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## **Publications of the Staff**

of the Henry Ford Hospital and the Edsel B. Ford Institute for Medical Research

Titles and Selected Abstracts

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

Crystal dynamics in gout and pseudogout. G. B. Bluhm, J. M. Riddle, M. I. Barnhart, H. Duncan, and J. W. Sigler. *Med Times* 97:135-44, Jun 1969.

These two crystalline deposition diseases present clinically as an acute inflammatory arthritis. Monosodium urate (MSU) crystals are regularly found in the synovial fluid in gout whereas the calcium pyrophosphate dihydrate (CPPD) crystals are present in the synovial fluid of pseudogout. Because the treatment of these two diseases is vastly different, it is imperative to ascertain the diagnosis. Although both crystals are birefringent, the use of compensated polarizing microscopy serves to distinguish the negative birefringence of MSU and the positive birefringence of CPPD. The fluorescent and electron microscopy findings are also different. The findings support the intracellular formation of MSU crystals within neutrophils, whereas CPPD crystals, when present in exudative leucocytes, were invariably within phagocytic vacuoles. A discussion is presented of the pathogenesis which appears different in the two diseases. A summary is provided of the pharmacodynamics of the available drugs used to treat the crystalline deposition diseases.

The immunofluorescent "band" test for lupus erythematosus. I. Morphologic variations of the band of localized immunoglobulins at the dermal-epidermal junction in lupus erythematosus. T. K. Burnham and G. Fine. *Arch Derm* 99:413-20, Apr 1969.

Biopsies of skin lesions and the clinically normal skin of patients with systemic lupus erythematosus (SLE), discoid LE (DLE), and various dermatoses were tested by the direct fluorescent antibody technique for the band of localized immunoglobulins at the dermal-tpidermal junction present in LE skin. In LE, three immunofluorescent band patterns were found: homogeneous, thready, and stippled. The homogeneous or solid band was seen only in chronic atrophic or hyperkeratotic lesions while the thready band was present in newer crythematous edematous lesions and in clinically normal SLE skin. The stippled band was found essentially only in clinically normal SLE skin even in SLE patients without LE skin lesions. In using the presence of the band as a diagnostic adjunct, awareness of the different immuno-fluorescent "band" patterns that may occur at the dermal-epidermal junction in LE tkin is essential to confirmation of a clinical diagnosis of LE—even in patients without LE tkin lesions.

#### **Abstracts**

The immunofluorescent tumor imprint technique. IV. The significance of "thready" nuclear immunofluorescence. T. K. Burnham, T. R. Neblett, G. Fine and P. Bank. *Arch Derm* 99:611-6, May 1969.

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Sera of 4,823 patients with connective tissue diseases, dermatoses, and various medical diseases were tested for antinuclear antibodies by the immunofluorscent tumor imprint technique. This technique employs touch imprints of tumors as nuclear substrate to detect anti-nuclear antibodies by indirect immunofluorescence. Thready nuclear immunofluorescence was seen much more frequently in systemic lupus erythematosus (SLE) (37.9% of the antinuclear factor positive patients) than in rheumatoid arthritis (4.3% of the antinuclear factor positive patients). If thready nuclear immunofluorescence is seen, systemic lupus erythematosus is statistically the best diagnosis in a clinically atypical patient who is suspected of having either SLE or rheumatoid arthritis. These findings emphasize the need for strict attention to nuclear immunofluorescent morphology, to enhance the diagnostic value of antinuclear factor tests.

Paget's disease of bone (Osteitis Deformans). H. Duncan, in Wolber, P.G.H., et al (eds): *Tice's Practice of Medicine*, Hagerstown, Maryland: Hooper Medical Div., Harper & Row Publisher, Inc., 1969, vol 5, chapt 54, pp 1-9.

This succinct review of Paget's disease of the bone alerts the physician to its asymptomatic onset after the age of 40 years. It is usually discovered when obtaining x-rays for other unrelated diseases. When the skull is involved, hearing may become impaired. A fracture can occur at the site of bone involvement. Rarely, sarcomatous bone change occurs. Etiology is unknown and therapy is empiric. Association with gout may be more than coincidental.

Comparative utilization of glycine-N<sup>15</sup> administered orally or parenterally. O. H. Gaebler and H. C. Choitz. *Metabolism* 18:416-21, May 1969.

