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Edsel B. Ford Institute for Medical Research

Titles and Selected Abstracts

Edited by G. B. Bluhm, MD


Von Willebrand's disease differs from classic hemophilia by its usually milder manifestations, prolonged bleeding time, predominance of mucous membrane bleeding, and autosomal inheritance. A review of the Henry Ford Hospital experience from 1959 to 1969 revealed 19 well-documented cases and 22 probable cases. The major diagnostic criteria were (1) significant history of abnormal bleeding; (2) reduced factor VIII activity; and (3) increased bleeding time. Supplementary criteria included family history of the disease, abnormal platelet morphological findings, decreased platelet adhesiveness, and positive plasma infusion tests. These 41 patients underwent a total of 171 surgical procedures. Without specific therapy, 75 procedures were associated with normal bleeding but in 35 it was excessive. On preoperative treatment with adrenocorticosteroids and fresh frozen plasma, in 40 procedures bleeding was normal and in 3 excessive.


The precise cellular, hormonal and enzymatic mechanisms which produce stasis edema are still unknown. Also the roles of the lymphatic capillary cul-de-sacs, the venous side of the blood capillaries and the extracellular fluids with its component parts are only partially known. This paper attempts to bring together some of the more pertinent available literature concerning the endogenous and exogenous factors which tend to regulate the formation of stasis edema. It also tries to pinpoint areas of differences of opinion hoping that investigators will be challenged to find more suitable answers.


Of 284 patients with thyroid carcinoma managed at the Henry Ford Hospital from 1952 through 1967, 25 (9%) had evidence at some time in the course of the disease of metastases to the anterior superior mediastinum. Metastases to lateral cervical lymph node were also present in all patients with metastases to the anterior superior mediastinum. Mediastinal metastases in these patients appeared initially and were restricted to the anterior superior component. In the 17 patients for whom dissection of the anterior superior mediastinum was performed at the time of the thyroidectomy, there is no evidence of recurrence in this region. Of the eight patients in whom anterior
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Mediastinal metastases appeared an average of 10 years following the original operation for ih-
carcinoma, three required further operative procedures. Lymphatics in the anterior superior me-
dium may provide the route for metastases to the contralateral neck. Such metastases occurred
in one patient who did not have evidence of carcinoma in the contralateral lobe of his thyroid.
Since the anterior superior mediastinum is not readily assessed by preoperative examination,
removal of lymph node bearing tissue in this region should be performed.

Renin release and the uteroplacental-fetal complex. O.A. Carretero, C. Polomska,

To determine whether the reninlike substance present in the uteroplacental-fetal complex of preg-
nant dogs responds similarly to stimuli known to produce a release of renal renin, pregnant
nephrectomized dogs were subjected to hemorrhagic hypotension, infusion of oxytocin,
norepinephrine, and acute hyponatremia. Plasma renin activity determinations were made be-
fore nephrectomy, 16-24 hours after nephrectomy, and at appropriate times after the various stimuli
were applied. As a group, the pregnant, nephrectomized bitches exhibited no significant release of a renin-
like substance from the uteroplacental-fetal complex. It is possible that the reninlike substance
was released in a small amount but was so diluted in the maternal blood that it became undetect-
able by the method used. On the basis of our experiments it can be concluded that if the reninlike
substance is released from the uteroplacental-fetal complex into the maternal blood of the dog,
it is in such small quantity that it would appear unlikely that this enzyme plays a systemic role
in that this enzyme has a physiological function, we would have to assume that it is at the local rather
than at the systemic level.


Studies investigating the effects of the auditory cortex upon auditory discriminations were
reviewed. Discriminations studied include frequency, intensity, duration and other temporal and
complex spectral differences, and changes in temporal patterning. Factors determining the effect-
iveness of lesions are size and completeness of lesion, whether the lesion involved one or both
hemispheres, nature of the testing procedure, size of the signal differences to be discriminated, and
nature of the discrimination. In view of the numerous factors, comparison of different studies
often difficult because of confounding. In terms of the factors listed above, (a) patterning changes
in which signals are not changed but merely rearranged in order of presentation, suffer more than
do tasks involving the detection of new signals or the recognition of different signals; and (b) discrimina-
tion tasks requiring recognition suffer more than do tasks requiring only the detection of
a new signal. It appears probable that the nature of the discrimination task interacts with the size
of the lesion and that failures on different types of tasks reflect different deficits.

