

- 49 *Effect of Furosemide on Renal Glycolysis and Oxygen Uptake in Rats.* T. YOSHIDA, P. R. LEWY, L. E. VOYER, A. B. WARD, Y. Y. AL-UBAIDI and J. METCOFF, Dept. of Ped., Michael Reese Hosp. and Med. Center, Chicago, Ill.

Furosemide (F), a potent diuretic agent, is known to inhibit tubular Na⁺ reabsorption. The mechanism of action of F is not known. Since Na⁺ reabsorption is energy dependent, F may inhibit this process by interference with renal energy metabolism.

Normal, fed, 200 g Sprague-Dawley male rats were used in this study. Homogenates of renal cortex and medulla were incubated in a medium containing 5 mM glucose (G). Addition of F (100–200 µg/ml) strongly inhibited formation of lactate ($p < 0.005$), α -glycero-P ($p < 0.005$), and all glycolytic intermediates below 1,3-diP-glycerate ($p < 0.05$) in both tissues; fructose-6-P increased sharply; triose-P formation did not change. The QO_2 of renal cortex and medulla slices obtained from controls, or 1 h after IV injection of F (20 mg/kg), were measured in a Warburg respirometer. Endogenous QO_2 was increased in the F-group cortex and medulla ($p < 0.02$); addition of G (5 mM) enhanced QO_2 in control cortex and medulla ($p < 0.05$) but not in F-group cortex. However, in F-group medulla, a synergistic effect of F+G on enhancement of QO_2 was observed.

Decreased lactate formation from G is consistent with inhibited glycolysis or enhanced Krebs cycle activity; our data indicate both may play a role. Inhibition of glycolysis may be a direct effect of F, or may result from increased Krebs cycle activity [NEWSHOLME *et al.*, *Nature* 193: 270, 1962]. The increased CO_2 with F in renal slices suggests uncoupling of the usual relationship between Na⁺ reabsorption and renal O_2 utilization.

- 50 *Increased Urinary Glomerular Basement Membrane Products in Pyelonephritis.* BORIS LUSTIK, WILLIAM T. KNIKER and CHARLES V. PRYLES, Depts. of Ped., State Univ. of N.Y., Downstate Med. Center, The Jewish Hosp. Med. Center of Brooklyn, and the Univ. of Texas Med. Sch., San Antonio.

Soluble glomerular basement membrane products (gbm-p) are excreted in urines of normal children, but increased excretion of these products occurs in various types of glomerular disease. [Abstracts, Soc. for Ped. Res., p. 9, May 1969.] Since pyelonephritis is a disease in which glomeruli may be involved, gbm-p were searched for in the urines of such patients.

Twenty-four hour urine samples from 83 subjects were concentrated and examined by immunodiffusion against sheep anti-human gbm globulin. Slight to marked increases in gbm-p were found in patients with untreated pyelonephritis. In one of these patients the level of gbm-p exceeded the level found in 3 patients with acute glomerulonephritis. In 2 additional children with acute pyelonephritis the quantity of gbm-p excreted equaled that found in one of the patients with glomerulonephritis. Patients with treated pyelonephritis, cystitis, and congenital renal anomalies without infection excreted gbm-p in the range found of healthy controls.

Sterile urine samples from normal subjects were inoculated with a strain of *E. coli* (0-6) isolated from a patient with acute pyelonephritis, and tested by the same technique in order to rule out cross-reactivity with bacterial antigen. All these tests were negative. These

preliminary studies suggest: (1) that increased excretion of gbm-p may be a manifestation of glomerular involvement in acute pyelonephritis, and (2) that this technique might prove useful in the differential diagnosis of upper vs. lower urinary tract infection.

- 51 *Chemical and Immunologic Characteristics of Glomerular Basement Membrane Fragments in Rat Urine.* S. RAYMOND WONG, CLAUDIUS KULVINSKAS, DONALD B. KAUFMAN and RAWLE M. MCINTOSH. Univ. of California Med. Center, Los Angeles (introduced by Solomon Kaplan).

Glomerular basement membrane (GBM) is composed of a collagen-like component and a carbohydrate rich glycoprotein. GBM fragments have been found in the urine of normal and nephritic man and experimental animals. This study was designed to isolate, purify and chemically and immunologically characterize GBM fragments of rat urine.

A glycoprotein, the major protein in normal rat urine (MUP), was isolated by DEAE ion exchange chromatography and purified by gel filtration on Sephadex G 200. MUP was shown to be a carbohydrate rich glycoprotein with an amino acid content similar to the non-collagen component of GBM. Fluorescein conjugated antisera stained rat glomeruli in a linear pattern. The antisera could be absorbed with rat GBM, rat glomeruli, 8 M urea solubilized GBM but not by rat collagen or the collagen component of GBM. The glycoprotein is similar to albumin in molecular size. In experimental nephrosis, the excretion of MUP is increased and the content of hexose altered.

- 52 *Chemically Induced Polycystic Kidney Disease in the Newborn*¹. JOHN F. S. CROCKER² and ROBERT L. VERNIER, Univ. of Minnesota Hosp., Dep. of Ped., Minneapolis, Minn.

KIME *et al.*, DARMADY and others have shown that diphenylamine (DPA), a fungicide, causes diffuse cystic disease in mature rats fed the compound for 6 months to one year. We report the development of polycystic changes in kidneys of newborn rats born of the mothers a) fed DPA (2 ½% in diet), and b) tube fed 2 ml of 1% DPA in alcohol, for the last 6 days of pregnancy. Controls received diet without DPA or were tube fed alcohol. All 70 newborn in the experimental group showed a) cystic dilatation of the collecting ducts, and b) vacuolar degeneration of the proximal tubules. Micro-dissection studies of the abnormal tubules will be presented.

This new model of cystic disease in the newborn animals demonstrates the increased susceptibility of the neonatal kidney to DPA and provides approaches to improved understanding of the enigma cystic disease.

- 53 *Prospective Study of Nephritis Associated With a New Nephritogenic Type at Red Lake.* PATRICIA FERRIERI, ADNAN S. DAJANI, S. STEPHEN CHAPMAN, JONATHAN JENSEN, LEWIS W. WANNAMAKER, Univ. of Minn. Coll. of Med. Sci., Dept. of Ped., Minneapolis, Minn.

In July 1969 a study of the pathogenesis of impetigo was initiated at the Red Lake Indian Reservation. Serial (3 × weekly) cultures of nose, throat, normal

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