Occurrence and treatment of secondary hyperparathyroidism in children on long-term hemodialysis. DONALD E. POTTER, BETTY S. ROOF, CAROLYN F. PIEL and MALCOLM A. HOLLIDAY. *Univ. of Calif., San Francisco, and San Francisco Gen. Hosp., San Francisco, Calif.*

Twelve children, 2–16 years of age (mean 9.7) were dialyzed 3× weekly for periods of 7–33 months. Bone resorption typical of secondary hyperparathyroidism was present on x-ray at the onset of dialysis in 3 and developed after periods of 3–17 months in 4 more. Mean individual predialysis values were BUN 57–89 mg%, calcium 8.9–10.1 mg%, and phosphorus 4.2–7.2 mg%; there were no differences between the group means of those with bone disease and those without. The mean duration of uremia and/or dialysis was greater in the children who developed bone disease and only 1 of 7 dialyzed >1 year failed to show bone resorption. Plasma parathormone levels were elevated in all children tested (9) but were highest in those with bone disease while alkaline phosphatase levels were elevated in all with bone disease and in only one without. Six children with bone disease were treated with vitamin D, 25–75,000 U daily, for periods of 4–11 months with complete resolution in 2, marked improvement in 3, and progression of disease until transplantation in 1. Fall in parathormone and alkaline phosphatase levels accompanied radiographic improvement. Hypercalcemia occurred in 2 but metastatic calcification, other than conjunctival, was not observed and the children were asymptomatic. The frequency of bone disease in these children was similar to that reported from adult dialysis centers, but the response to vitamin D and lack of toxicity were more favorable than has been reported in adults.

Mesangial nephritis; an entity characterized by mesangial IgA-IgA deposits. PAUL T. MCENERY, A. JAMES MCADAMS, and CLARK D. WEST. *Children's Hosp. Res. Found., Cincinnati, Ohio.*

Berger (Transpl. Proc. *1*:939, 1969) described a group of 55 patients who had divergent glomerular lesions by light microscopy, but by immunofluorescence had mesangial deposits of IgG, IgA and β1C-globulin. Most of the patients had a slowly progressive nephritis characterized by persistent microhematuria and mild proteinuria. Nephrotic syndrome was absent. Half of the patients had episodes of gross hematuria during a sore throat.

We have studied a group of 7 patients (ages 4–14 yrs) with mesangial deposits of IgG, IgA and β1C-globulin which by E. M. are located between mesangial cells and the glomerular basement membrane. Light microscopy revealed minimal increase in mesangial cellularity without matrix proliferation and an occasional mild focal lesion. Onset of disease was heralded by gross hematuria accompanying a respiratory infection and was followed by persistent microhematuria. Proteinuria was moderate with the gross hematuria and later diminshed or disappeared. At no time was hypocomplementemia or other signs of acute nephritis present. Initially many of the patients were considered to have benign recurrent hematuria but differed in that (1) they appeared to have respiratory infections with unusual frequency, each episode being accompanied by gross hematuria and (2) with time a persistent mild proteinuria developed in the absence of gross hematuria. In 3 patients the frequency of URI decreased and the microhematuria disappeared with prednisone therapy. Three patients not receiving prednisone and observed from 1 to 4 years had no evidence of progression of the lesion on repeat renal biopsy.

Subclinical and overt acute glomerulonephritis in children following infections with group A streptococci. INGE SAGEL, ANTONIA TY, AYSE M. YUCEOGLU, GERHARD TRESER, MARTIN SEMAR, EDWARD WASSERMAN, and KURT LANGE (Intr. by Miriam Lending). *N. Y. Med. Coll., New York, N. Y.*

Fluorescein (FIT) labelled IgG fractions from patients with acute poststreptococcal glomerulonephritis (AGN) stain parts of the basement membrane and mesangium of glomeruli from the same patients, provided renal tissue is obtained early in the disease. Staining is abolished by preabsorbing the IgG fractions with disrupted streptococci isolated from patients with AGN. Non-nephritogenic streptococci do not reduce staining. These findings were applied in an epidemiologic survey of a pediatric population with group A streptococcal infections. During a 12-month period 178 children with group A streptococcal infections were followed with weekly examinations including urinalysis and determination of serum complement (CH_{50}) and ASLO titers. Only children in whom these parameters were normal initially were kept in the study. 2 children developed typical AGN. 21 patients were asymptomatic but showed transient urinary abnormalities and decreased CH_{50}. Their renal tissue showed glomerular lesions ranging from mild mesangial increase and endothelial cell proliferation to the characteristic changes seen in AGN. The glomeruli showed granular staining with FIT labelled anti-human IgG and β1C. Streptococci cultured from the children were preserved. Only bacteria isolated from patients with demonstrable glomerular lesions reduced the staining capacity of FIT labelled sera from patients with AGN. Streptococci obtained from patients without evidence of renal involvement failed to preabsorb. It appears that nephritogenicity of streptococci can be predicted. This study suggests that incidence of glomerular damage following group A streptococcal infections is greater than suspected.

