was given 0.5 Gm. of gamma-globulin per kilogram of body weight per week for an additional 4-month period. She also was given methoin and phenobarbital in small daily doses as anticonvulsants. After 6 months' replacement of gamma-globulin, its serum level had increased more than threefold. Fewer grand mal seizures occurred, and petit mal attacks were rarely observed. Electroencephalograms were impressively better. Despite this striking improvement, there was no apparent connection between hypogammaglobulinemia and epilepsy. The patient was animated and cheerful, when previously she had been dull and lethargic. Respiratory infections and frequent inexplicable low-grade fever no longer occurred.

The patient's history suggested the presence of hypogammaglobulinemia 5 years at least before pulmonary tuberculosis developed, and tuberculosis was known to have been present for 2 years before gamma-globulin therapy was instituted. The association of hypogammaglobulinemia and tuberculosis is probably coincidental, and they bear no cause-and-effect relationship to one another. The natural course of tuberculous disease appears to be unaffected by hypogammaglobulinemia. Both delayed hypersensitivity and serum antibody response to tuberculosis appear to function normally in patients with hypogammaglobulinemia, so that in normal persons the 2 phenomena may be independent of gamma-globulin and may be to a large extent related to a cell mechanism (leukocytes and other body cells), although the possibility of an unidentified serum protein fraction sharing such immunological powers is not excluded.

Hypertension and Diabetes Mellitus. P. Freedman, R. Moulton and A. G. Spencer. Quart. J. Med. 27:293-305 (April) 1948 [Oxford, England].

The blood pressure was measured in 1,100 patients attending a diabetic clinic, and the data were analyzed in terms of the incidence of hypertension in each age and sex group. Hypertension was common in both sexes, and the incidence steadily increased with age to a maximum of 92% of the female and 81% of the male diabetics at 70 to 79 years. A strong clinical impression was gained that hypertension was more common in diabetics than in a general hospital population. Statistical analysis, however, clearly showed that this difference is largely a false impression due to the abnormal age and sex distribution of the diabetic population. From 10 to 69 years of age, in both sexes, there was no significant difference in the incidence of hypertension in diabetics as compared with a nondiabetic population. It was only at 70 to 79 years that high blood pressure was distinctly more common in diabetics.

Severe hypertension (diastolic pressure over 125 mm. Hg) is rare in diabetes, the incidence being 0.5% in the male and 1.4% in the female subjects, which is less than in a general hospital population. Advanced hypertensive retinopathy, excluding diabetic retinopathies, was not seen in any of the diabetic subjects, except in those with pheochromocytoma. Data are given on the apparent incidence of hypertension due to various renal and endocrine disorders in diabetes. Diabetic nephropathies were diagnosed in 27.5% of the patients whose diastolic blood pressure was over 100 mm. Hg. The arm circumference was measured in all the hypertensive diabetic subjects and was found to be an important factor in determining the level of the blood pressure in 26.5% of these patients.

SURGERY

Acute and Chronic Thrombosis of the Mesenteric Arteries Associated with Malabsorption: A Report of Two Cases Successfully Treated by Thromboendarterectomy. R. S. Shaw and E. P. Maynard. New England J. Med. 258:874-878 (May 1) 1958 [Boston].

The authors report on 2 men, aged 54 and 58 years, respectively, with occlusion of the superior mesenteric artery resulting in intestinal ischemia associated with malabsorption. The first patient had been admitted to hospital because of progressive bilateral intermittent claudication. Aortography showed a narrowed aortic bifurcation and complete occlusion of the right external iliac artery. The patient was operated on, and an aortic homograft was sutured end-to-side to the abdominal aorta, the right limb of the graft being anastomosed end-to-side to the common femoral artery and the left to the popliteal artery. On the third postoperative day the patient had abdominal cramps and passed a liquid stool containing occult blood. The abdomen remained nontender until the 16th postoperative day, when suddenly severe generalized abdominal pain occurred and peristalsis disappeared. At reexploration 9 hours later the entire small and large intestines from the ligament of Treitz through the midsigmoid appeared pale and cyanotic. There were no pulsations in the celiac axis, in any of its 3 major branches, or in the superior mesenteric artery and its branches. A pancreatic necrosis was observed, which appeared to be of at least 1 week's duration. The superior mesenteric artery was opened through a longitudinal incision and was found to be occluded by a brownish thrombus and atheroma in its proximal 2 cm. A proximal thromboendarterectomy was performed through this arteriotomy with resultant excellent flow from the aorta. An amazing recovery of the small intestine resulted, while the large intestine

remained cyanotic. A loop transverse colostomy was performed, so that the circulation of the colon could be observed in the postoperative period. Localized signs of peritonitis developed on the second day, and exploration was again carried out. The colon remaining within the abdomen was obviously viable, although there were 2 or 3 small necrotic areas in the wall of the defunctioned transverse colon. These were surgically patched with tabs of fat. The appendix was necrotic, and appendectomy was performed. Colostomy diarrhea and abundant drainage from the wounds, with the occasional casting out of a piece of pancreatic slough, continued for several weeks. The stools were found to contain increased amounts of fat. One month after the operation studies of intestinal absorption were performed, which showed a considerable defect in the absorption of fat, sugars, and vitamin B_{12}, with improvement during the 4-week period of observation. The patient was discharged 2 months after the thromboendarterectomy; he gained weight, was free from gastrointestinal symptoms on an unrestricted diet, and resumed full-time work.

These observations suggested that atherosclerotic occlusive disease in the arteries of the abdominal viscera may behave as it does in the brain, heart, and extremities, progressing more rapidly than collateral circulatory development and producing a picture of malabsorption, intermittent abdominal gain, and weight loss terminating in acute intestinal infarction. This was the sequence of events which occurred in the second patient in whom absorption studies were performed before and after the surgical correction of chronic intestinal ischemia and in whom the diagnosis was established preoperatively by aortography. Although major arterial branches to the abdominal viscera other than the superior mesenteric artery were involved with occlusive disease, restoration of continuity in the superior mesenteric artery alone was sufficient to provide symptomatic relief of ischemia. Since the absorptive functions of the intestine may be assumed to be dependent on its blood supply, it is not surprising that impairment of this supply should be accompanied by malabsorption. The diagnosis should be considered in certain patients with unexplained malabsorptive states, and thromboendarterectomy may represent an effective therapy in these patients, as well as in those in whom mesenteric vascular thrombosis results in intestinal infarction.

Lung Resection in Tuberculosis. I. S. Kolesnikov. Vestnik. khir. **80**:3-10 (March) 1957 (In Russian) [Leningrad].

Kolesnikov reports on 1,000 pulmonary resections performed for pulmonary tuberculosis in Leningrad during the past 5 years. The indications for elective resections were strict. The majority of the patients operated on had far advanced fibrocavernous tuberculosis. The sputums of all the patients were positive for tubercle bacilli. The patients selected for resection were those that showed no improvement from other methods, including collapse therapy. Pneumonectomy was performed on 23.3%, bilateral lobectomy on 4.6%, lobectomy on 30.6%, segmental resection on 28%, and various other types of resections on 13.5%. Endotracheal potentiated ether-oxygen anesthesia was used in 950 cases. Fifty patients were operated on under local anesthesia. The author stresses the desirability of resecting as little as possible of the lung. He does not rule out the employment of pulmonary collapse and of cavernostomy, each of these operations having its own indications. A closer contact between surgeons and internists should bring about earlier transference of patients to the surgeon and in that way should diminish the number of mutilating operations, such as pneumonectomy and bilateral lobectomy, and at the same time should increase the number of segmental resections.

Segmental Occlusion of the Femoral Artery and Femoral and Popliteal Aneurysms: Surgical Aspects. D. A. Felder and T. O. Murphy. Minnesota Med. **41**:322-326 (May) 1958 [St. Paul].

The authors used autogenous and homogenous veins, crimped braided nylon tubes, and compressed Ivalon sponge tubes for iliac-femoral arterial shunts or replacements in 24 patients and for femoral-popliteal arterial shunts or replacements in 73 patients. In the group of 24 patients, successful vein grafts existed more than 2 years in 7 of the 8 patients in whom they were used; the nylon tubes used at this level in 5 patients remained open for from 3 to 12 months. Of the compressed Ivalon prostheses used in the remaining 11 patients, 6 failed; the successful Ivalon sponge grafts were all patent over 14 months. In the group of 73 patients, vein grafts were used in 37, nylon tubes in 32, and Ivalon sponge prostheses in 4. Successful vein grafts existed 5 to 24 months after surgical treatment in 29 of the 37 patients. Sixteen of 32 nylon tube shunts were still open 3 to 12 months after the operation. The compressed Ivalon prostheses failed in all 4 patients in whom they were used. Thus, the most satisfactory results in patients with long segmental occlusions in the iliac-femoral and femoral-popliteal areas were obtained with the use of autogenous saphenous veins and braided nylon tubes, both as shunts and as replacements.