Relational and absolute cues in auditory discrimination by monkeys. D. N. Elliott,

Rhesus monkeys were trained to make auditory frequency, intensity, and duration discriminations.
Initial training was carried out with a procedure which allowed the utilization of either relation-
cues or absolute cues. Later tests with similar auditory parameters allowed only the utilization of
relational cues. Performance on these latter tests indicated that relational rather than absolute cues
had been utilized when both types were available on the frequency and intensity discrimination
tasks. However, absolute rather than relational cues were apparently utilized in making duration
discriminations.
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This is a review article of the responsible agents and influencing factors in pulmonary and systemic embolism. Occlusion of the pulmonary and systemic arteries by emboli continues to be an important clinical problem responsible for a variety of symptoms and death. In some instances they are of little or no clinical importance and may be only incidental necropsy findings. Thrombi remain the principal responsible agent, but new causes, some foreign to the body, have gained prominence being related to trauma (accidental, criminal, or self-inflicted) or to diagnostic and therapeutic procedures. Identification of the agent responsible for the vascular occlusion is therapeutically and prognostically important. Careful histologic examination of the embolus may indicate the possible site of its origin which may then be eradicated.


A 16-year-old girl was found to have co-existent polyostotic fibrous dysplasia and myositis ossificans progressiva. The authors postulate that both conditions result from a dysplastic connective tissue reaction involving bone in one instance and muscle in the other and leading to collagen deposition and metaplastic bone formation. Patients diagnosed as having either condition should be carefully scrutinized for evidence of the other to help determine whether this has been a chance occurrence or a more significant manifestation of a related fibrous and osseous metaplastic tissue transformation.


Using established organizational and statistical properties of biological systems, one can devise a strategy of skeletal research which respectably minimizes the probability that one will choose an inappropriate or irrelevant subject to study, and effectively enhances the probability that the subject of study and method of procedure will prove relevant to physiological and pathological problems related to human disease. This article sketches in very brief fashion some of the reasoning underlying such strategy, and one direction which one might take in attempting to implement it.


A case is described of left adrenal pheochromocytoma manifesting clinically as a cardiomyopathy. The symptoms of persistent sinus tachycardia and profuse sweating and an abnormal glucose tolerance test prompted the diagnosis, which was confirmed by the finding of increased urinary catecholamine excretion and observations at surgery. The predominant epinephrine secretion of the tumor could explain the relative normotension and abdominal cramps observed in this patient. Marked improvement in the hemodynamic findings and disappearance of the symptoms of congestive heart failure after removal of the tumor are supportive evidence of an underlying catecholamine-induced "myocarditis."


The binding of angiotensin by plasma proteins was demonstrated by equilibrium dialysis. Bound radioactive angiotensin could not be displaced by cold angiotensin, thus precluding the postulation of a physiological significance for this binding.


This article reviews present concepts of the diagnosis and management of parathyroid disorders especially from the orthopedic viewpoint. The major clinical manifestations of hyperparathyroidism
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(primary, secondary, and tertiary) and hypoparathyroidism (idiopathic and post surgical) are discussed with emphasis on the radiological features as these are commonly brought to the attention of the orthopedist. Also discussed are the parathyroid hormone resistant states such as pseudohypoparathyroidism (with or without osteitis fibrosa) and pseudo-pseudohypoparathyroidism. Diagnostic criteria are outlined with particular reference to the differentiation of parathyroid disorders from other conditions simulating them. Therapy is discussed in relation to the various disorders considered.


Eleven patients with borderline hypertension and high cardiac output were compared to 16 healthy volunteers. Cardiac output, heart rate, and intraarterial blood pressure were determined at rest, after administration of 0.2 mg/kg of propranolol iv, and after administration of an additional 0.04 mg/kg of atropine. In four additional patients, response to infusion of isoproterenol before and after administration of 0.2 mg/kg of propranolol iv was evaluated. Resting heart rate and cardiac output in patients with borderline hypertension were elevated. After propranolol infusion, the values decreased more in the patients with borderline hypertension, but remained significantly elevated. After atropine administration, the difference in cardiac output and heart rate between the two groups disappeared. Consequently, patients with borderline hypertension and hyperkinetic circulation simultaneously exhibit an increase of sympathetic and a decrease of parasympathetic tone.