Metabolism of identical amounts of N<sup>15</sup> from labeled glycine administered orally, subcutaneously, or intravenously was compared in three experiments on each of two female dogs. The observations were made during absorption of a complete mixture of amino acids originating from ingested protein. N<sup>15</sup> excreted in the urine, its partition between urea and ammonia, and its incorporation into fibrinogen and eight protein fractions obtained from plasma by dialysis and DEAE-cellulose chromatography, were determined 6, 12, 24 and 48 hours after labeled glycine was given. Excretion of N<sup>15</sup> as urea and incorporation of N<sup>15</sup> into plasma proteins both occurred more rapidly when labeled glycine was administered parenterally than when it was ingested. Thus, the net result was that utilization of the amino acid, as indicated by the amount of N<sup>15</sup> retained after 48 hours, or by atom per cent excess of N<sup>15</sup> found in plasma protein nitrogen after 12 hours, was not significantly different in the three types of experiments. Although the amount of N<sup>15</sup> excreted as urinary ammonia was relatively small, it was largest when glycine was administered orally, particularly during the first two 6-hour periods.

Basic pressures of voiding in the adult female. C. P. Hodgkinson and J. E. Morgan. Amer J Obstet Gynec 103: 755-72, Mar 15, 1969.

Basic extravesical and intravesical pressure changes involved in voiding were discriminated by electronically recording simultaneously the intravesical, intraurethral, and intravectal pressures in 65 adult females. Voiding was initiated by Valsalva stress in 39%, by detrusor contraction in 33%, and by mixed pressures in 28%. Once voiding was established the pressure of Valsalva stress frequently dropped out, leaving the evacuation phase of voiding to detrusor contraction. After-voiding contractions occurred as frequently from Valsalva stress as from detrusor contraction. Evidence in four patients with chronic partial urinary retention suggested that it might have been due to intense psychic trauma incidental to vaginal plastic surgery. A precise mechanism of voiding for the adult female could not be established. Willful control over detrusor function was confirmed.

### **Abstracts**

Tumors of major salivary glands in children. K. Hoffmann and M. A. Block. *Mich Med* 67:1461-4, Dec 1968.

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A review of 22 patients, up to 16 years of age at the time of diagnosis, emphasized the need for management of tumors of a major salivary gland, exclusive of acute inflammatory processes, in children in the same manner as in adults. Of this group of patients, representing approximately five per cent of all patients seen over a 21-year period, with tumors of the parotid or submaxillary glands, two of seven with mixed tumors and four with mucoepidermoid tumors were initially seen because of local recurrence following a previous local excision. Thus, an initial wide excision is required, consisting of at least a superficial parotidectomy or excision of the submaxillary gland, and not mere enucleation of the lesion. Tumors of major salivary glands in infancy are distinguished by being hemangioendotheliomas, angiomas, or other congenital lesions. Except for biopsy to rule out rare sarcomas or embryomas or excision because of size, ulceration, or hemorrhage, surgical removal of such lesions usually is avoided during the first two years of life to obviate facial nerve damage. Although chronic sialadenitis in children can usually be managed conservatively, operation is required occasionally for severe manifestations not responding to nonsurgical treatment.

Associated primary hyperparathyroidism and thyroid lesions. V. O. Laing, B. Frame and M. A. Block. *Arch Surg* 98:709-12, Jun 1969.

In a retrospective review of 72 patients with primary hyperparathyroidism, 29 (40%) were found to have clinically evident nodular change in their thyroids for which surgical definition was also considered necessary. The thyroid lesions found in the 29 patients included benign nodular thyroids in 21, thyroid carcinoma in four, chronic lymphocytic thyroiditis in three, and toxic nodular goiter in one. Combined thyroid and parathyroid disease was recognized preoperatively in 17 of the 29 patients, with an incidental parathyroid tumor found at the time of operation for nodular goiter in five patients, and a nodular thyroid recognized at the time of operation for hyperparathyroidism in seven patients. In a review of 100 consecutive autopsies, routinely performed, benign thyroid nodules were found in 14% and thyroid carcinoma in 1%. A comparison of this data with that of patients with primary hyperparathyroidism and with the experience of others indicates that benign thyroid nodules occur in hyperparathyroidism with a significantly increased incidence. Whether there occurs a significant increased coexistence of thyroid carcinoma in hyperparathyroidism is not conclusive. A patient undergoing surgery primarily for either thyroid or parathyroid disease should be evaluated preoperatively and at the time of operation for gross and functional abnormalities in the other gland or glands.