Effect of azathioprine in patients with lupus glomerulonephritis. JOHN P. HAYSLETT, CHARLES D. COOK, MICHAEL KASHGARIAN, and BENJAMIN H. SPARGO. *Yale Univ. Sch. of Med., New Haven, Conn.*

Recent studies have shown that the course of lupus glomerulonephritis is usually one of inexorable progression to renal failure despite intensive treatment with glucosteroids. Seventeen patients were treated with low doses of prednisone (<20 mg/day) and azathioprine (2–3 mg/kg/day) for 6 to 36 months. Diagnosis of the renal lesion, by biopsy, included lupus glomerulitis (1), moderately severe glomerulonephritis (4) and severe glomerulonephritis (12). Seven cases with severe nephritis had the nephrotic syndrome and 9/17 were less than age 16 at onset. In one patient proteinuria increased after 24 months of therapy and another with severe renal failure at onset failed to respond. In the remaining 15 cases GFR either returned to normal (3) or remained normal (12). There was a significant reduction in proteinuria in every case, including a remission in 6 patients with the nephrotic syndrome. There was no evidence of progression of the renal lesion, by biopsy, in 9 patients reexamined, including the patient with uremia at onset. In 8 a striking decrease in severity was found, characterized by a relative absence of proliferation and reduction in deposition of electron-dense material. After 24 to 36 months of treatment in 5 patients with severe glomerulonephritis initially there were prominent membranous changes, by electronmicroscopy, which were indistinguishable from membranous nephropathy. This study demonstrates improvement in clinical and histological

features of lupus glomerulonephritis with azathioprine-prednisone therapy. In addition, following suppression of the active proliferative lesion a new finding of membranous transformation was found.

Split products of fibrin in renal disease. ROSEMARY ANANIA and GEORGE A. RICHARD. *Univ. Fla. Coll. Med., Gainesville, Fla.* (Intr. by G. L. Schiebler).

Split Products of Fibrin (SPF) were determined by the tanned red-cell hemagglutination inhibition assay in 331 patients with various types of renal disease. The study included 77 sex-age matched controls. The mean value for SPF in the control group was 4.55 ± 2.46 S. D.

SPF were elevated in the Hemolytic-Uremic Syndrome (1/1), Lupus Erythematosis (SLE) (8/10), Steroid Resistant Nephrosis (SRN) (7/13), Acute Glomerulonephritis (AGN) (13/26), Steroid Dependent Nephrosis (SDN) (8/32), Renal Vein Thrombosis (3/3), Hereditary Nephritis (4/15), Active Anaphylactoid Purpura (2/3), and Hypocomplementaremic Nephritis (1/3).

To a lesser degree, the SPF were elevated in Steroid Sensitive Nephrosis (1/14), Idiopathic Hematuria (3/23), Post Acute Anaphylactoid Purpura (1/14), Post Acute Glomerulonephritis (2/20), Acute Urinary Tract Infection (2/18), and Post Urinary Tract Infection (2/81).

No elevation in the SPF was noted in Orthostatic Proteinuria (16), Idiopathic-Hypertension (15), Single Kidney (15), Hydronephrosis (9), and Chronic Glomerulonephritis without Azotemia (14).

A depressed Beta 1 C/Beta 1 A was closely correlated with the SPF in SLE (9/10) and AGN (24/26). Positive immunofluorescent staining of renal biopsy tissue for at least one immunoglobin was correlated with an elevated SPF in SRN (6), SLE (5), AGN (5), and SDN (3). Immunoflourescent stains for fibrinogen were seldom positive. These data indicate that SPF are not diagnostic, and may be elevated in several types of renal disease.