Success in treatment of hemorrhage from telangiectasia of skin and mucosal surfaces, which characterize Osler-Weber-Rendu Disease, depend on the location of these lesions and trauma to the lesions. The lesions involving the nasal mucosa have a deserved reputation for dramatic hemorrhage. Success has been reported uniformly by the replacement of the anterior portion of the nasal mucosa by split-thickness skin grafts, as advocated by Saunders. The case report describes the recurrence of telangiectasia in the skin grafts with subsequent hemorrhage. The patient was given a successful skin graft in a secondary operation which controlled his hemorrhages.


Studies of the urinary 17-ketosteroids of eight growth hormone-deficient prepubertal children showed levels much lower than those of normal subjects of similar age. After two years of growth hormone administration, both $C_{19}$O2 and $C_{19}$O3 androgen metabolites increased substantially in these subjects, but urinary corticoid levels had not increased proportionately. Androsterone levels demonstrated the most significant increase. 17-KS excretion in response to ACTH was increased after growth hormone therapy, although the corticoid response was not proportionately augmented.

Growth hormone is proposed as one factor responsible for the increasing androgen secretion that characterizes the maturing childhood adrenal.


Parotid masses logically suggest parotid pathology, but the examining physician must be aware that lesions of skin and subcutaneous tissue, parotid lymph nodes, muscles of mastication, mandible, parapharyngeal space, and cervical spine may present as lateral facial swelling. Although the final diagnosis may not be possible until tissue is removed for biopsy, the initial objective is to precisely identify the location of the lesion. Careful inspection and palpation are most important, but the history may suggest a systemic disease, one manifestation of which is the facial swelling. Parotid sialograms and other radiographs may be of some value. The anatomical boundaries of
parotid are so characteristic that the examiner may be able to state by inspection alone that a lesion
does or does not involve the parotid gland. Circumscribed masses usually arise from the gland,
lymph nodes, or skin and subcutaneous tissue. Diffuse swelling is seen with lesions in deeper tissues.
Diseases which affect parotid lymph nodes, producing such a circumscribed mass, may be clinically
indistinguishable from true parotid tumors. The paper presents patients with an epithelial cyst,
masseter hypertrophy, metastases to parotid nodes and mandible, primary tumor of the mandible
and cervical spine, inflammatory lesions of the mandible and tumors of the parapharyngeal space
in which a diagnosis of primary parotid tumor was considered.

Hypophosphatemic vitamin D refractory rickets and osteomalacia. A Parfitt,

The almost complete disappearance of dietary vitamin D deficiency from affluent countries was
a necessary prelude to the recognition that rickets and osteomalacia could occur despite a normal
intake of vitamin D. This led to the concept of vitamin D resistance, since the mineralization
defect could be overcome by vitamin D in amounts 50 to 1000 times larger than the normal require-
ment for prophylaxis. A large number of different diseases characterized by vitamin D resistance
have now been identified, many of which were formerly confused or thought to be variants of the
same condition. This process of subdivision is certainly not yet complete, but such is the power
of words over men’s minds that it is still widely assumed that patients given the same label must
have the same disease. Except for members of the same family, this assumption will always be
open to question until the pathogenesis is much more clearly defined. A major subdivision of this
group of patients comprises those in whom, apart from the consequences of rickets or osteomalacia,
the cardinal abnormality is persistent hypophosphatemia. It is with this subgroup that we are con-
terned in this paper.

Renal osteodystrophy. A.M. Parfitt, Orthopedic Clinics of North America 3:681-

The varied osseous manifestations of chronic renal failure, collectively referred to as renal
osteodystrophy, have become more common with the increasing use of maintenance hemodialysis
and renal transplantation. The subject has received extensive coverage in the literature of internal
disease during the past five years; the present paper emphasizes those aspects of special interest
to orthopedists, including some related soft tissue manifestations of uremia. The clinical, radiog-
aphic, and histologic features of renal osteodystrophy are primarily the result of varying combina-
tions of two major pathologic processes — defective mineralization leading to rickets or osteomalacia
and secondary hyperparathyroidism leading to ostetis fibrosa. Osteosclerosis is common but usually
asymptomatic, and osteoporosis is rare in the undialyzed patient but may be the principal lesion
in some patients on maintenance hemodialysis. Each of these abnormalities may resemble the same
abnormality occurring in the absence of renal failure, but together they produce some unique clinical
manifestations and a number of still unsolved problems in pathogenesis.