Necrotizing enteritis in Crohn's disease of the small bowel. M. Mogadam and R. J. Priest. Gastroenterology 56:337-41, Feb 1969.

Acute free perforation of the small bowel in regional enteritis occurred in six cases. In three cases, the clinical course was that of fulminating necrotizing enteritis (enteritis necroticans) characterized by "showers" of perforations, patchy necrosis of the bowel in areas not involved with regional enteritis, and fatal outcome. The roles of intestinal bacteria and corticosteroids in relation to this necrotizing process are discussed.

Observations on the mechanism of hemorrhagic toxicity in mithramycin (NSC 24559) therapy. R. W. Monto, R. W. Talley, M. J. Caldwell, W. C. Levin, and M. M. Guest. *Cancer Res* 29:697-704, Mar 1969.

The administration of mithramycin, a useful agent in the treatment of testicular tumors, has been accompanied by a marked hemorrhagic diathesis in many patients. A study was undertaken to evaluate toxic effects of this drug on the terminal vascular bed, platelets, coagulation, and fibrinolytic systems. Observations were made on 41 patients, eight of whom here studied serially. Abnormalities, varying in degree, were found in parameters of each

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patient's hemostatic mechanism. Vascular damage was noted in vivo and in vitro and was considered to be of major importance in initiating bleeding. In addition to significant throm-bocytopenia, altered platelet function was observed. Depression of Factors II, V, VII, and X occurred regularly. There appeared to be an increase in fibrinolytic activity in most patients tested. The degree of abnormality of any single factor in the hemostatic mechanism may be insufficient to produce a hemorrhagic diathesis, but a combination of such factors is capable of producing severe mucous membrane hemorrhage. The incidence of hemorrhagic toxicity was related to dose and appeared to be cumulative in subsequent courses. Interruption of mithramycin therapy because of hemorrhagic toxicity is based upon clinical judgment supplemented by the following guidelines: (a) marked facial flush and edema; (b) persistent epistaxis; (c) bleeding time (Duke) greater than 15 minutes; (d) platelet count less than 50,000 per cu mm; (e) prothrombin consumption of less than 17 seconds; and (f) significant increase in fibrinolytic activity.

A method for making color prints of gastrocamera photographs. K. Morehead, J. Kroll and B. M. Schuman. *Gastroint Endosc* 15:211-2, May 1969.

A method is described for providing a color Polaroid print to supplement the written report of a gastrocamera examination. A Polaroid MP-3 unit with a 16 mm macro lens, which has a fixed stop of F 4.5 and a Polaroid special shutter, is used. An Ascor unit model A423, with the flash tube three inches from the gastrocamera film strip transparency, allows a focus to be obtained. The Polaroid color print becomes a part of the patient's record.

Intravenous infusion drop artifacts. F. K. Redding, V. Wandel and C. Nasser. Eectroenceph Clin Neurophysiol 26:318-20, 1969.

In a series of electroencephalograms done on patients receiving intravenous infusions, about one third of the records were found to display a curious fast transient artifact, synchronous with the falling droplets of the intravenous infusion, and of a stereotyped form. Usually this was a brief series of one, two, three, or sometimes more, positive and negative fast waves at a frequency of 14-18/sec. Amplitude ranged from 50 to over 150 microvolts. These were recorded over wide areas of one or both sides of the head, or sometimes only one or a few electrodes. The artifacts are thought to be an electrical effect due to a static charge on the contents of the I.V. bottle. These have not been previously reported in the EEG literature.

Temporary transection of the left renal vein: a technical aid in aortic surgery. D. E. Szilagyi, R. F. Smith, and J. P. Elliott. Surgery 65:32-40, Jan 1969.

