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Publications of the Staff

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Titles and Selected Abstracts

Edited by G. B. Bluhm, MD

Effects of various protein-modifying agents and the aminonucleoside of puromycin on dithioerythritol-reducible disulfide in glomerular basement membrane.

P. D. Bartlett, M-H Tu, L. Katona and D. Glotzhober. *Research Communications in Chemical Pathology and Pharmacology* **10**: 673-680, 1975.

Comparative study of dithioerythritol-reducible (DTE) disulfide bonds in glomerular basement membranes (GBM) isolated from normal rats and from similar groups of rats treated with the nephrosis-producing aminonucleoside of puromycin emphasize not only the importance of such linkages in the interaction and structural organization of the macromolecular GBM collagen-glycoprotein matrix but also suggest a modality by which GBM semi-permeability might be engendered. Although DTE-reducible disulfide is significantly reduced in GBM of rats as early as the fourth day after administration of a nephrosis-producing

dose of the aminonucleoside, it has not been possible to demonstrate an unequivocal *in vitro* or direct effect of the drug on DTE-reducible disulfide in normal GBM. Several-fold increases in DTE-reducible disulfide in GBM subjected to the denaturing action of guanidine-HCl or the proteolytic action of pronase indicates that most of the disulfide lies buried in the GBM. Location of disulfide crosslinks in the innermost regions or core of the GBM might be expected to not only stabilize the membrane but also to protect the GBM from a considerable array of disulfide cleaving (reductases) within the kidney cortex.

Interpretative problems in endoscopic retrograde cholangiopancreatography. M. A. Block, B. M. Schuman, and M. L. Weckstein. *Am J Surg* **129**:29-33, 1975

The technic of endoscopic retrograde cholangiopancreatography (ERCP) has advanced and become sufficiently standardized and successful in experienced hands that assessment of real and potential problems of interpretation is justified. In a study of 41 patients with biliary tract disease, producing jaundice in 35, some difficulty in interpretation was noted for 10. The duodenal papillae were cannulated successfully in 83% of these patients, a total of 11 patients being examined during the period of study. Interpretative problems of a radiologic variety included incomplete filling of extrahepatic biliary ducts in 5 of 32 patients without mechanical obstruction to these ducts.

The gallbladder was visualized in 8 of 15 patients with intact gallbladders. Other limitations of ERCP included inability to define minute stones in the bile ducts, problems related to variations in the course and configuration of ducts due to anatomic and pathologic changes, and absence of visualization of ducts proximal to a stricture. The specific lesion producing biliary tract obstruction is not defined by ERCP. Limitations in endoscopic interpretation of ERCP included differentiation of inflammatory and malignant changes in the ampulla of Vater by visual and biopsy information. Findings from ERCP must be correlated with other available clinical data.

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Management of primary hyperparathyroidism in the elderly. M. A. Block, A. Xavier, B. E. Brush. *J Amer Geriat Soc* 23:385-389, 1975.

Of 166 surgical patients for whom the diagnosis of primary hyperparathyroidism was established over a 20-year period, about one-third were over 60 years of age. For an additional 9 patients, no operation was advised, usually because of other life-endangering disease and the presence of only a mild degree of hypercalcemia without complications. In recent years, nearly 50% of the patients did not have renal calculi or osteitis fibrosa cystica; this was unrelated to age. Most of the patients with management problems were seen since 1965. Age alone was not a dominant factor in relation to serious complications from hypercalcemia, the presence of other critical disease increasing the risk of operation, or the development of major postoperative complications. The only death from primary hyperparathyroidism

occurred in a 74-year-old patient who refused reoperation and died from an acute hypercalcemic crisis. A liberal, but selective, policy of surgical treatment is justified for primary hyperparathyroidism in the elderly. Patients for whom the diagnosis of primary hyperparathyroidism is established may be separated into three groups: those for whom early operation is indicated, those for whom operation should be delayed to permit recovery from other life-endangering acute disease, and those for whom operation is unjustified because of minimal uncomplicated hypercalcemia and other serious disease greatly limiting life expectancy. These categories encompass all age groups and are not restricted to the elderly. All patients require periodic re-evaluation.

Treatment of rheumatoid arthritis with gold. G. B. Bluhm. *Semin Arth Rheum* 5:147-166, 1975.

