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Titles and Selected Abstracts

Edited by G. B. Bluhm, M.D.


A review of hereditary amyloidoses is provided by papers from a 1969 international symposium on primary amyloidosis. These discussions allow comparison of the amyloid neuropathy with onset in the lower extremities (Portuguese-Japanese families), the neuropathy with onset in the upper extremities (Indiana-Maryland families), the neuropathy and nephropathy of the Iowa family, and the amyloidosis of familial Mediterranean fever. The importance of studies of genetic entities in understanding the pathogenesis of amyloidosis is emphasized.


Sixty-four patients, aged 65 or older, were examined using the new Olympus fiber esophagoscopy. Fifteen had inflammatory disease of the esophagus, ten carcinoma or lymphoma of the esophagus or proximal stomach, five had stomal ulcers after partial gastrectomy and three had esophageal varices. The procedure was well tolerated by all patients. The authors feel that fiberoptic esophagoscopy offers a thorough and reasonably safe method of examination of the esophagus and proximal as well as postoperative stomach in the geriatric patient.


The effects of accumulated tissue cholesterol concentrations on bile acid half-lives, pool sizes and excretion rates were studied in normal and hypophysectomized rats, and hamsters. High tissue cholesterol concentrations caused decreased bile acid half-lives in both normal and hypophysectomized rats. Total bile acid pool sizes remained static in both types of rats. In normal rats, there was a decrease in the cholic acid and a compensating increase in the chenodeoxycholic acid pool size. No change was observed in hypophysectomized rat pool spectra. Bile acid synthesis rates increased in both hypophysectomized and normal rats in response to elevated tissue cholesterol. Hamster bile acid net synthesis was unchanged by accumulated cholesterol, because an increase in the cholic acid half-life was compensated for by an increase in cholic acid pool size, and the chenodeoxycholic half-life and pool size were static. The relationship of these findings to comparative rates of tissue cholesterol accumulation in the three animals fed diets supplemented with cholesterol is discussed.
Abstracts


The observation that symptoms of some patients undergoing cholecystectomy for cholelithiasis are due to an associated esophageal hiatal hernia, requiring a second operation in at least some patients, led to a review of the problem. Of 301 patients for whom esophageal hiatal hernias were repaired from 1961 through 1967, at least 131 or 42 per cent had associated cholelithiasis. The hiatal hernia required a second operation for repair after cholecystectomy in 37 or 12% of the patients. Of the 37 patients, the hiatal hernia was repaired in nine within one year after cholecystectomy, the average interval being 8.5 years. Of 688 patients in whom cholecystectomy was performed in 1959 and 1960, in at least 100 or 15%, an esophageal hiatal hernia was evident at some time. Although the hernia was repaired prior to or at the time of cholecystectomy in only 23 and at a later date in only two patients, 63 or 9% of the 688 patients required operative correction or concentrated medical therapy. The authors suggest that prior to elective cholecystectomy or repair of an esophageal hiatal hernia, evidence of the possible presence of the other lesion should be evaluated. The selection of patients for repair of a hiatal hernia at the time of elective cholecystectomy is based on the patient’s age, general condition, and ease of the operation.


Hyperplasia, including papillary infolding, in certain benign thyroid lesions, including solitary autonomous functioning nodules and goitrous cretins, can lead to difficulty in histologic interpretation and to a suspicion or erroneous diagnosis of carcinoma. Evidence indicates that nodular goiters associated with congenital deafness (Pendred’s syndrome) also can produce similar difficulty. This hazard is particularly significant with the use of frozen sections at the time of operation on children, as emphasized in the authors’ experience with three children with solitary autonomous functioning nodules and a cretin with bilateral thyroid nodules. Although thyroid nodules in children require careful consideration for the possible presence of carcinoma, caution is needed in their pathologic interpretation and in the extent of operation performed for thyroid nodules. Because hyperplasia occurring in these nodules is likely related to defects in the synthesis of thyroid hormone and to an increased TSH stimulation and because such abnormalities are likely to be present in children, the continuous administration of adequately large doses of thyroid hormone, starting as early in life as possible, is indicated for such patients.


Without an etiological agent identified as a cause for rheumatoid joint disease, the authors present an integrated concept of inflammation as it relates to the diseased rheumatoid joint. The changes differing from “normal” synovium and synovial fluid are correlated with progressive disease as manifested by tissue, cellular and bio-chemical alterations in the diarthrodial joint. Particle formation contributed by the synovia and synovium as byproducts of the cellular and biochemical response to resolve the arthritis may act to self-perpetuate the disease. Differences of synovial fluid findings in rheumatoid arthritis and ankylosing spondylitis, a variant of rheumatoid arthritis, may be an indication of dissimilar pathophysiology. Therapeutic considerations may depend upon the stage of inflammation and the pharmacodynamics of a drug. Hence, concurrent use of several anti-inflammatory drugs with complimentary actions may be desirable during treatment. The optimum time for synovectomy may relate to fibrin formation in vivo and the stage of inflammation noted in the synovium and/or the synovial fluid.