Short term effectiveness and hemodynamic actions of guanadrel, a new symp-

Pharmacodynamic and hemodynamic effects of guanadrel, a new antihypertensive sympatholytic
agent, were studied in comparison with a known sympatholytic agent, guanethidine. Sixteen male
patients with moderately severe to severe hypertension were selected in a crossover study. Guanad-
rel was found to exert similar hemodynamic effect with guanethidine. It appeared to be as effective
as guanethidine in lowering blood pressure. Unlike guanethidine, guanadrel had a rapid onset and
offset of action, as observed in the study. This pharmacodynamic difference between the drugs
may explain the presence of early morning postural symptoms with guanethidine and their absence
with guanadrel. Apparently, the influence of the last evening dose of guanadrel had dissipated suf-
siently so as to avoid such early morning untoward effects, yet did not dissipate entirely, thereby
preserving satisfactory morning blood pressure control. Tolerance and comparative differences in
side effects to the drugs were discussed.

A system has been developed for the in vivo quantitative analysis of soft tissue. Preliminary work has indicated that $^{109}\text{Cd}$ is an ideal source for such an analysis. The use of this isotope has enabled the authors to determine the percentage of fat in a given sample with 2% accuracy. The attainment of this accuracy depends strongly on the initial assumptions regarding body composition. They consider 77.4% O, 9.03% C, 10.0% H, 2.69% N, .31% K, .24% S, .19% P, .089% N, and .08% Cl to be representative of fat-free tissue; whereas for fat, 77% C, 11.5% O and 1.5% H is the composition of choice. Absorption experiments on assorted fats and lean meats support these assumptions. The apparatus used in these measurements consists of a well collimated source, grazing apertures to reduce the contribution of scattered radiation, and a $1\frac{3}{4}'' \times 1\frac{3}{4}''$ NaI(Tl) crystal. The output pulse of the crystal is fed into a linear amplifier, two parallel single channel analyzers, and two timed scalers. In the course of our laboratory studies a curious anomaly was discovered, namely an apparent variation, with absorber thickness, in the experimental mass absorption coefficient of the lower energy. This problem was subsequently attributed to scattering of the lower energy radiation in the crystal, a problem inherent in the use of $^{109}\text{Cd}$. A mathematical correction, consisting of a subtraction of a constant fraction of the 88 keV intensity from the 85 keV intensity, has been successful in eliminating this error.


The case report of a 10-year-old girl is described. A discussion of the clinical, radiographic and pathologic features of osteoid osteoma is given. Intra-articular osteoid osteoma of the elbow is a rare lesion presenting both diagnostic and therapeutic problems. The differential diagnosis includes rheumatoid arthritis, traumatic synovitis, tuberculosis and osteochondritis. Laminograms of the elbow can be helpful in establishing the diagnosis and localizing the lesion. In children especially early diagnosis and treatment of intra-articular osteoid osteoma are important because the structural changes of the juxta-articular bone may result in permanent disability.


Involuntary motor derangements and calcification of the basal ganglia as manifestations of hypoparathyroidism have received periodic attention in the medical literature. An interesting patient is described who had an unusual paroxysmal motor disturbance due to idiopathic hypoparathyroidism that was corrected with vitamin D. Patients with extrapyramidal motor dysfunction should be screened for hypoparathyroidism irrespective of roentgenologic evidence of calcification in the basal ganglia. Treatment for hypoparathyroidism in such cases will usually result in substantial improvement. Certainly the possibility of hypoparathyroidism should be considered before other, less effective and more involved methods of therapy for syndromes of the basal ganglia are initiated.


In a double-blind test to determine whether the antinuclear factor (ANF) was present in patients with psychiatric disorders, a significantly greater number of positive ANF results was found in patients whose conditions were characterized by depression.