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Hypophysectomized rats, in contrast to normals, easily accumulated large quantities of tissue cholesterol when fed diets supplemented with this sterol. To study the mechanism of this effect and the hormones involved, we compared sterol and bile acid turnover in normal (N), hypophysectomized (H), I"-thyroidectomized (T), and hypophysectomized-thyroid-treated (HT) rats. Following injection of dl-mevalonic acid-2-C\textsuperscript{14} feces were collected for a 14-day period. When compared with normals, cumulative fecal bile acid-C\textsuperscript{14} excretion was reduced about 20% in H and T; while in HT, bile acid-C\textsuperscript{14} excretion approached normal rate. Cumulative fecal \( \alpha + \beta \)-sterol-C\textsuperscript{14} excretion was reduced 28% in T, but was similar to normal in H and HT. Total fecal cholesterol plus coprostanol excretion was reduced in both H (—45%) and T (—25%). Thyroid hormone treatment of hypophysectomized rats resulted in a small increase in fecal sterol excretion, but the daily rate was still below normal (—30%). The total steroid-C\textsuperscript{14} synthesized from mevalonic acid-2-C\textsuperscript{14} was reduced from normal in both T and H. HT synthesized almost normal amounts of total steroid-C\textsuperscript{14}. It was concluded that lack of the thyroid hormone in hypophysectomized rats accounts for some of the effects of hypophysectomy on steroid metabolism. However other hormones must also be important, since the effects of thyroidectomy were not the same as those of hypophysectomy, and thyroid administration did not restore some aspects of steroid metabolism to normal.


Serologists are constantly working toward the development of an ideal test which will detect syphilis with maximum specificity and sensitivity. As a clinical syphilologist, I hope for the development of a test to detect very early syphilis in the seronegative phase. There are several reasons why better tools for the diagnosis of early syphilis are needed. (1) A donor with very early syphilis (no clinical signs and a negative serologic test, but in a stage of spirochetemia) can readily infect a recipient of his fresh blood in transfusions. Storage of blood is reasonably effective in eliminating this danger. (2) Very early syphilis (STS-negative) may be missed in routine serologic testing, especially in the absence of a physical examination, as in public health detection programs. (3) Dark-field microscopic examination may fail to detect T. pallidum simply because, in practice, clinician and technician employ it only occasionally. Fluorescent technics may or may not eliminate this problem in the future.


A survey was made by means of a standard questionnaire and spirometric test of 1,584 postal employees, aged 40 years or more, for respiratory symptoms and ventilatory impairment. "Chronic" cough and phlegm was recorded in 156, "chronic" wheezing in 108, and shortness of breath which interfered with ordinary activity in 67. Respiratory illness which caused at least a week's absence from work during the previous three years was noted in

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104 subjects. Chronic respiratory symptoms, absences from work for respiratory disease, and diminished values in ventilatory tests were highly correlated with the amount of cigarette smoking. No relationship was found between chronic respiratory symptoms and prior exposure to silica dust.


For the purposes of this chapter, the term allergy is used in its broadest sense as "an altered capacity to react." Sections are included on eosinophilic pneumonias, diffuse interstitial fibrosis of the lungs, pulmonary alveolar proteinosis, and sarcoidosis. All are discussed from the viewpoint of etiology, pathology, clinical features, diagnosis, prognosis, and treatment, with special reference to sensitivity manifestations. In some cases the relationship of allergy is tenuous, in others, well established. Liberal case material is supplemented with pertinent illustrations. The classification of eosinophilic pneumonias adopted is that of Crofton, which recognizes five categories:

- **Group 1. Simple pulmonary eosinophilia ("Loeffler's syndrome"; transitory pulmonary infiltrations with eosinophilia, "P.I.E." syndrome)**
- **Group 2. Prolonged pulmonary eosinophilia**
- **Group 3. Tropical eosinophilia**
- **Group 4. Pulmonary eosinophilia with asthma**
- **Group 5. Polyarteritis nodosa**

Only the first three of these are discussed in this chapter. Diffuse interstitial fibrosis is considered as the comprehensive term covering several synonyms: Hamman-Rich syndrome, chronic interstitial pneumonia, and muscular cirrhosis of the lungs. A selected bibliography is appended for each section.


