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WEGENER'S GRANULOMATOSIS (WG) IN CHILDHOOD WITH PROLONGED SURVIVAL FOLLOWING CYTOTOXIC THERAPY. A. Vishnu Moorthy, Russell W. Chesney, William E. Segar, and Ted Groshong. The University of Wisconsin Center for Health Sciences, Children's Hospital. Depts of Pediatrics, Medicine and Pathology, Madison, Wisconsin.

Wegener's granulomatosis is a systemic disease of unknown etiology involving mainly the kidney and respiratory tract in a necrotizing and granulomatous vasculitis, though other organ systems may be affected. Only 6 cases have been reported in children under age 16 years and each had a rapidly fatal outcome despite supportive therapy and corticosteroids. Although several studies have reported a good response in adults to cytotoxic therapy, this form of therapy has not been tried in children with WG. We have treated 2 girls, aged 10 and 13 years, with a combination of prednisone and cyclophosphamide therapy for generalized WG with renal, ocular, nasopharyngeal, sinus and cutaneous involvement. One patient also had middle ear pulmonary and laryngeal granulomata. Multiple biopsies of involved tissues confirmed the diagnoses. Cyclophosphamide was capable of inducing remission in disease activity initially and during subsequent relapses. Proteinuria decreased in one patient from 5.2 to 0.8 gm/24 h and her serum creatinine concentration fell from 2.1 to 1.3 mg/dl. Pulmonary granuloma regressed in the second patient. Hemorrhagic cystitis was the only complication of therapy, but did not recur with readministration. These patients have survived 2½ and 5 years respectively. Both are in good health and attending school at present. These are the first children of which we are aware to receive this form of therapy for WG.

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RENAL TUBULAR ACIDOSIS (RTA) IN A PATIENT WITH PARTIAL PERIPHERAL RESISTANCE TO THYROID HORMONES (TH). T. Moshang, Jr., B. Falkner, and R.D. Utiger, Hahnemann Med. Coll., Dept. of Ped., and Univ. of Pa., Dept. of Med., Phila.

In the syndrome of peripheral resistance to TH, variable degrees of resistance in different organ systems have been described. In several reported patients, persistent tachycardia has suggested a lesser degree of resistance of the myocardium to the elevated levels of TH. A 6 yr. old white male with this syndrome had a mild RTA which corrected during treatment with propylthiouracil (PTU). Clinical features included failure to thrive, short stature, mild mental retardation, speech defect, elongated face with slanted eyes, medially displaced large toes, bilateral inguinal hernias, a hydrocoel, and normal cardiovascular findings. Initially, he did not have a goiter but subsequently developed a goiter. Laboratory data: Bone age retarded (2-1½ yrs.) but no stunting of epiphyses. T4=22ug%. T3RU=44%. T3=321ng%. TSH=6uIU/ml. 24 hr. RAIU=63%. The TRH test showed a ΔTSH of 11.5uIU/ml. Venous pH=7.32. CO₂=18mEq/L. Urine pH was 7.0, with a generalized aminoaciduria. Urine Ca excretion was 6mg/24 hrs. Mg=0.09mEq/L. Ca=9.6mg%. The association of hyperthyroidism and RTA has been recorded but the etiologic role of excessive thyroxines in renal tubular dysfunction has been debated. There was no evidence for nephrocalcinosis in this patient. The correction of the RTA during PTU therapy suggests that the kidneys in this patient with partial peripheral resistance to TH was more sensitive to the excessive levels of TH. As importantly, this finding supports the possibility that excessive TH can be toxic to renal tubular function.

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ALTERNATIVE COMPLEMENT PATHWAY (AP) IN CHILDREN WITH NEPHROSIS (CN). Michael E. Norman, Arlene Taylor, and Ulf R. Nilsson (Spon. by Mary Ann South). University of Pennsylvania School of Dental Medicine, Department of Pathology, and Children's Hospital of Philadelphia, Philadelphia, Pa.

In surveying the AP in children, 7 CN with normal serum C3 but low-normal or low-Factor B were studied. Heavy proteinuria was found in all, impaired renal function in 2. Two received daily and 2 alternate day prednisone. Renal biopsy revealed minimal changes in 2, mesangial nephritis in 2; focal, post-strep and congenital nephritis in one each. C3, C4, C5, B, properdin (P), and B₁H were measured by radial immunodiffusion. C function was evaluated by lysis of EA (CH50) or EAC142 in the presence of EDTA (C3--9), lysis of glutathione-treated human E (APLys) and C3 and B conversion on immunoelectrophoresis in fresh serum and following 37°C incubation with buffer or inulin (C3-B/C). All data were compared to age-matched normal children.

	C3	C4	C5	B	P	B ₁ H	CH50	C3--9	APLys	C3-B/C
NL	7	6	7	4	6	7	3	3	4	7
LOW	-	1	-	3	1	-	2	3	2	-

B correlated with APLys, not so well with P, and not at all with B₁H or C3-B/C. B was found in concentrated urine specimens of 2 with low-normal serum B. Classical C activation was present only in post-strep nephritis. Low B levels cannot be explained simply by urinary loss or consumptive depletion, and may reflect depressed synthesis. The relationship of normal C3 to low B remains to be explored, but our data clearly emphasize the importance of age-matched controls in evaluating the AP in children.