Of 20 patients with popliteal aneurysms, 11 underwent lumbar sympathectomy with subsequent resection of the aneurysm in 3, 1 had a simple resection of the aneurysm, and in 8 primary resection with autogenous vein grafting was attempted after sympathectomy. Sympathectomy followed by im-

mediate resection appeared to be the most satisfactory method of treatment for the symptomatic or asymptomatic popliteal aneurysm. In 4 of the 8 patients in whom attempts at replacement with autogenous vein grafts were made, encouraging results were obtained in that these patients have functionally good extremities without claudication.

Short segment thromboendarterectomies were performed in 5 patients with acute arterial occlusions. Two of these were due to embolism and 2 to thrombosis. One of the 5 patients died within 24 hours after the operation, and autopsy revealed multiple emboli in the renal, splenic, and cerebral vessels. Another patient required a saphenous vein graft of the common femoral artery, since the remaining vessel after endarterectomy was too friable to hold sutures. This patient is well, with good peripheral pulses, 30 months after the operation. The remaining 3 patients had patent vessels on follow-up examination 3 months to 1 year after the operation. For short segments, and particularly in cases of acute occlusion, either by embolism or spontaneous thrombosis in severely sclerotic femoral arteries, endarterectomy is definitely necessary for a successful result.

Lung Resection in Tuberculosis. A. M. Dyhno. Vestnik. khir. 8:10-16 (March) 1958 (In Russian) [Leningrad].

The author reports on 127 patients with fibrocavernous tuberculosis who were operated on. There were 5 pneumonectomies, 72 lobectomies, and 50 segmental resections. The onset of the disease dated from 1½ to 14 years. All the patients were treated preoperatively with antibiotics, artificial pneumothorax, and sanatorium rest. There were 8.8% postoperative deaths, the cause being shock in 4 patients, hemorrhage in 2, and empyema in 2. The postoperative course was complicated in 4.9% by a bronchial fistula and in 12.7% by empyema.

Surgical Methods of Treatment of Tuberculosis of Children and Adolescents. M. L. Shulutko. Vestnik khir. 80:16-23 (March) 1958 (In Russian) [Leningrad].

Cavernous types of tuberculosis of children and adolescents give unfavorable prognosis when treated conservatively. The introduction of streptomycin and of other chemical therapeutic substances has not solved the problem. Surgical methods are beginning to play an important role in the complex treatment of children and adolescents with cavernous pulmonary tuberculosis. An analysis of 131 patients operated on gave a postoperative mortality of 3%; there was empyema in 2.3% and bronchial fistula in 3.8%. Follow-up revealed deaths from tuberculous process on the operative side in 2 patients. The remaining 120 patients (91.6%) are practically well and free from tubercle bacilli. Attention is called to the fact that the mediastinum in children and adolescents has considerable mobility. The author therefore advocates introduction of a pneumothorax 3 to 5 days before the operation. This results in gradual replacement of the mediastinum and in giving the general organism an opportunity to adapt itself to new conditions. Pulmonary resection is indicated for the following conditions: (1) in the presence of multiple cavities of the lung; (2) in patients with marked fibrosis surrounding a pulmonary cavity; (3) in the presence of tuberculous lesions and bronchiectasis; (4) in patients with bronchial stenosis; (5) in the presence of diffuse lobar infiltration after preliminary but ineffective antibacterial therapy; (6) in cases of caseation of the lung; (7) after prolonged but ineffective pneumothorax; and (8) after ineffective thoracoplasty, extrapleural pneumothorax, and oleothorax; employment in these patients of thoracoplastic procedures and of extrapleural pneumothorax is seldom successful. One of the peculiarities of the course of tuberculosis in children and adolescents is bilateral involvement. Of the 441 children treated in the author's clinic, 45 to 50% presented bilateral involvement. They were treated by artificial pneumothorax of one side and operative resection of the other side. The important problem in the treatment of bilateral tuberculosis is the maximal sparing of healthy tissue. This is best accomplished by a sparing bilateral resection.

Aneurysms of the Thoracic Aorta. F. H. Ellis Jr. Minnesota Med. 41:335-338 (May) 1958 [St. Paul].

The author reports on 24 patients, between the ages of 5 and 73 years, with aneurysms of the thoracic aorta which were arteriosclerotic in 10, syphilitic in 5, traumatic in 4, congenital in 2, mycotic in 2, and dissecting in 1. Resection of the lesion was done with the aid of hypothermia in 18 of the 24 patients. The main cause of inoperability was the location of the aneurysm in either the ascending aorta or its proximal arch. Grafts were used in 17 of the 18 patients on whom resection was done. Homografts were used in 14 patients, an Ivalon sponge graft in 2, and a crimped nylon tube in 1. Hypothermia was used as a means of avoiding ischemia of the spinal cord during cross clamping of the aorta. By reduction of the arterial oxygen requirement of the central nervous system, a safe period of aortic occlusion up to 1 hour is permitted. Six patients died in the first week after the operation. Hemorrhage, complications of hypothermia, or both accounted for most of the deaths. In only 1 patient were neurological signs and symptoms recognized in the postoperative period. Three other

patients died later, and death resulted from hemorrhage in all. Aneurysm of the thoracic aorta is a serious threat to health and life, and its surgical removal should be considered seriously despite the high mortality rate.

Clinical Importance of Traumatic Fat Embolism. H. Kühne and K. H. Kremser. Beitr. klin. Chir. **195**:385-394 (No. 4) 1957 (In German) [Munich, Germany].

Autopsies in 643 fatal traffic accidents during the years from 1954 to 1956 revealed fat embolism of the lungs in 95%; it was massive in 59%, and the systemic circulation was involved in 23%. Since autopsy findings indicate the terminal status and do not permit deductions regarding clinical conditions, the authors investigated the presence of air embolism in patients with comminuted and open fractures, in those with traumatic décollement, and in those subjected to fracture nailing. One hundred fifteen of a total of 2,956 patients with such injuries died, and whereas fat embolism was found in all of those who died, the clinical diagnosis of fat embolism was made during life in only 7 of the patients whose histories are presented. Five of these 7 patients had sustained severe traffic accidents, and the other 2 had fallen from great heights. They had sustained multiple fractures. In 1 case extensive décollement was associated with a pelvic fracture and fractures of the leg and femur.

All the patients were conscious on admission to hospital, but they were in shock. After measures were taken to counteract the shock, 6 patients responded with rapid recovery, but 5 died after intervals of from 1 to 4 days with signs of respiratory insufficiency. Case 7 is of particular interest, because pulmonary as well as cerebral symptoms indicated extensive fat embolization, but the patient apparently was able to cope with these emboli, because at the time of his discharge he was free from all neurological disturbances. The severe shock existing in all patients decided the therapeutic measures. Only 1 of the patients (case 7) could be given specific therapy in the form of dehydrocholic acid (Decholin) and eupaverin, whereas in the others death occurred so rapidly that there was no time for such treatment. In the further discussion of fat embolism, the authors consider not only the cases reported but also literature reports.

Cavernous Hemangiomas, "Cavernomas" of Liver. F. Niemann and W. Penitschka. Beitr. klin. Chir. **195**:257-277 (No. 3) 1957 (In German) [Munich, Germany].

The authors report on a 44-year-old woman with cavernoma of the liver who was operated on at the surgical clinic of the University in Bonn, Germany. She had severe epigastric pain during the 7 months before surgical intervention and had lost a considerable amount of weight. Roentgenologic examination of the gastrointestinal tract, heart, lungs, and urogenital tract did not reveal any abnormality. Laparotomy revealed a partly nodulated and partly smooth tumor, the size of the head of a child, which partly adhered to the parietal peritoneum; it occupied the entire left epigastrium up to the umbilicus and was connected with the liver. There was a distinct border line between the diseased and the normal tissue of the liver. The left enlarged lobe of the liver which was entirely occupied by the tumor was resected. Microscopic examination of the surgical specimen revealed a typical cavernoma. The course of healing was delayed for 8 weeks by a seropurulent secretion which originated in a cavity below the left costal arch at the border of bone and cartilage, suggesting a cartilaginous necrosis. The patient was discharged in excellent general condition 10 weeks after the operation. She had gained 5 kg. (11 lb.).

One hundred two additional cases of surgically removed cavernoma of the liver were collected from the literature. Thirteen (12%) of these tumors had perforated. The primary mortality rate among patients operated on was 11%. The best operative results were obtained with the radical extirpation of the tumor, whether the tumor had ruptured or not. Despite the fact that hemostasis was frequently difficult, only 2.5% of the patients undergoing resection died, as compared with 90% of those in whom only tamponade was used for a perforating cavernoma. In 7 patients the size of the tumor decreased as a result of roentgenotherapy, injections promoting sclerosis, or galvanocautery. Late results of surgical treatment were reported in 16 of the 102 patients with cavernoma of the liver who were followed for 2 to 10 years; all of them were in good health and completely free of complaints. True recurrences were not reported.