An analysis was done of the relationship between physical loads on bones and the regulation of drifts caused by osteoblastic and osteoclastic cell activities at bone surfaces. It was found that load induced changes in curvature of the surfaces of bones correlated consistently with known patterns of bone resorption and formation. Tension and compression stresses and strains each failed to correlate. The features considered in the analysis included the loads, the three principal stresses and strains, surface curvature, and the direction of each with respect to bone surfaces. On the basis of the analysis, it is postulated that strain generally is a major biomechanical factor which influences cell behavior patterns in live bone. It is postulated specifically that when a bone surface becomes less concave as an external load is applied, net loss of bone appears at that surface as the result of osteoclastic activity. When a bone surface becomes more concave while an external load is applied, net increase in bone appears at that surface as a result of osteoblastic activity. An electrical voltage is known to be generated at the surfaces of bones that are deformed by bending and may be associated with a biological signal that is created at these surfaces. This signal may be the agency responsible for the correlation reported here.


Further studies of a patient with resistant osteomalacia have been presented. Balance studies have been performed in conjunction with tetracycline labeling of bone. Possible defects in intestinal calcium absorption, renal phosphate transport and the skeleton, and their respective roles in the pathogenesis of resistant osteomalacia, have been discussed. Important features in the patient described include normal parathyroid anatomy; an intestinal mucosa with the potential for absorbing calcium without the need for large doses of vitamin D; biopsy specimens of bone which were diagnostic of osteomalacia and consistent with severe inhibition of new bone formation and cellular proliferation; and decreased renal tubular phosphate transport. A pathogenetic mechanism involving combined defects consisting of impaired renal phosphate transport and an intracellular derangement at the skeletal level is proposed for this patient. It is suggested that resistant osteomalacia is a syndrome resulting from a variety of metabolic abnormalities.

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Most of the confusion about this subject can be traced to the inability to correlate morphologic facts with ideas of function. Previously, it was assumed that the secret of stress urinary incontinence was tied inexorably to pathologic function of a muscle sphincter at the urethrovesical junction; however, recent evidence has suggested that sphincteric action of the urethra is of minor importance in urethrovesical function. Previously, in an attempt to be consistent with knowledge of other retention-expulsion systems, theories of urethrovesical control were postulated and fixed to the singular idea that the control of urinary function required a bladder for a reservoir, a urethral muscle for a sphincter, and a urethra for a conduit. This reservoir-sphincter-conduit concept seemingly has blinded experimental physiologists and research has been conducted, for the most part, as though the bladder and the urethra functioned as isolated units apart from general body function. Sometimes, in appraising the conclusions of a study, one has the idea that fact has been made to conform to theory, rather than theory to conform to fact. In this reappraisal of the contributions of the past decade on stress urinary incontinence in the female, the following fundamental aspects of the problem have appeared to need up-dating and clarification: (1) definition and identification of stress urinary incontinence, (2) classification of types, (3) anatomy of the detrusor muscle, (4) anatomy of the urethra, (5) vesicourethral topography, (6) vesicourethral pressure relationships, (7) willful control of smooth muscle, (8) vesicourethral function, (9) gravity and urethrovesical function, and (10) the fundamentals of treatment. These perplexities are inherent in the unsolved physiology of urethrovesical function and, until urethrovesical function is better understood, they are likely to persist.


Paralytic ileus secondary to myxedema is an exceedingly rare cause of intestinal obstruction and one in which surgical intervention may be disastrous. It exemplifies the ultimate functional expression of the syndrome of gastrointestinal myxedema. A recently observed case of advanced athyrotic myxedema in which a paralytic ileus developed prompted us to ascertain the incidence of this complication in our institution. The records of 89 cases of myxedema seen at the Henry Ford Hospital from 1953-1963 were reviewed and three additional cases of myxedema ileus, one of which complicated a possible gallstone ileus, were encountered. In view of the paucity of literature dealing with this unusual manifestation of myxedema and to emphasize the importance of its recognition, these four cases are presented.


Death of patients with Marfan's syndrome is often sudden and unexpected. It is natural under such circumstances to suspect a cardiac arrhythmia as one possible explanation. Recently it has been our opportunity to study two young men with Marfan's syndrome who developed disturbances in cardiac rhythm or conduction during their terminal illness. In these two patients with Marfan's syndrome there were significant pathologic changes in the sinus node and AV node, involving particularly the nodal arteries. The clinical significance of these changes is indicated by the occurrence of arrhythmias and conduction disturbances in the terminal illness of both patients. Similar pathologic changes were observed in the small arteries of the ventricular myocardium and lungs.