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HYPERLIPIDEMIA IN CHRONIC RENAL INSUFFICIENCY (CRI); THE ROLE OF PARATHORMONE (PTH). Z. Papadopolou, L. Tina, R. Sandler, P. Jose, P. Calcagno, Department of Pediatrics, Georgetown University School of Medicine, Washington, D.C.

The onset and pathogenesis of hyperlipidemia in CRI is not well documented in children. Glomerular filtration rate (GFR), total serum lipids (TL), cholesterol (chol), triglycerides (Tg), lipoprotein electrophoresis and PTH levels were measured in 25 non-nephrotic children 4-17 yrs old. GFR was measured by clearance of creatinine, PTH by radioimmunoassay. Group A consisted of 5 children with normal GFR and served as controls, Group B 6 children with GFR 60-95 ml/min/1.73 M², Group C 7 children with GFR 10-40 ml/min/1.73 M² and Group D 7 children on maintenance hemodialysis. The data are tabulated below:

Groups	TL(mg%)	Chol(mg%)	Tg(mg%)	PB*(%)	PTH(pg/ml)
A	465±31	157±12	61±6.0	10.6±1.9	ND
B	531±49	184±20	56±8.7	11.8±3.0	268±45
C	661±37**	208±14**	103±9.0**	13.9±2.7	348±67
D	631±62**	195±19**	135±7.7**	26.0±3.6**	538±85+

*pre beta lipoproteins ND not done **p<0.05 as compared to controls + p<0.05 as compared to group B

The data demonstrate for the first time that the alterations in TL, chol, Tg occur early in CRI when GFR values decrease below 40 ml/min. PB increased only after the onset of hemodialysis. PTH was increased in 2 of 7 children in Group C and in all of Group D. The correlation between PTH and Tg was 0.51 suggesting that additional factors may be associated in the pathogenesis of hyperlipidemia of CRI.

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THE INCIDENCE OF END-STAGE RENAL DISEASE IN CHILDREN Donald E. Potter, Carolyn F. Piel, and Malcolm A. Holliday Univ. of Calif. School of Medicine, Department of Pediatrics, San Francisco.

There is little data concerning the incidence of end-stage renal disease (ESRD) in children. Estimates of 3.5 children 1 to 14 yrs. of age/million total population/year and 3.5 children 1 to 16 yrs./million/yr have been made from death certificate data in the United Kingdom and a hospital survey in Germany respectively. A program of dialysis and transplantation in children started at the Univ. of Calif. in 1966 is the only program in Northern California and Northern Nevada and serves a population area of 7.9 million. The number of children < 17 yrs. of age referred from this area with ESRD is shown below. Children who died with acute renal failure are excluded.

	1966	1970	1974	1975	1976
1	6	12	15	6	18
2	5	11			
3	11	15			
4	13	12			

From 1968 to 1976 inclusive, the incidence of ESRD was 1.59 children/million/yr. With the exception of an unexplained decrease in 1975 and a "rebound" increase in 1976, yearly fluctuations in incidence were small. The mean age of the children was 10.0 yrs.; no child was < 1 yr. of age. The incidence in 3 age groups 1-5, 6-10, and 11-15 yrs. was 0.34, 0.45, and 0.68/million/yr. respectively. Of 124 children referred, 119 were treated with dialysis and/or transplantation. We believe these figures provide a reasonable estimate of the number of children who reach end-stage disease each yr. and are candidates for dialysis and transplantation.

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EFFECT OF GLOMERULAR POLYANION REMOVAL ON PROTEINURIA Edward R. Root, Susan B. Conley, Alan M. Robson. Wash Univ Sch of Med, Dept of Ped, St. Louis

Recent evidence suggests that in addition to the mechanical barrier to glomerular filtration, there is an electrical barrier, probably provided by glomerular polyanion (GPA), a negatively-charged glycoprotein lining glomerular epithelial foot processes. Loss of GPA may cause proteinuria in glomerulonephritis. Conversely, albumin infusion into normal animals reduces GPA and increases proteinuria. Since loss of GPA can be produced by perfusion of kidneys with a polycation (e.g. protamine sulfate, Seiler et al. Science 189:390, 1975) without apparent damage to the glomerular basement membrane, we determined whether polycation infusion increases proteinuria. Systemic infusion of protamine (at doses lower than those used by Seiler to avoid systemic toxicity) resulted in transient (<80 min) but significant decreases in GPA as determined by double-blind reading of both control and affected kidneys stained with alcian blue and colloidal iron. In 12 additional animals infusion of comparable doses of protamine was associated with increase in proteinuria from 24.1±4.4 (SE) to 61.2±17.0 ug/min (p<0.05 by paired t test) during the period of decreased polyanion. Since GFR fell from 1.98±0.41 to 1.48±0.29 ml/min, proteinuria increased even more per unit of GFR. Serum protein levels did not increase.

These observations support the thesis that glomerular polyanion reduces the passage of protein into the glomerular filtrate and that loss of polyanion contributes to the proteinuria in glomerular diseases.