A Further Description of the Pathologic Physiology of Congenital Megacolon and the Results of Surgical Treatment. R. B. Hiatt. Pediatrics **21**:825-831 (May) 1958 [Springfield, Ill.].

The author reports follow-up results of 63 patients who were operated on for congenital megacolon at the Columbia-Presbyterian Medical Center, New York, between 1947 and 1955. There were 5 deaths, 3 of which occurred in infants whose age at the time of the operation was less than 12 months and were due to severe enterocolitis occurring from 3 months to 1 year after the operation. The 4th early postoperative death occurred also in an infant less than 12 months of age, and was due to acute aspiration in the nursery. The 5th death occurred in a child whose age at the time of operation was 18 months and who died at 3 years of age of acute

membranous colitis. The 58 surviving patients had undergone a "pull-through" procedure, consisting of a surgical intussusception of the entire rectum and the lower two-thirds of the sigmoid through the anus, with replacement by more proximal colon and with an end-to-end anastomosis of the anus and sigmoid in one stage. Twenty-nine (50%) of these patients were completely continent immediately after the operation or within 1 year after the operation; 20 patients (34%) became completely continent within 2 to 5 years after the operation; and in 9 patients (16%) fecal staining or actual incontinence is still a persistent problem after many years. Careful observation of these 9 patients with imperfect anal control revealed that enterocolitis and psychological maladjustment are the 2 prominent factors which contribute to this difficulty.

In congenital megacolon one is dealing with a slowly progressive disease as a result of gradual development of hypertrophy in the proximal portion of the aganglionic segment of the colon; this hypertrophy in time increases the degree of obstruction, because its response to the constant physiological stimulus of feces occurs in the form of nonpropulsive spasm. This hypothesis explains why good initial results may be obtained from a segmental resection of the transitional segment, since, although only a part of the aganglionic segment is removed, the hypertrophied portion which is responsible for most of the obstructive element is removed. This initial good result, however, can only be temporary, since obstruction is bound to occur when hypertrophy develops again in the remaining achalasic segment. The replacement of the rectum and the lower sigmoid by proximal colon in patients with congenital megacolon has proved successful, as manifested by the long-term follow-up study.

NEUROLOGY & PSYCHIATRY

Barbiturate Narcomania as Problem in Medical Department with Resident Psychiatrist. E. Kåss, N. Retterstøl and T. B. Sirnes. Tidsskr. norske lægefor. 78:341-345 (April 15) 1958 (In Norwegian) [Oslo].

Of 3,750 patients admitted to a medical department with a resident psychiatrist during a 2-year period, 63 were drug addicts. Sixty patients (40 men, 20 women) were addicted to barbiturates alone or combined with other narcotics, 44 of them being admitted because of acute intoxication. In more than half of the cases there was also chronic alcoholism. Fifteen patients had had long-term treatment with narcotics prescribed for illness. In the remaining patients the main cause of the addiction was attributed to personality deficiency. More than half of the patients were without work. Abundant amounts of vitamins B and C were given, often combined with insulin in small doses. Some patients were also given ataraxics (chlorpromazine, reserpine, meprobamate). In general, treatment of narcomania cannot be carried out well in a medical department, where the treatment of somatic symptoms is important. The patients were prepared by the psychiatrist to be motivated, if possible, for a long-term treatment in psychiatric institutions. There are no possibilities for narcomaniacs unwilling to be treated. The prognosis for permanent recovery in established narcomania is unfavorable. Greater weight should be put on prophylaxis.

Primary Amyloidosis with Special Reference to Involvement of the Nervous System. R. A. Chambers, W. E. Medd and H. Spencer. Quart. J. Med. 27:207-226 (April) 1958 [Oxford, England].

Primary amyloidosis has been divided into cases in which there is 1 localized tumor and those in which the deposits are more generalized. The present paper describes 6 patients with the generalized forms, 3 of whom initially presented neurological problems. Various aspects of amyloidosis are discussed on the basis of these case histories and of literature reports. Approximately two-thirds of all cases occur in men, and the clinical form is partly related to age, neuropathy occurring relatively early and cardiac myopathy relatively late. The clinical picture varies but frequently shows the gradual onset without fever or toxemia, in adult life, of impaired function of the myocardium, kidneys, or peripheral nerves. The illness is progressive despite treatment and, if the heart or kidneys are involved, leads to death in a few years. The polyneuritis affects first and most severely the longest fibers. The symptoms are predominantly sensory, and usually the first symptom is pain, often lightning pains. The motor signs are those common to all types of chronic polyneuritis and may be of any severity. The characteristic sensory abnormality is diminished appreciation of temperature and pain. The ankle jerks, and later the other tendon reflexes, are lost, but they may be present when symptoms and cutaneous sensory signs are advanced. Additional clinical features include diarrhea, impotence, vitreous opacities, abnormal pupils, and thickened peripheral nerves.

That the diagnosis of amyloid neuropathy is difficult is demonstrated by the fact that chronic tonsillitis, dermatitis artefacta, hysteria, malingering, disseminated sclerosis, spinal tumor, tabes dorsalis, and leprosy were the diagnoses considered in the 3 patients who initially presented neurological problems. Amyloid polyneuritis may mimic tabes, but this diagnosis should be doubted if the motor symptoms are symmetrical and sphincter symptoms are absent. Examination of the blood and cerebrospinal fluid may be necessary. If leprosy

is likely, the social consequences make biopsy essential. Sensory radicular neuropathy is similar in many respects, including the family history and, sometimes, diarrhea and abnormal pupils, but wasting and weakness and enlarged peripheral nerves, all characteristic of amyloid polyneuropathy, are usually absent. Serum protein examination, the Congo red test, and biopsy are valuable diagnostic aids. Serum protein changes include diminished total protein, diminished albumin, and increased globulin values and the fiinding on electrophoresis of an abnormal protein, which may appear in the urine, in the region of the a_2—β globulin bands. In five of the 6 reported patients the total protein content and the albumin content were reduced or at the lower limit of normal. The Congo red test was performed for 3 of the patients. The result was positive in case 3, equivocal in case 1, and negative in case 6; the authors accepted 90% retention of dye in 1 hour as positive. The result probably depends on the amount of amyloid and its affinity for Congo red, and, although a negative result is of no significance, falsely positive results are rare. The authors conclude that amyloidosis, whether primary or secondary, is a single disease process, with variations in distribution determined by such factors as inheritance, age, and sepsis.

Tuberous Sclerosis: Case Report. H. Mavor and G. A. Schumacher. J. Maine M. A. 49:179-182 (May) 1958 [Brunswick].

The patient, a 37-year-old woman, was admitted to the neurology service of the DeGoesbriand Memorial Hospital in Burlington, Vt., on July 16, 1957, in status epilepticus. The history obtained on admission was meager. The patient apparently had had intermittent convulsive seizures for many years and had been treated with Dilantin capsules. This medication had been omitted for 2 days prior to admission. The onset of repetitive seizures occurred approximately 1 to 2 hours prior to admission. When first seen the patient was having successive focal and generalized convulsive seizures, consisting of tonic and clonic movements of the right upper and lower extremities, with occasional spread to the left, associated with apnea and cyanosis and followed by hyperpnea, coma, and widely dilated, unreactive pupils. The seizures were controlled with a total of 910 mg. of phenobarbital sodium given intravenously in divided doses over a 2-hour period. The presence of facial skin lesions resembling adenoma sebaceum, convulsions, and the deteriorated state implying mental retardation suggested a diagnosis of tuberous sclerosis. Hints of a familial incidence were obtained in that the patient's son suffered from "spells" and had never been able to attend school.

Tuberous sclerosis or epiloia, one of several recognized neurocutaneous syndromes, has as its outstanding manifestation the triad of convulsive seizures, mental deficiency, and skin lesions. Over 450 cases have been reported. In hospitals and colonies for the epileptic, the incidence among new admissions appears to be approximately 1 in 200. The disorder is congenital, and strong heredofamilial tendencies are present. Two major hypotheses are (1) that it is a disorder of prenatal development, i. e., of embryogenesis (blastomatous in origin), and (2) that it is actually a slowly progressive neoplastic process. One view has held that tuberous sclerosis and neurofibromatosis are similar, the former a central, the latter a peripheral neurospongioblastosis. Attention is usually called to the disease by the occurrence of convulsive seizures of both the major generalized type and the minor petit mal variety early in life. The coexistence with convulsions of mental deficiency and the characteristic butterfly distribution of small skin nodules, spreading from the nose over the cheeks and usually also involving chin and forehead, is sufficient to make the diagnosis. The brain in epiloia reveals grossly firm white nodules at the surface as well as deep in the cortex. Similar foci appear in the subcortical white matter. Tumor nodules may project into the ventricular cavities. Less often, nodules are also found in the basal ganglions, brain stem, and cerebellum. No specific therapy for the basic disease process is available. The usual anticonvulsants are employed to counteract seizure activity.