The increasing number of geriatric patients in the past decade or two has brought an increasing awareness of the different response in the aged patient to a given disease entity or to its treatment. It has long been observed that the elderly patient with an acute abdominal disorder, myocardial infarction, hyperthyroidism or almost any acute disease process, presents an unusual picture that is often confusing and at times confounding to the clinician. It is as though a complete new set of criteria has to be considered for this group of patients. The effects of digitalis, diuretics, anticoagulants and sedatives in elderly cardiac patients are reviewed. Experience indicates that there are drug problems peculiar to the geriatric patient. Therefore, it should be emphasized that this group of patients presents a reservoir of new problems each time a different drug is used. Their responses are unpredictable. Undesirable reactions lead to difficulties far more frequently than in any other age group.
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From January, 1962 to October, 1963, 12 pools of human plasma, (15 to 18 liters each) from healthy blood bank donors were bioassayed for virus neutralizing antibody content. Certain enteric viruses of the poliomyelitis, Coxsackie, and ECHO families were consistently present throughout the year. These pools showed that the same antibody titers for the respective viruses remained fairly constant throughout the year with a two-fold variation from the average titer. Thus we were able to establish a standard average antibody response for the evaluation of individual antibody response to these viruses. Such standards could not be established with the upper respiratory viruses because of low antibody titer and inconsistency of response in the pooled plasma throughout the year. An attempt was made to correlate the quantitative measurements of the individual’s immune globulins with his virus antibody response as measured by the standard average antibody response determined for the Greater Detroit Area. The results show that there is no correlation between the quantity and antibody content (or quality) of the immune globulins. Individuals with hypergammaglobulinemia may even have more antibody content than individuals with normal or hypergammaglobulinemia. The term serum globulin dyscrasia has been ascribed to that condition in which normal or hypergammaglobulin quantities are present but the virus neutralizing antibody response is lacking. In our two year study, globulin dyscrasias were found in a variety of clinical conditions, in both sexes, and at all ages. The clinical conditions included: infectious mononucleosis, pneumonitis, meningitis, septicemia, lupus erythematosus, multiple myeloma, generalized herpetiform infections with superimposed pyoderma, and recurrent conjunctivitis with corneal opacity from herpes simplex.


The thyroid scintigram is a map of the distribution of radioactive iodine within the thyroid gland. To extract clinically useful information from it, correlation with palpable thyroid abnormalities, pathophysiology, and microscopic anatomy is required. The initial attempt at such correlation was undertaken in cases presenting a problem in preoperative identification of the malignant nodule. As the low level of functional activity of thyroid cancer was well known, it seemed reasonable to attempt to correlate apparent function in terms of scintigram activity and pathological anatomy. The hot nodule on the scintigram can be identified as autonomous or TSH-dependent. The former represents a well defined pathophysiologic entity and can be correlated with a benign histologic picture. No case of a primary thyroid cancer fulfilling the criteria for the diagnosis of an autonomous hot nodule and masquerading as a benign lesion has been reported. It is a theoretical improbability. Papillary carcinomas have been reported within presumably autonomous nodules. These observations would seem to be of the same significance as the incidental discovery of cancer in any other type of thyroid. The frequency of association of the hot autonomous nodule and thyroid cancer has not been determined.


Clearly, inspite of the impressive advances that have been made toward solution of problems of prosthetics, large areas remain for exploration. Progress in the future will be achieved, as it has been in the past, by the cooperative effort of many gifted and devoted persons representing a vast interdisciplinary scheme.


Another cause of intrahepatic portal hypertension has been introduced recently into the literature, and it has been called congenital hepatic fibrosis. A new case meeting the characteristics of this condition is presented here. It is believed that this disease slightly predominates in female children. Splenoportography is suggested as a routine method of differential diagnosis in patients with portal hypertension and well preserved liver function. Splenorenal anastomosis with transesophageal ligation of the varices is advocated as a combined procedure favorable for the presinusoidal type of portal hypertension with bleeding esophageal varices.

Non-syphilitic sera which demonstrated antinuclear factor with tumor imprints also produced a reactive fluorescent treponemal antibody (FTA) test whose intensity seemed to parallel closely the intensity of the nuclear immuno-fluorescence. Such reactive FTA results were rendered negative by absorption with human tumor homogenates; they were diminished partially by normal tissue homogenate absorption, but remained unaffected by animal tissue powder absorptions. Patients furnishing such sera were considered non-syphilitic, although four had reactive lipoidal antigen tests, presumably false positive. Known syphilitic sera absorbed with tumor or normal tissue homogenates could not be rendered negative to the FTA, and these did not produce nuclear immuno-fluorescence. These findings suggest that false positive FTA test results may indicate the presence of an autoimmune disorder.