The clinical benefit from gold therapy in rheumatoid arthritis (RA) was first suggested by Forestier. Only recently have controlled evaluations of gold therapy, by objective and subjective clinical measurements, confirmed significant relief from joint swelling and pain, as well as improved function, in patients who received gold. Because gold salts can also reduce or arrest progression of rheumatoid joint disease as evaluated by x-ray, its continued use is appropriate for treatment until such time as prevention and cure

of RA is discovered. From 1927 to 1975 a wealth of published reports about gold preparations, tissue distribution, mode of action, selection of patients, regimens for administration, clinical results, and drug toxicity has accumulated. Representative articles are cited for these points and used to outline a practical regimen of gold therapy for the patient with active rheumatoid disease. Guidelines for treatment are detailed in the article and will hopefully permit the patient to reap the maximum benefit of gold therapy.

Spontaneous closure of paravalvular leak after mitral valve replacement. W. F. C. Duvernoy, L. Gonzalez-Lavin, and D. T. Anbe. *Chest* 68:102-104, 1975.

Complications after prosthetic valve replacement may be multiple. In biologic valves, valve detachment and cusp perforation may occur. If this is of significant magnitude, reoperation may be required. This report describes recurrent mitral regurgitation after mitral valve replacement with a

Hancock porcine xenograft. The regurgitation subsided spontaneously three months later. We felt that a paravalvular leak closed, with progressive fibrosis and tightening of the annulus. Functional results in this patient were excellent.

Diagnosis and management of the common congenital cardiac defects. G. M. Folger. *Mich Med* 74:623-633, 1975.

The neonate with symptomatic heart disease presents a challenge to the pediatrician, neonatologist, and pediatric cardiologist. Proper care, including prompt diagnosis and surgical management where indicated gives this infant, although

desperately ill, significant chance to survive. Often there are no sequelae associated with the condition or its treatment. This communication outlines the maneuvers in recognition of the stressed newborn and the differentiation of pul-

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monary disease from cardiovascular. Attention is called to the need for prompt diagnosis when the child is cyanotic and stresses the importance of immediate management of an underlying malformation of the heart as well as the resultant hypoxemia. The more commonly encountered cardiovascular lesions are considered in respect to the

presence or absence of cyanosis and the diagnostic and therapeutic management is outlined. Those abnormalities resulting in hypoxemia are stressed and it is emphasized that these infants, regardless of the severity of the malformation, should be given every opportunity for survival.

Inherited antithrombin-III deficiency causing mesenteric venous infarction: A new clinical entity J. C. Gruenberg, R. C. Smallridge, and R. D. Rosenberg. *Ann Surg* **181**:791-794, 1975.

Primary superior mesenteric venous thrombosis is sometimes preceded by peripheral thrombophlebitis. Inherited antithrombin-III deficiency is a recently recognized autosomal dominant trait, which is characterized by thrombophlebitis and pulmonary embolism. This case report illustrates many features of both entities and strongly suggests a causal relationship. While long-term therapy has yet to be established, prophylactic therapy is recommended when asymptomatic in-

dividuals with known antithrombin-III deficiency are at increased risk of thrombosis. The efficacy of heparin alone has been unreliable, whereas Coumadin has been encouraging. Antithrombin-III concentrates are being developed and theoretically should be helpful. Patients with thrombophlebitis or pulmonary embolism should be suspected of having antithrombin-III deficiency. Such individuals also represent one mechanism to explain "primary" mesenteric venous thrombosis.

Citrobacter diversus at Grace Hospital, Detroit, Michigan. A. Madrazo, J. Geiger, C. B. Lauter. *Amer J Med Sci* **270**:497-501, 1975.

Over a six-month period from December 1973 to June 1974, isolations of *Citrobacter diversus* were obtained from nine patients at Grace Hospital. Our initial experience was with a patient who developed pneumonitis and a massive fatal empyema due to this organism. Seven of the nine patients were 50 years of age. Three patients had an underlying malignancy. Four patients experienced significant clinical infections. Isolations in three patients were considered to be commensal,

and two isolations were of indeterminate significance. Our *Citrobacter diversus* isolates, which can be confused with *Escherichia coli*, were uniformly resistant to ampicillin and carbenicillin and sensitive to the cephalosporins, tetracyclines, and gentamicin. These results agree with previous reports. *Citrobacter diversus* appears to be capable of causing serious clinical disease. Patients most at risk are elderly compromised hosts and infections are usually hospital acquired.

Massive empyema due to Citrobacter diversus. A. Madrazo, M. D. Henderson, L. Baker, V. K. Vaitkevicius, and C. B. Lauter. *Chest* **68**:104-6, July, 1975.