Is Cortisone Contraindicated in the Acute Phase of Polioencephalitis? R. De Mattia and F. Di Nola. Minerva med. 49:1183-1187 (March 31) 1958 (In Italian) [Turin, Italy].

The authors believe that cortisone may be used effectively in the management of acute polioencephalitis when the functional blockage can be ascribed to the compressive action of edema and is thus at least partially reversible. Cortisone was given to 8 patients with polioencephalitis in 6 of whom the disease was accompanied by tetraplegia and by paralysis of the bladder muscles. Paralysis of respiratory and of swallowing muscles affected 2 patients, and paralysis of respiratory muscles alone affected 2. Cortisone was given parenterally to all patients, 3 of whom received it in a single dose in combination with hydrocortisone (25 mg.) by the intrathecal route. Total dosage of 450 to 900 mg. of cortisone was administered in decreasing divided daily dosages, from 200 mg. in the beginning to 100 mg. at the termination of treatment, for a period of 4 to 6 days. Six of 8 patients survived with fair chances of functional restoration. The results were good, although they may be only partially attributed to the effect of cortisone.

GYNECOLOGY & OBSTETRICS

Intra-Aortic Transfusion: Discussion of Technic and Report of Five Cases. H. L. Riva, J. L. Breen, R. P. Hatch and W. L. Pickhardt. Obst. & Gynec. 11:537-542 (May) 1958 [New York].

Five women, between the ages of 28 and 43 years, 2 with spontaneous rupture of the uterus associated with intrauterine pregnancy, 2 with ruptured ectopic pregnancy, and 1 with carcinoma of the uterine cervix, who underwent abdominal surgery, were in severe shock and responded inadequately to intravenous transfusion of blood. The abdominal aorta then was used as a site for transfusion. By displacing the intestinal tract onto the abdominal wall, rather than packing it, time was saved and better exposure of the aorta was obtained. The transfusion was carried out with an angulated aortic needle, which was inserted just above the bifurcation of the aorta. Exposure of the aorta was performed by vertically splitting the posterior peritoneum to allow better exposure for placing the needle and for repair of the vessel, if the need should arise, thus avoiding concealed retroperitoneal hemorrhage. Hemorrhage was controlled by clamping either the aorta or the common iliac arteries with vascular clamps.

Intra-aortic transfusion of about 500 cc. of blood brought about a rapid change in all the patients, with complete stabilization of blood pressure occurring within 5 to 20 minutes. In addition, the immediate perfusion of the coronary and cerebral vessels was of great importance at the time of intra-aortic transfusion. Intra-aortic transfusion was accomplished in each patient within several minutes. The danger of air emboli was avoided by discontinuing the transfusion just before its completion. In none of the patients was it necessary to repair the aorta after the transfusion, and no retroperitoneal hematomas were observed. There was no morbidity or mortality in this small group of patients. The aorta at the time of abdominal surgery is easily accessible for transfusion and has many advantages over other arterial vessels. Intra-aortic transfusion is simple and requires a minimum of equipment. It is of unquestionable value in many cases in which death from hemorrhage seemes inevitable.

Mumps Mastitis in the Nursing Female, with a Case Report. R. J. Weaver and T. Neal Petry. J. Indiana M. A. 51:644-648 (May) 1958 [Indianapolis].

A 28-year-old woman was first seen on March 11, 1956, complaining of swelling and tenderness of her right jaw for 1 day. She was the mother of 3 children, 2 of whom had had mumps 2 weeks before, and the third and youngest was a nursing infant of 11 weeks. She returned 8 days later because her baby had "choked" while nursing. She said that 3 days after the previous visit her breasts had become very tender and swollen, but not hot. In a few days lactation decreased, and the physician thought this accounted for the infant's choking. At the second visit her left parotid was swollen, and she was ordered to cease nursing the child. The administration of stilbestrol, 0.1 mg. daily, was started, and 3 days later lactation had ceased, with caking of the breasts absent 6 days later. The infant was followed closely but manifested no signs or symptoms of mumps.

Although mumps mastitis is a recognized complication of epidemic parotitis, it has been reported rarely. The authors found reports of only 2 other cases, and only 1 of them concerned a nursing mother. Neither the infant of this patient nor the infant of the nursing mother cited had signs of mumps. The immunity existing in infants up to 6 or 8 months of age is generally considered passive immunity from the transfer of maternal antibodies across the placenta. The mothers were not immune in these 2 instances, and presumably the maternal circulation carried no antibodies. Therefore, the mechanism of the immunity displayed by the infants is apparently different. An alternate possibility is that the infants had subclinical mumps. The authors suggest that serologic tests be done on apparently well infants whose mothers have the disease, and that observations be made and reported as to whether nursing mothers with mumps mastitis can nurse after subsequent pregnancies.

Testosterone Pellet Implants for Advanced Breast Carcinomatosis in the Female: Preliminary Report. C. P. Lamar and P. R. Rezek. J. Am. Geriatrics Soc. 6:397-404 (May) 1958 [Baltimore].

The authors report on clinical and pathological observations made during a 10-year period at the Jackson Memorial Hospital, Miami, Fla., on 100 women who were treated by subcutaneous implants of testosterone pellets for palliation of advanced and otherwise intractable breast carcinomatosis. Testosterone (pure crystalline) compressed pellets (75 mg. each) were implanted, 10 at a time, into the subcutaneous fat through a special trocar. Implants were made at weekly intervals for 6 or more times. Then they were spaced farther apart—up to twice a year in a patient who survived for more than 8 years, and 3 to 6 times a year in other patients who survived for periods ranging from 3 to 6 years. Implants of pure testosterone have the advantage of more prolonged effect and less frequent administration than intramuscular injections of testosterone esters. Masculinizing changes seemed to be less conspicuous than with other forms of less intense androgenic therapy. Edema was minimal, and there was no hypercalcemia. In 2 patients

tetanic muscular contractions were relieved by parenteral administration of calcium. As a rule, serum levels of protein, calcium, phosphorus, and alkaline and acid phosphatase remained within normal limits. Exacerbations of neoplastic activity were accompanied occasionally by a transient increase in the serum levels of alkaline and acid phosphatase, and more frequently by an increase in serum protein-bound iodine concentration and radioactive iodine uptake by the thyroid gland along with decreased glucose tolerance. Subjective responses were good in more than 90% of the patients, as manifested by reduction or even suppression of severe pain, production of euphoria, and gain in appetite, weight, and strength. The duration of remissions was variable, averaging 28 months, with a range of 8 weeks to more than 8 years.

The cases of 3 of the 100 patients are described to illustrate some gross and histological changes observed and the relatively low incidence of masculinizing changes. In a patient whose remission has persisted for more than 8 years, mammary biopsy was performed both before and after a radical mastectomy 3 years after onset of therapy. There was gross reduction in the size of the primary breast tumor and lymph nodes, but the histological picture showed no changes. In another patient impressive histological changes took place after androgenic therapy; there was remarkable new epithelization of all ulcerated areas with distinct healing and shrinkage of all lesions. Sex chromatin was observed in some of the tumor cells both before and after treatment; and again at autopsy, after hypophysectomy, sex chromatin was found in the skin, adrenal cortex, and tumor tissue.

Tuberculosis of the Endometrium: A Report on 250 Cases with the Results of Drug Treatment. A. M. Sutherland. Obst. & Gynec. 11:527-536 (May) 1958 [New York].