Early detection of carcinoma is foremost among geriatric gynecologic problems, but many other disorders occurring frequently among elderly women also merit careful attention. An elderly woman may seek medical aid for a seemingly minor complaint because she is lonely and wants attention. The complaint deserves careful investigation; it may be serious. Even if it is not, the time required to give her comfort and reassurance is well spent.


Pronouncements concerning the effectiveness of new forms of treatment are not meaningful unless concomitant information is available about the dangers of such therapy. Although an extensive dialogue has appeared in the medical literature concerning the worth of AC drugs in various thromboembolic states, there are few reports of long-term observations of the complications of such therapy. Because a large group of outpatients receive long-term AC's at the Henry Ford Hospital, it was decided to evaluate the incidence and severity of complications that appeared in this group of patients, and to detect the ease of control of prothrombin times during a one-year period of time. With proper precautions, long-term outpatient anticoagulant therapy during a one year period is safe and practical. In 978 patients given long-term anticoagulants, 15 patients (1.5 per cent) experienced major hemorrhage, and 218 patients (22 per cent) reported minor bleeding not necessitating hospital care. No significant correlation was observed between the prothrombin time and major complications. Fifty-five deaths occurred during this period, and in four of these patients, anticoagulants may have been a contributing factor.


The fifth, sixth, or seventh ribs from 97 metabolically normal people of all ages were examined. Mineralized longitudinal sections were specially stained to show both osteoid seams and osteoblasts. In 19 persons, the mean number of osteoblasts per mm² of active osteoid seam surface on III seams was 4500. In 66 persons, a layer of osteoblasts was present on only 29% of 121 seams. The seams without layers of osteoblasts nevertheless were part of actively forming Haversian systems as judged by other criteria. No significant age differences were observed in either value.


Osteoporosis may be defined as less bone than a comparable standard of normal. A decrease in bone mass is the one factor common to all of the osteoporoses, since there are also qualitative changes in the bone tissue in many of the osteoporoses. In order to
determine the decline in skeletal mass, some standard of normal is necessary. Many investigators have attacked this problem in a variety of ways, and a large amount of data is available. The provision of an adequate microscopic index of normal bone quantity was the object in this study. The measurement of total cross-section area, marrow-space area and the area of cortex is over 600 undecalified, complete cross sections of midrib diaphysis in 139 normal and 60 abnormal subjects of all ages showed: The total area of the sections in the normal individuals increased from birth until age 20, then remained stable for several decades and subsequently rose again gradually. The area of the marrow space increased in a fashion similar to that of total area and marrow area, while the cortical area increased until early adult life and then underwent a gradual decline. The ratio of cortical area to total crosssection area was highest in infancy and decreased gradually throughout life. In 18 patients with well-controlled diabetes mellitus, there were no changes in the indices cited, whereas in a group of known osteoporotics, the values for cortical/total ratio and cortical area were low.


A diagnosis of ankylosing spondylitis can be made at an earlier stage of the disease if the subtle clinical manifestations are appreciated, important physical signs are elicited, certain laboratory aids are utilized, and radiographic changes are detected in the axial skeleton. The early use of available measures aids in maintaining functional posture. In mild disease permanent changes will be minimized, and in severe disease even the development of a “poker spine,” if straight, may be a relatively minor handicap.


Serum antirachitic activity (SARA) has been determined in 116 women from Michigan and sixty-five Puerto Rican women, age forty-five and over, with particular emphasis on its relationship to age, season, climate, degree of vertebral osteoporosis and vitamin D therapy. SARA for all Puerto Rican subjects was relatively independent of season and averaged 4.4 units per ml., compared to 2.6 units for all Michigan women in whom the levels during summer were nearly twice those during winter. For Michigan women, SARA was significantly less in symptomatic osteoporotic subjects than in the skeletally normal; it increased significantly more in the latter during the summer, and for osteoporotic subjects in particular it was lower in the older age groups. Vitamin D given orally in conventional doses to osteoporotic subjects restored SARA to levels obtained naturally in normal subjects during the summer and in Puerto Rican residents. Unexpectedly, serum calcium and phosphorus levels were found to average significantly higher in Puerto Rican than in Michigan women, respective values being 10.4 versus 9.6 and 3.8 versus 3.1 mg. per cent. Although other explanations may be presented for the higher values in Puerto Rican women, the latter are consistent with the known actions of vitamin D and suggest a better calcification potential in the island resident. The over-all findings are considered relevant to the current efforts to define the respective roles of endocrine imbalance and disordered mineral metabolism in the genesis of involutional osteoporosis. A link between these two casualties is suggested by the fact that androgens promote sebaceous secretion, a dermal function essential to vitamin D formation.