Clinically normal skin biopsies from 220 patients were tested by the direct fluorescent antibody technique for the “band” of localized immunoglobulins found at the dermal-epidermal...
Abstracts

junction in lupus erythematosus (LE) skin. Diseases studied included systemic lupus erythematosus (SLE), discoid lupus erythematosus (DLE), rheumatoid arthritis, scleroderma, and various miscellaneous dermatoses including bullous diseases. Only SLE and bullous pemphigoid demonstrated the band. The SLE band differed morphologically from that of bullous pemphigoid. The band-positive SLE patients had more severe disease and a higher incidence of certain laboratory abnormalities associated with more severe SLE than the band negatives. In the band positive patients, kidney involvement occurred three times, fever 3½ times, and marked weight loss two times as frequently. The presence of the band in clinically normal skin is diagnostic and probably prognostic, confirming a clinical diagnosis of SLE even in patients without LE skin lesions, and simultaneously suggesting a poorer prognosis.


Four cases are described of a lower mediastinal mass due to esophageal varices secondary to portal hypertension. These changes may be discovered as a lower posterior mediastinal mass seen through the heart shadow on a plain chest film. This is more likely to be seen in the supine position rather than in the upright position, but when seen in the upright position the possibility of portal vein thrombosis should be strongly considered. Confirmation is made by celiac and superior mesenteric arteriography whereas splenopancreatography may not confirm it.


In recent years, a number of results having behavioral implications have emerged from neurophysiological studies of *Aplysia*. Since little is known about the actual behavior of *Aplysia*, the author attempted to study one type: free operant responding. Experiments were performed in which the operant was passage of the animal into a specified area of the chamber (as measured by photocells), and the reinforcement was an increase in the chamber water-level. The first experiment suggested that a higher water level in the chamber was "preferred" to a lower level. The second experiment showed that a 3-minute increase in water depth, contingent upon an arbitrary response, maintained the emission of that response at a level higher than that for control subjects. The third experiment supported a learning interpretation for these findings by utilizing true yoked controls and a "probe" technique.


A head position response measured by photocells was differentially reinforced in *Aplysia californica*, the sea hare, to produce higher motions in a vertical tube. Reinforcement was an increase in the tank water-level. Two different types of contingencies were used in studies employing yoked controls. In Experiment I, reinforcement was provided for the duration of the programmed response. In Experiment II, passage of the animal into the programmed position was reinforced with a fixed duration of reinforcement. Subjects in both experiments responded with higher head positions. In Experiment II, a high-effort response was maintained steadily for periods up to 15 hours.


The observations presented are based on the study of two cases of diphtheric myocarditis. Pathologic changes in the heart were correlated with the cardiac conduction disturbances that preceded death. Extensive patchy necrosis and universal fatty degeneration of myocardial fibers were found in both cases. Except for the absence of fat in the sinus and atrial ventricular node
Abstracts

fibers, the changes seen in the specialized tissue of the heart were similar to those affecting the working musculature. Unlike myocarditis complicating other infectious diseases, the cardiac lesions associated with diphtheria are primarily parenchymal rather than interstitial. This study suggests that necrosis of specialized cardiac tissue is responsible for the permanent conduction disturbances while intramyocardial accumulation of fat might be the pathologic basis for the transitory conduction disturbances.


Fatalities associated with varicella are rare and almost always attributed to pneumonitis or meningoencephalitis. This report describes a fatal case of disseminated varicella in a 10-month-old child. Death resulted from myocarditis with extensive inflammatory involvement of the bundle of His and bundle branches. It is suggested that viral tropism for the specialized tissue of the heart may result in cardiac conduction disturbances severe enough to cause death.


The authors report 49 cases of bilateral radical neck dissection done at the Henry Ford Hospital and the University of Michigan Hospital between 1954 and 1969. Sites of the primary tumors were primarily the mucous membrane surfaces of the head and neck. There were two thyroid carcinomas and one melanoma. Fifty of the patients had staged neck dissections. Seven had simultaneous operations. The incidence of operative complication and operative death was greater in the group which had simultaneous dissection. The 50-month survival rate for all patients was 24%. Prognosis is inherently poor in patients with bilateral cervical metastases. Staged neck dissections are preferred to the simultaneous operation because of the higher incidence of complications and operative death in the latter group; however, simultaneous dissections should be done if staging would compromise resectability of disease. An aggressive surgical approach to bilateral cervical metastases is suggested.