Two hundred fifty women, between the ages of 16 and 53 years, with endometrial tuberculosis, were treated at the David Elder Infirmary in Glasgow during the past 7 years. Twenty-eight patients were unmarried, and only 29 gave a history of previous pregnancy. A history of definite or possible extragenital tuberculosis was obtained from 137 of the 250 patients. The interval between the earlier tuberculous manifestations and the discovery of the endometrial infection varied widely but was 5 or more years in most of the patients. Principal symptoms consisted of infertility in 104 patients, abdominal pain in 54, profuse and sometimes irregular bleeding in 41, amenorrhea in 25, and vaginal discharge in 12. Fourteen patients had no complaints. Chest roentgenograms revealed unsuspected active pulmonary lesions in 8 and healed pulmonary lesions in 103. Cervical biopsy revealed unsuspected cervical tuberculosis in 4 patients. A provisional diagnosis of endometrial tuberculosis was based initially on the histological findings in the curettings in most patients. Bacteriological proof was sought in 229, and a positive result was obtained in 170. In 132 of the latter patients, the tubercle bacilli were of the human type. Antituberculous agents were given to 242 patients. Streptomycin and aminosalicylic acid (PAS) were given for 84 days to 152 patients. Of these, 102 (67%) had a persistently negative endometrium after an average follow-up period of 25 months, 32 (21%) had recurrences of the endometrial infection, and 18 were lost to follow-up. Streptomycin and isoniazid were given for 84 days to 69 patients. Fifty-nine patients remained negative after an average follow-up period of 16 months. Recurrences were observed in 6 patients in the second and the third year after treatment. Four patients were lost to follow-up. Aminosalicylic acid and isoniazid were given to 19 patients for 6 to 12 months. It is still too early to compare the results obtained with those in the other groups. Two patients were treated with isoniazid alone, but the use of a single drug is undesirable and this method was abandoned. Recurrences occurred in 40 of the 242 patients, and 22 of the 40 patients were cured after a second course of drug therapy, the average time of follow-up being 22 months. Toxic drug reactions, such as vestibular disturbances, skin rashes, and gastrointestinal disturbances, occurred in 35 (14%) of the 242 patients, requiring discontinuation of therapy in all these patients.

From a consideration of the results of treatment obtained in these patients, it appears that the results obtained are better than those observed in control patients. It is too early to assess the value of streptomycin and aminosalicylic acid as compared with that of streptomycin and isoniazid, although the results to date suggest that the latter combination is at least as effective as the other and is less likely to be associated with toxic drug reactions. The occurrence of major drug reactions in 35 patients is disturbing. Although a few control patients did become negative without chemotherapy, the reported data show that it is not justifiable to withhold treatment from any patient with proved endometrial tuberculosis. Most of the controls remained positive at follow-up, and an appreciable number showed clinical deterioration in the course of the control year and required immediate treatment. In contrast to that, most of the treated patients have been cured of their principal complaints, apart from those with infertility. A continued follow-up of the patients will show whether these conclusions should be modified in the light of further experience.

Postclimacteric and Menopausal Hemorrhages. G. F. Winter, R. Häntsch and P. Rotter-Pool. Ztschr. Geburtsh. u. Gynäk. **150**:19-28. (No. 1) 1958 (In German) [Stuttgart, Germany].

The authors regard as the postclimacteric phase the period between the last menstruation and the definite menopause, defining the onset of the latter as 3 years after the last menstruation. They admit that the definition of these 2 concepts varies in the literature, and since they wanted to compare their findings with those of other clinics, they limit the postclimacteric period in this study to 2 years after the last menstruation. They investigated the postclimacteric and menopausal hemorrhages of patients treated at the University Women's Clinic in Berlin during the 5 years from 1950 to 1954 inclusive. A total of 1,623 patients were involved. It was found that 57.5% of the postclimacteric and menopausal hemorrhages were due to malignant lesions, whereas the average in the world literature is 53.7 or 55.2%. Malignant lesions were the cause of 35% of the genital hemorrhages during the postclimacteric and of 60% of those during the menopausal period, whereas in sexually mature women, up to the age of 45, a total of 15% of the nonmenstrual hemorrhages were due to malignancies. Cervical carcinoma was found to cause 66%, carcinoma of the body of the uterus 22%, and carcinoma of the ovary 5.7% of all the postclimacteric and menopausal hemorrhages that were due to malignant causes.

Studies on the incidence of hemorrhage in the presence of ovarian tumors revealed that 34% were accompanied by hemorrhage, or abut 1 in 3. An ovarian tumor was found, on the average, in 1 woman in 17 with postclimacteric or postmenopausal hemorrhages. Cervical polyps were the most numerous among the nonmalignant lesions responsible for genital hemorrhages, accounting for 16.2% of the postclimacteric or menopausal hemorrhages traceable to benign causes. One of 3 "benign" postclimacteric hemorrhages originated in the endometrium under hormonal stimulus, whereas only 1 in 9 of the menopausal hemorrhages was due to this cause. In 40% of all the women with bleeding from a hormonally activated endometrium, the history revealed treatment with estrogens. The percentage was even higher (50%) when the women were questioned regarding the use of hormone ointments and creams. Myoma, which together with glandular hypertrophy is the most frequent cause of hemorrhages during the climacteric, plays only a subordinate role in this respect during the postclimacteric period and during the menopause, accounting for 6.2% of benign and for 2.6% of all hemorrhages.

PEDIATRICS

Serum Oxaloacetic Transaminase Activity in Acute Rheumatic Fever: Values in Cases With and Without Salicylate Therapy. R. W. Massie and M. Stahlman. A. M. A. J. Dis. Child. **95**:469-476 (May) 1958 [Chicago].

Eighteen patients with acute rheumatic fever were studied over long periods with serial determinations of serum glutamic oxaloacetic transaminase (SGOT) activity, C-reactive protein (CRP), antistreptolysin-O (ASO) titer, and erythrocyte sedimentation rate (ESR). SGOT activity was elevated in some patients with acute rheumatic fever. These elevations were inconstant, however, and equally ill patients sometimes showed no elevation. Elevated values of SGOT occurred only in the patients with active rheumatic carditis. Rheumatic carditis was frequently not accompanied by elevation in SGOT. A single determination of SGOT activity was of little value in diagnosing acute rheumatic fever or in following the course of the disease. Some values that were not above the "upper limit of normal" were demonstrated to be significantly elevated when serial determinations were performed. A rise and fall in SGOT values were often well correlated with ESR, CRP, and ASO-titer determinations as well as with the clinical status of the patient. Administration of acetylsalicylic acid did not affect SGOT activity in the absence of active rheumatic carditis. The effect of salicylates on SGOT activity in the presence of active rheumatic carditis was uncertain, and inconstant results were obtained in several patients.

Bilateral Choanal Atresia, a Surgical Emergency in the Newborn. R. C. Morrow. J. Maine M. A. **49**:135-136 (April) 1958 [Brunswick].

Some cases of neonatal asphyxia are due to undetected bilateral congenital atresia of the posterior nares. The author presents observations on 4 infants with bilateral atresia observed at the Mary Fletcher Hospital in Burlington, Vt., and reviews the recent literature on this problem. The fact that the 4 cases were observed in 3 years suggests that this defect cannot be regarded as rare. The persistence of the nasobuccal membrane, which normally ruptures in the 7th week of fetal life, is the most widely accepted embryologic mechanism of this anomaly. The newborn infant is often unable to survive nasal obstruction, as though it were not instinctively aware of the simple expedient of breathing through the mouth. The clinical picture is that of obstructed breathing, with the varying degrees of intermittent success in getting a little air through the mouth. Usually the infant can be kept breathing by any expedient which serves to

hold the mouth open and the tongue down and forward. Feeding is difficult, because sucking, swallowing, and breathing cannot be carried on simultaneously. Even infants who can achieve mouth breathing are in danger of death by starvation. Once the condition is suspected, the diagnosis can be clarified by attempting to pass catheters through the nasal cavities into the pharynx, and by obtaining x-ray films with the instillation of contrast media into the nostrils.

Every breath of the infant should be supervised until adequate surgical relief is achieved. The mouth can be kept open by means of a small oral airway of the type used in anesthesia. The surgical management is early penetration of the choanal obstruction. Three of the 4 newborn infants with bilateral choanal atresia observed by the author were operated on, on the 1st, 2nd and 16th day of life respectively. The 4th infant had, in addition, multiple anomalies of the heart and great vessels and died on its 9th day. The choanal problem was recognized, and, by constant nursing attention, oral breathing and adequate feeding were being maintained, while corrective surgery was to have been done had the infant survived its cardiac anomalies a few more days. The 3 infants responded well to prompt operation in the newborn stage, followed by a program of periodic dilatations and the intermittent use of polyethylene breathing tubes. The possibility of bilateral choanal atresia should be thought of in threatened neonatal asphyxia.

Acute Cerebellar Ataxia of Childhood: Report of 9 Cases. G. King, G. A. Schwarz and H. W. Slade. Pediatrics **21**:731-745 (May) 1958 [Springfield, Ill.].