Citrobacter diversus is a gram-negative rod member of the Enterobacteriaceae family. A patient is described from whom this organism was isolated twice in pure culture from empyema fluid. Our isolates of *Citrobacter diversus* were resistant to ampicillin and carbenicillin and sensitive to cephalothin. *Citrobacter diversus* should be

distinguished from *Citrobacter freundii*, *Enterobacter cloacae* and *Klebsiella pneumoniae*. This organism joins *Streptococcus pyogenes*, bacteroides species, anaerobic streptococci and *Escherichia coli* as a slight pneumonia with extensive empyema.

Natural history of uncomplicated valvular pulmonic stenosis. M. R. Mody. *Amer Heart J* **90**:317-321, 1975.

Sixty-eight patients, with isolated valvular pulmonic stenosis with intact ventricular septum

diagnosed by cardiac catheterization, underwent a repeat study one to twelve years later which

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documented the progression of the lesion. These 68 patients were classified into two groups according to age. Group I comprised 37 patients who were less than one year of age at the initial study, and Group II comprised 31 patients who were older than one year of age at the time of the initial study. These 68 patients were divided into three groups according to their systolic right ventricular pressure and classified as mild, moderate, or severe. Increasing severity of the lesion was noted much more frequently in Group I, even with patients who were noted to have mild stenosis at

initial cardiac catheterization. This was not as marked in Group II. The incidence of patient foramen ovale was noted to be much higher in Group I. Also, a much greater number of patients required surgery after repeat cardiac catheterization in Group I. The data suggest that mild cases of pulmonic stenosis in Group I can become severe at a later date, whereas this was less likely in Group II. Those with moderate and severe stenosis can remain the same or become more severe as age advances in both groups.

Colonoscopy in inflammatory bowel disease. N. T. Tawile, R. J. Priest, and B. M. Schuman. *Gastroint Endosc* 22:11-13, 1975.

Utilizing colonoscopic examination in 40 patients with inflammatory bowel disease, the authors were often able to detect bleeding sites, obtain biopsy specimens for histologic confirma-

tion, and more accurately assess the linear extent of disease than was apparent in radiographic studies.

Effect of cellulose phosphate on calcium and magnesium homeostasis: studies in normal subjects and patients with latent hypoparathyroidism. A. M. Parfitt. *Clin Sci & Mol Med* 49:83-90, 1975.

The bivalent cation-binding agent, cellulose phosphate, was given for six days to four normal subjects and six patients with latent hypoparathyroidism (diagnosed by impaired response to EDTA infusion), all of whom were on a moderately low calcium diet.

In normal subjects, there was a prompt and sustained fall in urinary calcium with no change in plasma calcium, indicating increased tubular reabsorption. Plasma and urinary magnesium fell, without increase in tubular reabsorption. The urinary total hydroxyproline increased and $T_{m,P}$ /glomerular filtration rate fell after two days; these changes were transient and were consistent with a transient increase in parathyroid hormone secretion.

In the hypoparathyroid patients, urinary calcium fell more slowly and a fall in plasma calcium occurred in several subjects, the extent and dura-

tion of which corresponded with parathyroid status determined by EDTA infusion. Urinary conservation of calcium was impaired but plasma and urinary magnesium fell as in normal subjects. Urinary total hydroxyproline did not change and $T_{m,P}$ /glomerular filtration rate fell more slowly than in the normal subjects.

The relative contributions of increased tubular reabsorption and reduced filtered load to calcium conservation in response to calcium depletion depend on the prevailing level of parathyroid function; the former is more important when parathyroid function is normal, the latter when parathyroid function is impaired.

In the detection of reduced parathyroid reserve, the assessment based on the plasma calcium response to cellulose phosphate agrees closely with the assessment based on the degree of recovery from EDTA-induced hypocalcemia.

Effect of cellulose phosphate and dietary calcium restriction in primary hyperparathyroidism. A. M. Parfitt. *Clin Sci & Mol Med* 49:91-98, 1975.

The bivalent cation-binding agent, cellulose phosphate, together with a low calcium diet was given for six days to nine patients with primary hyperparathyroidism subsequently verified at surgery.

Urinary calcium fell promptly by $8.4 \text{ mmol}/24 \text{ h}$, and by 70%, and reached amounts below 4.0

$\text{mmol}/24 \text{ h}$ in five of the nine patients. The magnitude of fall may have been related to increased synthesis of vitamin D by the skin in a subtropical environment. Plasma magnesium fell steadily and urinary magnesium fell by 80%.

The plasma calcium showed two types of response. In five patients there was no significant

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change because a reduction in calcium load was offset by a further increase in the already high tubular reabsorption of calcium. In the remaining four patients, the tubular reabsorption of calcium was at a higher level initially and failed to increase further on the experimental regimen, with a corresponding fall in plasma calcium.