The authors report a case of postoperative carotid-artery rupture resulting from injury to the vessel by a partially resected thyroid ala and review some aspects of nine additional cases. The site of perforation was often the common carotid below the bulb. Two patients died before treatment. Of eight patients who were treated with carotid ligation, seven survived. Two had neurological sequelae. The incidence of this complication can be reduced by control of factors which impede wound healing, thoughtful skin incisions, and carotid protection with autogenous materials. Treatment is carotid ligation. Other treatment methods are uncertain and subject the patient to the risk of subsequent fatal hemorrhage.


The gastrocamera has been supplanted by the combined gastroscope and gastrocamera as a diagnostic instrument. The important considerations of safety, durability and performance of the gastrocamera are emphasized. Under special circumstances and indications, it is superior to direct viewing endoscopes.


The current status of both investigational and practical chemotherapy according to tumor types and chemotherapeutic agents is presented. Drugs are subdivided according to mechanism
of action, ie, alkylating agents, antimetabolites, and others. Recommended dosage regimens and anticipated toxic reactions are listed according to generic and trade names. The problems inherent in cancer chemotherapy are outlined from the testing of agents in preliminary animal experimentation through the approval of the Federal Food and Drug Administration to guarded “Phase I trials” conducted simultaneously in a number of institutions, using carefully prepared and scrupulously monitored protocols. Of the approximately 25,000 new compounds annually tested in animal laboratories, one in 10,000 may show activity significant enough to warrant extensive and expensive preclinical pharmacology. Since many solid tumors are resistant to cancer chemotherapeutic agents currently available, investigational programs continue to be important facets of clinical oncology. Examples are given of the development of drugs through Phase I, II, and III studies. Also, the major malignancies are listed and the best available therapeutic regimens are discussed. However, it is emphasized that the principal contribution of chemotherapy programs has been an increased awareness, on the part of physicians, nurses, and other health personnel, of the multiple medical, social and other problems of the patient with cancer; also, the fact that the patient is the most important factor in any therapeutic program.


A succinct presentation of chemotherapy and hormonal programs of choice describes the results to be anticipated from such programs for the majority of common solid tumors. Based on extensive experience at Henry Ford Hospital, guidelines are given for selection of patients, choice of drug or hormone, proper dosage regimen, toxic effects, response, and duration of response. Commercially available and investigational chemotherapeutic agents are listed according to mechanism of action. In the majority of solid malignant tumors, chemotherapy and hormonal therapy are only palliative. However, such treatment can bring worthwhile subjective and objective improvement in a significant number of patients. At the present time, chemotherapeutic agents or hormones are usually recommended when curative surgery or radiotherapy is impossible or when recurrent malignancies are untreatable by either modality. The one notable exception to this is the treatment of choriocarcinoma of the placenta. With early diagnosis and prompt treatment, “five year cures” occur frequently with the use of chemotherapy. Surgery or irradiation should be considered only if chemotherapy fails. In addition to choriocarcinoma, the paper discusses carcinomas of the breast, lung, kidney, prostate, bladder, testicle, ovary, cervix, endometrium, and head and neck; malignant melanomas; and sarcomas, ie, fibrosarcomas, rhabdomyosarcomas, leiomyosarcomas, and osteogenic sarcomas.


Several experiments have been completed dealing with auditory performance of brain-damaged cats. Subjects with the auditory areas of both cortices ablated are able to discriminate auditory stimuli whose frequency components are present in an ongoing neutral background. Further, it appears that ablated subjects are able to discriminate in situations demanding responses to more than one positive cue over trials, though not within trials. Transfer tasks provided evidence that the basis for the auditory discrimination could not have depended exclusively on the occurrence of a “greater neural event.” The inability of the brain-damaged subjects to perform a Neff pattern discrimination was again demonstrated. However, these same subjects easily performed a frequency discrimination whose frequency components and intensities were identical to those in the pattern task. Both conditions lend credence to the results found in the prior investigations and attest to the adequacy of the ablations performed on the subjects. The results of the main experiment are difficult to interpret in terms of Neff’s neural theory [Neff, W. D. (1961). “Neural Mechanisms of Auditory Discrimination” in Sensory Communication, W. Rosenblith, Ed. (John Wiley & Sons, Inc., New York) pp. 259-278]. Some further research on these problems has been specifically outlined, and some general questions about pattern discriminations have been put forth.
Abstracts


A 22-year-old woman with an acute variant of myelofibrosis and agnogenic myeloid metaplasia was found to have a consistent chromosomal aberration in her megaloblasts, cultured from the peripheral blood. This marker was interpreted as a 1-3 translocation. The lymphocyte karyocyt in this patient was normal. Bone marrow fibroblasts, obtained by needle biopsy, were successfully cultured, also yielding a normal karyotype. These observations point to a secondary role of the fibroblastic proliferation in myelofibrosis, and suggest that the primary fault in the pathogenesis of this disease is located only in the hematopoietic cell lines.