The authors report on 6 boys, between the ages of 2½ and 11 years, and on 3 girls, between the ages of 17 months and 3 years, with acute cerebellar ataxia. The neurological sign of most clinical significance was the ataxic gait. This occurred in varying degrees of severity in 8 of the children. Truncal ataxia, action tremor, and dysmetria were also frequently noted, but nystagmus, hypotonia, and hyporeflexia were infrequently observed. Choreiform movements and hemiparesis with hyperreflexia occurred in a few patients and indicated that the pathological process was not limited to the cerebellum in these patients. Fever was present in 5 patients. Seven of the patients had some degree of disturbance of personality and state of consciousness as part of the illness. The most pressing diagnostic problems presented were the degree of increased intracranial pressure and the possibility of a neoplasm of the posterior fossa. Changes of the optic nerve heads in 4 patients and bilateral early evidence of papilledema in 2 were suggestive of increased intracranial pressure. The indications were such that ventricular tap and ventriculography were performed in 5 of the 9 patients; in none of them was the intraventricular pressure increased. Five patients made a complete recovery. Residual disturbances in behavior were observed in 4 children: there was simple retardation in 1 and a schizoid personality change requiring institutionalization in another; in the remaining 2, only mild apathy and irritability at school were reported. The causation was not determined in any of the 9 patients. The children were quite healthy when the acute ataxia began, and none of them had a history of head trauma or preceding infection. Four of the patients had the onset of their illness in the months from January through March, and 5 in the months from August to October; these findings might suggest that these cerebellar disorders of childhood are due to different seasonally prominent pathogens.

Similar cases were collected from the literature, which had been recorded as "acute cerebellar encephalitis" or "acute cerebellar ataxia," a form of nonsuppurative encephalitis. The concept is proposed that these cases represent a toxi-infectious process of variable causation with the cerebellum or its systems as the major or only target organ. The main significance of these relatively benign forms of cerebellar disorder in children is their differentiation from cerebellar tumor. In the cerebellar medulloblastoma, the course is inevitably progressive with increasing papilledema or hydrocephalus. In acute idiopathic cerebellar disorders, the papilledema does not increase; there is usually no progression of signs, and in several weeks the signs begin to recede. A careful, watchful waiting would seem to be the best procedure in such cases, but ventricular tap and ventriculography may be the methods of choice in settling the diagnostic problem finally.

Multiple Sclerosis in Children: A Clinical Study of 40 Cases with Onset in Childhood. J. C. Gall, A. B. Hayles, R. G. Siekert and H. M. Keith. Pediatrics **21**:703-709 (May) 1958 [Springfield, Ill.].

The authors studied 26 girls and 14 boys with disease of the central nervous system, characterized by several attacks of neurological dysfunction and disseminated lesions, with onset in childhood and clinically typical of multiple sclerosis. In 8 of the 40 patients who were admitted to the Mayo Clinic between 1920 and 1952, the age at the onset of the disease was 10 years or less, and in the remaining 32 it was between 11 and 14 years. The disease as it occurred in these children did not appear to differ clinically from the disease as observed in adults, in respect to mode of onset, symptoms, physical findings, and changes in the cerebrospinal fluid. In contrast, however, to the equal occurrence of multiple sclerosis in men and women according to reports on adults by other workers, the girls predominated among these chil-

dren in a ratio of 2:1. Follow-up data were available by letter on 32 patients; 10 were still ambulatory, 10 were bedfast, and 12 had died. Death presumably resulted from multiple sclerosis or its complications. The youngest patient to die was 16 years old. A pediatrician confronted with a child showing evidence of scattered neurological deficits that remit, particularly a disturbance of vision and coordination, should consider the possibility of multiple sclerosis.

Acute Epiglottitis in Childhood: A Serious Emergency, Readily Recognized at the Bedside. W. Berenberg and S. Kevy. New England J. Med. **258**:870-874 (May 1) 1958 [Boston].

The authors report on 26 boys and 16 girls, between the ages of 3 months and 14 years, with epiglottitis, who were admitted to the Children's Medical Center in Boston between 1946 and 1954. The onset of the disease was abrupt, and in 39 patients the initial complaint was one of difficulty in breathing. In patients who were able to express themselves, extreme pain in the throat was impressive and usually associated with marked dysphagia. There was a striking retention of secretions, with visible and copious puddling of pharyngeal mucus in 20 patients. Irritability and marked restlessness appeared fairly early. Hoarseness was present in 12 patients at the time of admission to the hospital. Definite stridor occurred in 30 children. A croupy crow was described in 15. Temperatures ranged between 100 F (37.7 C) and 105 F (40.5 C), with an average of 102.5 F (39 C). The respiratory rates varied between 22 and 60 respirations per minute. There was definite involvement of the epiglottis in all the patients. Although this varied somewhat in severity and in the apparent degree of inflammation, constant features were edema and a striking, fiery-red appearance, so that on depression of the tongue and examination of the pharynx, a "cherry-red" epiglottis came into view of the examiner. Diminished breath sounds indicated poor air exchange in 24 patients. A history of prostration and marked respiratory obstruction was obtained in the 3 patients who were found to be dead on arrival at the hospital. Two additional children died within 3½ hours after admission.

Blood cultures were obtained in 16 of the 39 patients who were alive at the time of admission to the hospital. Positive cultures for Hemophilus influenzae, group B, were obtained in 11 of the 16 patients. One blood culture yielded pneumococci. Throat culture yielded H. influenzae, group B, in 17 patients and a hemolytic Staphylococcus pyogenes var. aureus in 2. Direct cultures from the epiglottis at the time of tracheotomy, which was carried out on 18 patients as a lifesaving measure, yielded pneumococci in 1 patient, beta-hemolytic streptococci in 1, and H. influenzae, group B, in 11. Penicillin and streptomycin were given to 16 patients, penicillin, sulfadiazine, and streptomycin to 10, streptomycin and sulfadiazine to 5, penicillin, streptomycin, and chloramphenicol to 2, penicillin and sulfadiazine to 1, penicillin and chloramphenicol to 1, all four agents to 1, and chlortetracycline and chloramphenicol to 1. Penicillin and streptomycin were administered intramuscularly for 24 hours, and then orally as soon thereafter as the patient could tolerate that route. Sulfadiazine was given orally, subcutaneously, and, to 3 patients, intravenously.

Acute epiglottitis is a serious and often fatal condition that, although infrequently recognized, lends itself to accurate bedside diagnosis with consequent institution of specific lifesaving therapy. Its recognition and management should become familiar to all concerned with the care of sick children. The reported data emphasize the importance of H. influenzae, group B, as the predominant but not the only micro-organism producing this clinical picture, and the lifesaving value of tracheotomy to relieve the rapidly developing obstruction of the upper airway. The chemotherapeutic agent of choice is chloramphenicol in doses of 100 mg. per kilogram of body weight given intravenously for the first 24 to 36 hours and then reduced to 50 mg. per kilogram orally if it is tolerated.

Diabetes and Growth in Children: Comments on the Mauriac Syndrome and Its Treatment. H. Lestradet. Presse méd. **66**:582-584 (April 2) 1958 (In French) [Paris].

The appearance of a significant insulin deficiency in children during the period of growth may give rise to clinical manifestations which should be given individual consideration. One of these clinical forms, presented only by patients capable of significant adrenocortical response, is the Mauriac syndrome, in which retardation of growth may or may not be associated with evident signs of hypercorticism. Retarded growth and delay in puberty in juvenile diabetic patients, however, should be ascribed solely to nutritional deficiency and to a poorly regulated insulin therapy, and not to a metabolic derangement peculiar to the disease itself. In some of the author's patients with the Mauriac syndrome, a slight increase in the dietary supply of glucides was followed by a dramatic regression of hepatomegaly, resumption of growth, and a rapid onset of puberty.

Treatment then consists of (1) a normal, well-balanced diet, with a sufficient supply not only of proteins and vitamins but also of glucides, and (2) a well-supervised insulin therapy. Twice the average dose of insulin required by diabetic adults may be needed by children with diabetes, if they are to have a satisfactory physiological development during the period of puberty. Thereafter these large

doses of insulin can be reduced, sometimes rapidly, to those usually regarded as normal in adults. Regular insulin is sometimes poorly tolerated by children with the Mauriac syndrome. Thus, no improvement was obtained from total doses of 120 to 140 units of regular insulin administered in 6 injections daily to a 10-year-old boy in whom ketosis and hypoglycemic reactions occurred alternately. The administration of 2 injections daily of 30 to 40 units (one-third of the previous dose) of protamine zinc insulin, however, resulted in the immediate disappearance of ketosis and hypoglycemia, while at the same time the hepatomegaly disappeared and growth was resumed. Six months later this patient had grown 6 cm. (about 2½ in.) in height, and the usual treatment with a mixture of regular insulin and protamine zinc insulin administered in a single injection in the morning could be resumed. Delay in growth, whatever clinical aspect it assumes as a result of individual hormonal reactivity and of the degree of insulin insufficiency, should disappear completely if children with diabetes are treated according to physiological therapeutic principles, i. e., if they are given a rational diet and insulin therapy adapted to their needs, which are generally great during the period of growth.

Intestinal Diseases After Antibiotic Therapy: Clinical and Bacteriological Aspects of Bacterial Superinfection After Treatment with Broad-Spectrum Antibiotics. G. Möbius, L. Möbius and L. Weingärtner. Ztschr. Kinderh. **80**:615-641 (No. 6) 1958 (In German) [Berlin].