The hypercalcemia of primary hyperparathyroidism can be explained by increased gastrointestinal absorption and increased renal tubular reabsorption of calcium; net bone resorption makes only a small contribution but an additional factor dependent on the blood-bone equilibrium is not ruled out.

Comparison with other published data suggests

that the fall in urinary calcium in response to a calcium-depleting regimen is prevented by concurrent depletion of inorganic phosphate and may be enhanced by concurrent depletion of magnesium.

Persistence of hypercalcemia combined with an increase in tubular reabsorption of calcium in response to cellulose phosphate may be of diagnostic value in suspected primary hyperparathyroidism.

Cellulose phosphate may be of value in stone prevention in patients with primary hyperparathyroidism who are unsuitable for surgical treatment.

Patterns of care — radiation therapy in Michigan. J. E. White. *Mich Med* 74:639-640, 1975.

A survey of the type and location of radiation therapy resources in the state of Michigan was undertaken under the auspices of the Michigan Society of Therapeutic Radiologists. Nearly half of the institutions performing therapy have no megavoltage equipment. Only 6.7% of institutions with megavoltage equipment also have specialized treatment planning equipment such as simulators. Less than half of institutions with megavoltage

equipment (less than 25% overall) utilize computerized dosimetry. County maps detailing geographic distribution of equipment are available. The importance of megavoltage therapy, ancillary planning equipment, and specially trained personnel are discussed. The problem of cost-effectiveness related to geographic distribution is also discussed.

Synovial fluid analysis. S. R. Yehia and H. Duncan. *Clinical Orthopaedics and Related Research* 107:11-24, 1975.

Synovial fluid analysis plays an important role in the differential diagnosis of various forms of arthritis. The results of macroscopic, biochemical, bacteriological, and microscopic techniques of evaluating synovial fluid must be correlated to

establish the diagnosis of each of the various forms of arthritis. The principle of polarized microscopy as applied to the differential diagnosis of crystalline arthritis is currently of special interest.

The diagnosis of cancer of the biliary tract and pancreas by endoscopic retrograde cannulation. M. C. Zonca, B. M. Schuman and K. H. Wong. *Gastrointestinal Endoscopy* 21:129-132, 1975.

The authors' experience indicates that where cancer of the biliary tract or pancreas is highly suspected but not proven, endoscopic retrograde

cannulation will provide important positive or negative findings to assist in the decision for surgical exploration.

Listed by title only:

Fitzgerald trait deficiency, a hitherto unrecognized agent. Fitzgerald factor, participating in surface-mediated reactions of clotting, fibrinolysis, generation of kinins, and the property of diluted plasma enhancing vascular permeability (pf-Dil). J. P. Abraham, R. Waldmann, O. Ratnoff and H. Saito. *Journal of Clinical Investigation* 55:1082-1089, 1975.

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Fitzgerald factor. A hitherto unrecognized coagulation factor. J. P. Abraham, R. Waldmann, J. A. Caldwell and J. Rebeck. *Lancet*, May 1975.

Tumors of the thyroid. M. A. Block. *Current Diagnosis*, Philadelphia: W. B. Saunders Co., H. F. Conn, M.D., and Rex B. Conn, Jr., M.D., eds., 4th edition. pp. 731-35, 1975.

Antinuclear antibodies—Clinical significance of the nuclear immunofluorescent patterns. T. K. Burnham and P. W. Bank. Letter to the editor, *American Journal of Clinical Pathology* **64**:289-90, 1975.

"Band" test in connective tissue disease. T. K. Burnham. Letters to editor. *Ann Intern Med* **83**:909, 1975.

Electron paramagnetic resonance study of the interaction of a spin-labeled analog of adenosine diphosphoribose with paramagnetic cobalt (II) liver alcohol dehydrogenase. H. R. Drott, D. Santiago and J. D. Shore. *FEBS Letters* **39**:21-23 (Amsterdam) 1974.

Counseling parent and teacher regarding the effects of mild hearing loss. A. B. Graham. *Transactions, American Academy of Ophthalmology and Otolaryngology* **80**:ORL 73-78, 1975.

Proton equilibria and kinetics in the liver alcohol dehydrogenase reaction mechanism. J. D. Shore, H. Gutfreund, R. L. Brooks, D. Santiago and P. Santiago. *Biochemistry* **13**:4185-4191, 1974.

The role of metal in liver alcohol dehydrogenase catalysis. J. D. Shore and D. Santiago. *Journal of Biological Chemistry* **250**:2008-2012, 1975.