The clinical, angiographic, and pathologic characteristics of 33 cases of congenital arteriovenous communications of the extremities and pelvic and shoulder girdles are presented. Attention is called to the unitary pathogenesis of these morphologically highly variable lesions, formerly suggested by other authors, and a classification based on the events of the fetal development of the vascular system is proposed. Some diagnostic pitfalls in the recognition and the usefulness of arteriographic studies in the therapeutic evaluation of congenital arteriovenous communications are pointed out. The refractoriness of all but the most sharply localized lesions to radical surgical treatment, their essential benignity, and their satisfactory response to conservative management are documented.

Although the majority of cardiac myxomas originate in either the right or left atrium and, therefore, disturb tricuspid or mitral valve function, these tumors frequently produce a capricious clinical picture which makes their recognition difficult. Two patients with atrial myxomas, one arising in the right and one in the left atrium are presented to illustrate certain diagnostic and surgical features. The changing clinical findings produced by these tumors were brought about by disturbance of mitral and tricuspid valve functions. Both tumors were successfully excised using extracorporeal circulation. The pedicle of origin and underlying atrial myocardium were excised in each instance. Invasion of the underlying myocardium was not demonstrated.


This report deals with a previously unreported property of individual bone resorption and formation processes. It provides evidence of a temporal and physical relationship which is concealed from those who study the entire skeleton as a unit. While changes in cell behavior in adults are felt by most biologists to reflect regulation of cells by factors in their environment, we prefer to speculate over the possibility that in this instance the cells are executing some form of pre-programmed behavior, determined by a mechanism existing inside the cell which functions in concert with factors arising from the without, as suggested previously by one of us.


Hepatic injury in the form of intrahepatic cholestasis due to allergic drug sensitivity has been reported for many drugs. The prototype most extensively studied is that of cholestatic jaundice caused by chlorpromazine. This report describes a case of cholestatic hepatitis due to sodium oxacillin (Prostaphlin). Cholestatic hepatitis occurred following sodium oxacillin administration and was documented by liver biopsy. Oxacillin was not previously included among drugs with potential of causing this type of hepatic injury.


Partial fractionation of Mg++ + Na+ + K+ - activated from Mg++ activated ATPase activity in deoxycholate extracts of rat kidney subcellular particulate (i.e., the fraction sedimenting between 10,000 and 105,000g) has been accomplished on CM Sephadex C 50 columns. The preparative procedure is reproducible and preparations having activity ratios of 1.44 are strikingly similar to those reported by Skou. In vitro inhibitory effects of aminonucleoside on the partially purified Mg++ + Na+ + K+ -activated preparation appear to be completely ascribable to inhibition of the Mg++ activated ATPase activity, constituting a major portion of the enzymic activity.


Under normal conditions, due to the countercurrent multiplier mechanism operating in the loops of Henle of the renal medulla, an increasing concentration of sodium from cortex toward the papilla is seen. The maintenance of this medullary hypertonicity partly depends upon the flow of blood through the vasa recta, which act as countercurrent diffusion exchangers. An increased rate of medullary blood flow would reduce medullary sodium concentration, whereas a decreased flow would exert an opposite effect. In a series of 25 experiments, a good inverse relationship between the sodium concentration and electrical resistance of renal tissue was seen. Through the use of electrodes of varying length and


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diameter it was established that: (1) The concentration of sodium progressively increases from cortex to inner medulla (papilla), whereas electrical resistance progressively decreases. (2) Medullary and papillary concentrations of sodium and electrical resistance could be significantly altered by the renal vasodilator hydralazine, without any essential cortical changes.


This report concerns electron microscopy of the ultrastructure of normal and bronchitic human bronchial mucosa and is related to current studies on the cytology and etiology of bronchitis (whether caused by occupation, disease, or excessive smoking) and of bronchogenic carcinoma. The structure of the human bronchial mucosa has been well described by light microscopy. Although other species (rat and mouse) have been fairly extensively studied by electron microscopy, the published work on the human bronchus is meager. The present paper confirms and extends Rhodin’s work with the normal human bronchus and offers, in addition, some initial observations and impressions of the bronchitic condition. Detailed observations on the ultrastructure of the normal cells of the epithelium of human bronchial mucosa discussed on the basis of electron microscopy are compared briefly with preliminary observations made on the bronchitic bronchus studied by the same methods. Particular attention has been given to the pellicular structures, which are here described for the first time in detail. The ciliar structure is also emphasized.

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