The authors list 5 groups of secondary effects that may occur after treatment with broad-spectrum antibiotics, particularly after penicillin, streptomycin, chloramphenicol, chlortetracycline (Aureomycin), and oxytetracycline (Terramycin). These are (1) toxic effects, (2) allergic complications, (3) damage to the hematopoietic system, (4) bacteriolysis-induced secondary effects resembling the Herxheimer reaction during syphilis therapy, and (5) complication resulting from effects on the physiological bacterial flora in the respiratory or intestinal tracts. This paper is especially concerned with observations on 13 children, in whom serious intestinal disturbances developed during treatment with broad-spectrum antibiotics. High temperatures, watery stools, and vomiting occurred from 4 to 11 days after onset of the antibiotic therapy. All except 1 of the children were less than 2 years, and 7 were less than 1 year old. Eight of the children died, and 5 survived. All except 1 child had been treated with chloramphenicol, a few had received penicillin or chlortetracycline in addition, and 1 had received only chlortetracycline. The feces or intestines of all the children contained resistant staphylococci, and in 2 of the infants who died pathogenic fungi (Candida and Aspergillus) were found in addition.

On the basis of clinical, bacteriological, and pathological investigations on the 13 patients and of a review of literature reports, the authors emphasize that intestinal disorders after treatment with broad-spectrum antibiotics are to be characterized as superinfections, which are produced most frequently by staphylococci that are resistant to antibiotics and occasionally by saprophytes that may become pathogenetic or by fungi. The causal organism that is resistant or not responsive to antibiotics originates in the physiological, oral, or intestinal floras, in which it becomes dominant and unrestrained after the selective elimination of susceptible organisms. The resistant staphylococci are often transmitted to the patient within the hospital, because here they are usually predominant. While the pathological changes in the intestine vary, they are usually characterized by a pseudomembranous inflammation. As an unexpected and hitherto not described finding, the authors observed in 3 of the children severe edema in the cecum, which on histological examination was found to be restricted to the submucosa, where it had caused extensive dissolution of fibers. This tissue-destructive edema is regarded as a manifestation of a disturbance in permeability with formation of an exudate high in protein content and with fermentative effect. The effect of the intestinal disorder on the body in general usually becomes evident in symptoms of the central nervous system. Edema of the brain, central follicular necrosis of the spleen, and fatty degeneration of the liver are generally found and are attributed to the action of staphylococcic toxins. However, septicopyemia could be excluded in the reported cases.

Retrolental Fibroplasia: A Case Report on Preventable Blindness. W. H. Havener. Ohio M. J. **54**:496 (April) 1958 [Columbus].

The boy whose history is presented weighed 3 lb. 15 oz. (1,800 Gm.) at birth, the estimated length of pregnancy being 7 months. Oxygen was given for 3 days in unknown concentration. Although both eyes were normal shortly after birth, at the age of 6 months this child had markedly impaired vision. Reexamination at this time showed traction bands which displaced the large central retinal vessels. Fibrovascular membranes swept across the macular area, obviously destroying central vision. Retrolental fibroplasia occurs almost exclusively in premature infants who have received supplemental oxygen. Central vision may be destroyed by fibrovascular membranes, as in this case, or the whole retina may become detached and pulled forward to produce the "retrolental" membrane. No therapy is known to be effective once the disease has manifested itself. It is extremely hazardous to use oxygen in the care of premature infants, except when obvious cyanosis or other evidence of anoxia exists.

THERAPEUTICS

Acute Glutethimide (Doriden) Poisoning: The Use of Bemegride (Megimide) and Hemodialysis. G. E. Schreiner, L. B. Berman, R. Kovach and H. A. Bloomer. A. M. A. Arch. Int. Med. **101**:899-911 (May) 1958 [Chicago].

Glutethimide has been used widely as an hypnotic and a sedative. Chemically, glutethimide is α-ethyl-α-phenylglutarimide. While working with a new barbiturate antidote, β-methyl-β-ethylglutarimide, known as bemegride (Megimide), the authors were impressed by the clinical similarity and disparate pharmacology of α-ethyl-α-phenylglutarimide, the depressant, and β-methyl-β-ethylglutarimide, the stimulant. Shortly thereafter they had the opportunity of contrasting the response to glutethimide in barbiturate poisoning to the clinical response in a patient who was admitted with presumed barbiturate intoxication but proved subsequently to have negligible amounts of barbiturate and a substantial concentration of glutethimide in the serum. The authors describe their observations on 6 patients with severe glutethimide poisoning whom they treated with varying combinations of supportive measures, bemegride, and external hemodialysis. There was 1 fatality. The first patient, who had severe poisoning from the ingestion of 7.5 Gm. of glutethimide responded dramatically to bemegride. The second patient, who presumably had taken approximately 10 Gm. of glutethimide and possibly a small amount of secobarbital (Seconal), also responded immediately to bemegride. The depression of respiratory rate in this patient was extreme. It may have been related to the associated barbiturate intake or to the ingestion of alcohol or some other unknown drug.

The 3rd patient was admitted unresponsive after the ingestion of 10 Gm. of glutethimide. She also had taken alcohol and possibly other drugs. This patient died. A surprise finding at autopsy was the presence of a massive coronary atherosclerosis, which must be considered most unusual in a 24-year-old woman. The authors wonder whether circulatory impairment could have contributed to her death. The 4th patient had marked hypotension, even after return of a reasonable degree of consciousness in response to bemegride. There was also the possibility of chronic cumulative toxicity of glutethimide, since she appeared groggy before her acute ingestion. She demonstrated apnea on manipulation. Anoxemia worsened the coma, and this patient might not have survived without hemodialysis, which reduced the blood glutethimide level. Patients 5 and 6 were treated with bemegride, and in the latter hemodialysis was also used. The authors stress the difficulties of treating patients poisoned by drugs. The great variety of tranquilizing drugs and the numerous hypnotics and sedatives produce a great multiplicity of possible interrelationships of drug effects. The toxicologist dealing with patients must take cognizance of such factors as inaccurate history of dosage, ratio of ingested dose to absorbed dose, time elapsed before treatment, underlying physical state, and individual drug tolerance.

The authors define the bemegride-glutethimide relationship as a functional antagonism. Bemegride stimulates the respiratory and circulatory center and restores reflexes and consciousness. However, the drug also produces exaggerated reflexes, muscle twitching, tremor, clonus, hyperventilation, and epileptic potentials in the electroencephalogram. Discussing a therapeutic plan for acute glutethimide intoxication, the authors show that, in patients with the mild form, symptomatic therapy and patience are enough. In patients with a moderate degree of intoxication, treatment should include lavage of the stomach. The use of endotracheal suction and oxygen and pressor drugs for hypotension are valuable, but care is necessary to avoid overhydration. Cerebral edema represents a major threat. It is well to be suspicious if more than 1,500 mg. of bemegride is required to lighten anesthesia. The administration of bemegride should be stopped immediately if clonus or convulsions are produced. Patients with severe glutethimide intoxication should be titrated with bemegride immediately after a sample has been taken for the determination of glutethimide blood level before bemegride is given. In the event of failure to elicit a light reflex or plantar withdrawal, a bemegride requirement greater than 1,500 mg. on titration, convulsions from bemegride, or later deterioration of the clinical state, plans should be made for external hemodialysis.

On the Mechanism of the Diuretic Action of Chlorothiazide in Human Beings. V. Bonomini and P. Zucchelli. Policlinico (sez. prat.) **65**:487-496 (March 31) 1958 (In Italian) [Rome].

Diuretic action of chlorothiazide was studied in 19 patients of both sexes, between the ages of 19 and 68 years. Cardiovascular or renal disorder was present in 9 patients, cardiac decompensation of the congestive type in 6, and edema in the lower extremities ascribed to chronic kidney disease but unrelated to hyperazotemia in 4. Chlorothiazide was administered intravenously in a single injection, varying from 100 to 500 mg., without causing toxicity. Chlorothiazide produced an increased urinary output in patients with cardiovascular disorders, but only a slight effect in patients with a renal disorder. Larger doses of the drug had an effect on duration of the action rather than on its intensity. Chlorothiazide did not affect either the glomerular filtration rate or the renal blood flow. The drug exerted its diuretic effect only through

the tubular action. Like mercurial diuretics, chlorothiazide blocked the reabsorption of sodium chloride. The drug also produced an increased excretion rate of phosphate, bicarbonate, and sodium chloride. It caused a decrease in both ammonia and titratable acidity excretions. The pH of the urine increased in patients with cardiovascular decompensation, but it did not change much in patients with severely damaged renal tubules. Diuretic response to chlorothiazide resulted from blockage of sodium chloride reabsorption in the renal tubules. This study confirms the effective diuretic action of chlorothiazide in human beings.