Antigen identification in Goodpasture's syndrome. RAWLE M. MCINTOSH and WILLIAM R. GRISWOLD (Intr. by Fred G. Smith). *UCLA, Los Angeles, Calif.*

Although there is unquestionable evidence that an anti-basement membrane antibody is involved in the development of the renal lesion in Goodpasture's syndrome the specific antigen has not been clearly identified. In an attempt to clarify this problem serum and antibody eluted from a patient with Goodpasture's syndrome was studied by fixation to normal human glomerular basement membrane (GBM) before and after treatment with collagenase, neuraminidase and 8 M urea. Controls for buffer, pH and temperature were employed. Absorption studies and spleen cell and lymphocyte transformation studies using GBM glycoproteins prepared by method of Kefalides were also performed.

Double layer immunofluorescent studies demonstrated that both serum and eluate fixed to the GBM of untreated normal human kidney and normal human kidney treated with 8 M urea, and neuraminidase. However they did not fix to collagenase treated kidney. This suggests that the collagen like glycoprotein rather than the non-collagenous or sialic acid rich glycoprotein is the antigen which induces autoimmune nephritis in Goodpasture's syndrome. Although cell transformation studies were inconclusive this finding was confirmed by absorption studies.

Nature of kidney-bound antibody in the renal disease of bacterial endocarditis. ROBERT L. LEVY and RICHARD HONG. *Univ. of Wisconsin Med. Ctr., Madison, Wis.*

It is thought that the renal disease which sometimes accompanies bacterial endocarditis is due to antigen-antibody complex mechanisms because of the demonstration of immunoglobulin and complement in histologic specimens; however, the specificity of the antibody is not known. We have attempted to further define the pathogenetic mechanism by elution of kidney-bound protein and investigation of its properties. A patient with no previous renal disease who died of bacterial endocarditis and renal failure was studied. He presented with bacterial endocarditis accompanied by elevations of serum immunoglobulins and ultimately developed a monoclonal IgM. Light microscope examination of the kidney revealed segmental nephritis; fluorescent staining showed deposits of the 3 major classes of immunoglobulins and complement along the glomerular basement membrane (GBM) in a "lumpy-bumpy" distribution. Protein was eluted from the *post-mortem* kidney and radiolabeled with I^{125}. Radioautographic studies showed the presence of IgG and IgA. The eluted antibody was shown to selectively combine with bacteria (formalin fixed) cultured from the patient *ante-mortem*. There was also evidence for anti-GBM antibody activity of the eluate. The eluted antibody was not anti-antibody (i.e. did not selectively combine with IgG coated human red blood cells). The demonstration in the kidney eluate of antibacterial antibody specific for the organism cultured from the patient strongly supports the concept of antigen-antibody complex disease in the pathogenesis of the nephritis which accompanies SBE.

Tamm-Horsfall glycoproteinuria: An early index of human renal allograft rejection. ROBERT H. SCHWARTZ, ALLYN G. MAY, ERIC A. SCHENK, RICHARD B. FREEMAN, MICHAEL F. BRYSON, and JAN VAN ESS. *Univ. of Rochester Sch. of Med., Rochester, N. Y.* (Intr. by Douglas Johnstone).

Urinary glycoprotein of Tamm and Horsfall (T & H) is a renal substance found in the ascending limb of the loop of Henle and the distal convoluted tubule. Excretion can be measured by 0.58 M NaCl precipitation. Normal excretion = (1.7–2.1 mg/hr/1.73 sq. m. body surface area). Increased excretion occurs with dichromate-induced renal tubular damage in rats. This observation suggested that monitoring T & H excretion might provide an early index of kidney damage in human allograft rejection. Eight patients (4 males, 4 females. Age 9–49 years) were studied during the first 37–120 days post-transplantation. Seven rejection episodes in 5 patients were diagnosed clinically. In each instance T & H excretion exceeded 25 mg/24 hours (½ upper limit of normal adult excretion = normal excretion of one kidney) prior to the onset of clinical rejection. The interval between onset of increased excretion and clinical rejection was between 4 and 14 days (mean = 9 days). Peak excretion rates up to 110 mg/24 hours occurred. High excretion rates in chronic rejection (1 patient) and in glomerulonephritis of the transplanted kidney (1 patient) were also observed. In these instances T & H was primarily in the form of insoluble urinary casts. Since anti-rejection measures are likely to be more effective when the diagnosis of a rejection episode is early, T & H measurement has a practical clinical value.

The "swan-neck" lesion in childhood cystinosis. CHARLES P. MAHONEY, GARY E. STRIKER, and GEORGE H. FETTERMAN. *Univ. Wash. Med. Sch., Seattle; Children's Hosp., Pittsburgh, Pa.* (Intr. by Robert P. Igo).