In the process of freeing the abdominal aorta in the region of its large visceral branches in particular at or near the renal arteries, dissection may be seriously hampered by the anatomical disposition of the left renal vein. The presence of this structure in the operative field may be particularly troublesome when the surgeon tries to gain access to a right renal artery which is in an anomalously posterolateral position, or when he is dealing with a high aortic occlusion or with a large aortic aneurysm encroaching on the renal arteries, both latter circumstances calling for the freeing and clamping of the suprarenal aorta. In such instances temporary transection of the left renal vein and the lateral retraction of its stumps make exposure remarkably easier and faster. Experience with this maneuver in 20 instances over a four year period has shown that the left renal vein can be safely interrupted without damage to the function of the left kidney provided the principal tributaries, in particular the left gonadal and the adrenal veins, are preserved. The resuturing of a divided vein is recommended since the performance of the anastomosis is simple and quick, the adequacy of collateral venous circulation in a given case is impossible to determine without extensive dissection and the renal parenchyma—physiologically often substandard in the cases under discussionmay be vulnerable even to the relatively minor effects of permanent venous congestion.

Toluene-diisocyanate asthma. L. C. Sweet. Univ Mich Med Cent J 34(1):27-9, Jan-Feb 1968.

Toluene-diisocyanate (TDI) is a reactive organic compound used in the manufacture of lacquers, adhesives, plastics, rigid elastic foams, and synthetic rubber. TDI is a known potent respiratory tract irritant; however, some workers exposed to supposedly "safe" concentrations of TDI vapor have developed lower respiratory tract symptoms indistinguishable from bronchial asthma. A 49-year-old engineer engaged in the manufacture of polyurethane foam dolls had developed this syndrome and was studied by means of provocative nebulization of TDI. Diminution of pulmonary function and the onset of wheezing supported the apparent association of TDI and the patient's asthma. The exact mechanism by which TDI produces asthma, however, remains in doubt.

Bypass flow requirements during thoracic aneurysmectomy with particular attention to the prevention of left heart failure. R. E. Taber and H. R. Hug. J. Thorac Cardiov Surg 57:203-213, Feb 1969.

This investigation concerned the bypass flow requirements necessary to decompress the left heart and prevent myocardial failure from overdistention. Thirty dogs were divided into five groups. A control group underwent clamping of the aorta without bypass, and bypass without clamping of the aorta. The other groups were bypassed at flow rates varying from 40 to 90 cc per kilogram per minute. Evidence of left heart failure was detected by noting elevations of the monitored ventricular diastolic pressure and of the left atrial mean pressure. Ventricular work was also calculated using the planimetric method. Clamping the canine thoracic aorta for 30 minutes without bypass resulted in a high incidence of left heart failure and subsequent death. The bypass group without aortic clamping did not show signs of failure. Bypass flow rates of 40 and 60 cc per kilogram per minute were inadequate to decompress the left heart in the majority of animals during aortic clamping. To avoid any signs of myocardial strain or failure, it was necessary to regulate the bypass flow rate at 60 to 100 cc per kilogram per minute to maintain a normal left atrial pressure. Thoracic aneurysmectomy experience with left heart bypass is presented in five patients using the flow regulation principles developed in these experiments.

Treatment of metastatic hypernephroma. R. W. Talley, E. L. Moorhead II, W. G. Tucker, E. L. San Diego, and M. J. Brennan. *JAMA* 207:322-8, Jan 13, 1969.

Conventional therapeutic methods (radiotherapy, surgery, and chemotherapy) have been unsatisfactory in the treatment of metastatic hypernephroma. Early detection is thwarted because hypernephroma often is asymptomatic until far-advanced. A retrospective six-year review, of 72 patients treated at Henry Ford Hospital, revealed that patients in whom metastass occurred 18 months or longer after initial diagnosis had a median survival of almost 15 months as compared to approximately eight months for patients with earlier metastases. Currently, radiotherapy is not recommended as primary treatment for hypernephroma; the value of postoperative radiation remains controversial. In this series, radiation therapy frequently palliated symptoms produced by local metastases but did not alter survival patterns. Excision of single metastatic deposits was associated with increased survival in three of four patients with pulmonary metastases, and in two of three patients with thyroid metastases. As rule, systemic chemotherapy was unrewarding. Two excellent objective regressions were blained in 16 patients treated with progestational agents. Case histories are presented of the wo patients in whom objective regressions were observed, one patient received hydroxyrogesterone caproate; the other patient received medroxyprogesterone acetate. After 46 and months respectively, both patients are alive with continuing arrest of their disease. Results of trials with various chemotherapeutic agents, androgens, corticosteroids, and progestational agents are summarized in detail.

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