Sodium Balance During Prednisone Treatment. S. Gjørup and J. H. Thaysen. Ugesk. læger **120**:471-476 (April 10) 1958 (In Danish) [Copenhagen].

Prednisone is not suitable as the only substitution therapy in Addison's disease. It is particularly adapted for long-term treatment in cases where cortisone has caused troublesome fluid retention or where cortisone has been regarded as contraindicated because of edema or tendency to edema. No potassium addition should be given during treatment with prednisone. Although with the usual doses applied in the treatment of chronic polyarthritis and with free choice in diet the development of a salt-poor syndrome is hardly to be feared, the possibility should be borne in mind if fall in blood sugar, shock, and so on suddenly occur in patients treated with massive prednisone doses. This applies especially if the patient's salt intake is simultaneously reduced. In stress situations patients with secondary insufficiency of the adrenal cortex as the result of long-continued prednisone treatment should receive the addition of cortisone or hydrocortisone.

Pancytopenia and Granulocytopenia After Carbutamide in Diabetes. S. Aarseth and H. Willumsen. Nord. med. **59**:564-565 (April 17) 1958 (In Norwegian) [Stockholm].

Three cases of hemorrhagic complications on carbutamide treatment are reported, 2 with fatal outcome. Diabetes mellitus developed in a man, aged 81 years, who had previously been well. Carbutamide was given in the usual therapeutic doses of 28 and 13 Gm., with an interval of 6 months. There was progressive bone marrow depression, with anemia, thrombocytopenia, and total disappearance of white blood corpuscles. Death occurred 12 days after the carbutamide was withdrawn. In the second case, in a woman, aged 70, with long-continued heart disease and recently diagnosed diabetes mellitus, polyclinical treatment with carbutamide in the usual doses was effective in reducing the blood sugar. After 4 weeks general dermatitis and fever set in, with almost total disappearance of neutrophil granulocytes. The patient died. The total carbutamide dose was 43 Gm. in 7 weeks. The third patient, a man, aged 68, with moderate diabetes of 3 years' standing, was treated with a total of 30 Gm. of carbutamide in the course of 4 weeks. Because of fever and diarrhea the treatment was discontinued; another not readily resorbable sulfonamide was given for a couple of days. Examination of the blood showed anemia and complete granulocytopenia. The patient recovered after massive doses of penicillin and blood transfusions. Carbutamide involves a not inconsiderable risk of hematological complications threatening life, especially granulocytopenia. Since similar complications have not been observed on tolbutamide treatment, and since the effect in reduction of blood sugar is the same as that of carbutamide, carbutamide therapy should not be employed in the treatment of diabetes.

PATHOLOGY

The Spread of Lung Cancer to the Brain. W. I. B. Onuigbo. Brit. J. Tuberc. **52**:141-148 (April) 1958 [London].

It is a striking feature of lung cancer that brain and adrenal metastases frequently coexist. In a previous paper the author had demonstrated that the topographic distribution of adrenal deposits accords well with lymph-borne and not artery-borne metastasis. This finding posed the question of whether a similar pattern was demonstrable in the case of brain secondaries. Because it has been denied that the brain has lymphatic connections, the current view is that lung cancer metastasizes to this organ via the arteries. Theoretically, arterial scattering of tumor emboli should result in an even distribution of deposits on either side of the brain. Lymphogenous dissemination to the brain, however, would lead to ipsilateral preponderance of deposits. The author reviewed cases of bronchial carcinoma from the autopsy records of the Scottish Medical Schools and the Stobhill General Hospital, Glasgow. In every case showing unilateral metastases in the cerebral or cerebellar hemisphere, it was noted whether the deposits were ipsilateral or contralateral. For bilateral metastases, the side containing the larger deposits was similarly noted.

Two hundred fifty cases fulfilling these criteria were analyzed. Of 177 patients showing unilateral deposits, 100 were ipsilateral and 77 were contralateral; of 73 patients showing bilateral growths, 43 contained the larger deposits ipsilaterally and 30 did so contralaterally. Thus, in the whole series of 250 cases, ipsilateral tendency was exhibited on 143 occasions, and the contralateral trend was manifest 107 times. This finding is statistically sig-

nificant and is in keeping with lymphatic metastasis. Fifty-five cases collected from the literature also exhibited a statistically significant ipsilateral preponderance. Other factors indicating that the spread of lung cancer to the brain takes place by way of the lymphatics, rather than the arteries, are as follows: 1. Subdiaphragmatic tumors metastasize to the brain more often than do infradiaphragmatic tumors. 2. The relatively nearer cerebellum is a site of metastatic predilection. 3. The outstanding histopathological features of brain metastases include the common finding of tumor cells in perivascular spaces and the difficulty of demonstrating them inside vessels. Two controversial questions are asked. First, do lymphatics effect connections with these perivascular spaces? Many anatomists thought so. Secondly, are the subarachnoid spaces and the lymphatic system connected? Indian ink introduced into the cranial subarachnoid appeared within 4 hours in cervical nodes and ultimately in intrathoracic nodes.

Rheumatic Fever and Rheumatic Heart Disease: II. Life Expectation and Natural History. E. Waaler. Acta med. scandinav. **160**:293-303 (No. 4) 1958 (In English) [Stockholm].

The authors report on 211 patients who died at the University Hospital in Bergen, Norway, between 1941 and 1955 and in whom a diagnosis of rheumatic heart disease was made on autopsy. History revealed rheumatic fever in 46 (60%) of the 76 men and in 61 (45%) of the 135 women. This higher incidence of rheumatic fever in men, as compared with women, was not apparent in the younger age groups, but it was significant in the older age groups. Chronic valvular disease was recorded as the cause of death in patients whose average age was 52 or 53 years at the time of death. Death occurred at an earlier age in patients with bacterial endocarditis than in those with pure rheumatic lesions. The average interval between the first attack of rheumatic fever and death was 30 to 32 years in patients dying of chronic valvular disease. The mean age at death was strikingly higher in these patients than in those whose cases were collected from the United States literature. It seems that rheumatic fever and rheumatic heart disease have had a milder course in Norway than in the northeastern part of the United States. The difference may be partly due to the fact that the patients in Norway were less selected, but it must also be remembered that rheumatic heart disease in more recent years has had a tendency to run a milder course than in the years between 1900 and 1920, the period with which the American studies were concerned.

Acute rheumatic fever occurs mainly in children and adolescents. A severe valvular lesion is more likely to occur in patients with rheumatic heart disease and a positive history of rheumatic fever than in those with a negative history of rheumatic fever. Rheumatic heart disease acquired in childhood and adolescence takes a more severe course than that starting in adult life. The findings in the 135 women also indicated that in adult life the silent insidious types of rheumatic heart disease are particularly common in women. The preponderance of women among the 211 patients is partly due to the fact that women are apparently more susceptible to the hyperergic inflammatory type of reaction than men. Microscopic evidence of active rheumatic inflammation was found in only 5 men and 9 women with chronic disease, but the small number of patients does not permit any conclusions concerning a possible difference between men and women. This low incidence of activity on microscopic examination is probably partly due to the fact that 34 of 92 patients who died of chronic valvular disease were above 60 years of age. The longest interval between clinical signs of activity and microscopic findings of activity was 35 years. The clinical ability to make a diagnosis of activity of rheumatic heart disease seems to be lacking, and inflammatory scarring of the valves may take place without being revealed by definite clinical signs.

Presence of Neoplastic Cells in the Peripheral Arterial Blood of Patients with Bronchial Cancer. C. Colombo, G. Maggi and F. Rolfo. Minerva med. **49**:725-730 (Feb. 28) 1958 (In Italian) [Turin, Italy].

Peripheral arterial blood of 13 patients with bronchial cancer was investigated for possible presence of neoplastic cells. Specimens of 5 cc. of serum were obtained from the femoral arteries before the surgical operations. Tumor cells were found in the serum of 2 patients. The first patient was a 56-year-old man who had a squamous tumor in the right main bronchus, with diffusion in the carina and metastases in the hilar lymph nodes during a period of 8 months. Sixteen tumor cells were found in his peripheral blood. After he underwent pneumonectomy, histological examination revealed malignant infiltration of the wall of a large thrombotic vein, with invasion of tumor cells into the vessel's lumen. The second patient was a 59-year-old man who had a tumor in the upper part of the left bronchus, which could not be reached by forceps. Bone metastases were roentgenologically visible. Five tumor cells were counted in the peripheral blood. Tumor cells in the peripheral arterial blood of these patients were 2 to 4 times larger than neutrophils and were round or egg-shaped. They had a large cytoplasm clearly outlined, were slightly eosinophilic, and had no granulation. Nuclei were large, some of them vesical, with spots of chromatin which were arranged irregularly. Nucleoli were identifiable and in some instances well marked.