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Pathology of Thymus Insufficiency.

The morphology of the thymus at post mortem may be misleading. Acute illness and stress lead to lymphophagocytosis and outflow of of lymphocytes (thymocytes) resulting in lymphodepletion of cortex obscuring cortico-medullary differentiation, shrinkage of the whole organ and often a relative increase in central medullary epithelium and Hassall bodies (H.B.) (involution). Longstanding debilitating disease and/or drug therapy will lead to similar changes, but in addition, possible disappearance through attrition of differentiated central epithelium and H.B. (hyperinvolution), morphologically resembling the thymus found in Severe Combined Immunodeficiency Disease (SCID). The thymus in adenosine deaminase (ADA) deficient SCID is of the hyperinvoluted type, rather than the embryonal non-differentiated type found in ADA positive cases.

The morphological interpretation of the thymus does not permit firm conclusions relating to function. Small size, weight and diminished lymphocyte content are of little value. Size of the "corpus thymicum" and size and number of blood vessels may simply indicate hyper-involution. Distinguishing hyper-involution from non-differentiation at an embryonal level may only be possible with serial sectioning and close scrutiny of the whole of the epithelial structure.

Firm conclusions of the functional competence of the thymus can only be drawn after taking into account morphology, clinical course and in-vitro assessment of thymic epithelial function.

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Pathomechanisms of anemia in chronic renal failure(CRF).

Erythrocyte life-span (ELS) was determined in 16 children with CRF on conservative treatment (CT) and 6 children on regular haemodialysis (HD). Intestinal blood loss was measured during 5-6 days in 4 CT and 6 HD children. Blood loss in the HD equipment (parallel flow dialyzer Gambro) was determined in 6 children at the end of 3 consecutive HD sessions (each 8-10 hrs.) after reperfusion with air and 0.9% NaCl. For all measurements labeling of red blood cells with acetylacetonate mediated ^{111}Indium was used, the advantage of this isotope being a high counting yield and a physical half-life of only 2.8 days. On CT, ELS (M±SD) was significantly lower in the group with BUN >60 mg% (61±18%) vs. the group with BUN <60 mg% (76±12 %)vs.adult controls (100%). On HD ELS was 74±17 %. No correlations were found between ELS and serum creatinine or bicarbonate. Intestinal blood loss amounted to 6.7±2.5 on CT and 11.1±1.2 ml/day on HD. Blood loss in the equipment used for HD was 9.2±5.1 ml per dialysis (25 % in dialyser, 51% in connecting tubing system, 24 % in swabs by cannulation). In conclusion, besides bone marrow dysfunction, haemolysis and blood loss by intestine and by trapping in equipment used for HD contribute essentially to the anemia observed in CRF.

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Total body potassium in children with chronic renal failure (CRF).

Total body potassium (TBK) was determined in 21 non-dialyzed patients with CRF aged 4 to 18 years. Glomerular filtration rate measured concomittantly (usually by C_{Inulin}) ranged between 3 and 63 (mean 17) ml/min/1.73 m^2. The mean duration of CRF was 36 months. TBK was calculated from K^{40} content assessed by a whole body counter. Compared to predicted values adjusted for weight, height, sex and age (Burmeister, W. and A. Bingert, Klin.Wschr. 45, 409,1967) TBK was reduced in 18 of 21 patients, with a mean of 85.7 % of normal ($p < 0.01$). No correlations were found between TBK and serum K, K clearance, renal function,duration and cause of renal failure, These results suggest that total cell mass is reduced early in the course of CRF and persists up to the end-stage. An adequate K intake seems to be important for maintaining a positive K balance and, thereby, for allowing a sufficient nutritional status and body growth in children with CRF.

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Assessment of uraemic cardiomyopathy in childhood by systolic time intervals.

Systolic time intervals (STI) are recorded in 48 children with chronic renal failure (CRF) for quantitative determination of impaired myocardial performance as a result of uraemic cardiomyopathy under conservative treatment or on haemodialysis (HD). Duration of total systole (DTS), pre-ejection-phase (PEP), ejection time (ET) and systolic quotient (SQ = ET/PEP) are estimated from simultaneous high speed tracings of the EKG, PKG and the external carotid pulse. The measured values are compared to the calculated values related to age and heart rate according to GOLDE. In non-dialysed children (mean S_{CR} 9 mg%) there is a prolongation in PEP of 32% above normal ($p < 0.05$), indicating a reduced myocardial performance. The SQ is found shortened to 80% of normal ($p < 0.05$) corresponding to a diminished left ventricular ejection fraction. A correlation is also found between PEP, SQ and serum haemoglobin (r = 0.75/0.76). Following administration of digitalis PEP decreases ($p < 0.05$) and SQ increases ($p < 0.05$). On HD PEP and SQ improve significantly ($p < 0.05$) in the case that they have indicated a negative inotropic myocardial state before HD.

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Plasma-HGH, -TSH and -cortisol in children with chronic renal failure(CRF).

Growth retardation in children with CRF were ascribed to malnutrition and hormonal imbalances. In 20 children with CRF , age 6-18 y., serum creatinine (SCR) 4-10mg%, human growth hormone (HGH), thyroid stimulating hormone (TSH) and cortisol (F) were measured by radioimmunoassay with a combined arginine-(A), TRH- and ACTH-stimulation test. In patients below 3rd perc. in height HGH basal values were low (1,9±1,5ng/ml), rising to an upper normal range (43±12ng/ml) after A-stimulation. Patients with a height above 3rd perc. had elevated basal values (25±12ng/ml) with an excessive HGH-release (80ng/ml) following A-stimulation. In contrast TSH- and F- values before and after stimulation allowed no differentiation between both groups. Basal and TRH-stimulated TSH increased with rising SCR. Basal and ACTH-stimulated F remained in the lower normal range in all children. The results indicate that normal growth in CRF is associated with increased basal and excessive stimulatory HGH-levels, whereas growth retarded children show a HGH-release within upper normal range. We speculate that high levels of endogenous HGH may compensate growth retardation in CRF. TSH-release seems to be related to the extent of renal dysfunction, reaching levels seen in hypothyroidism. Plasma-F is slightly depressed, but shows a normal rise.

165 S. LEISTI* (Intr. by J. Perheentupa). Childrens' Hospital, University of Helsinki, 00290 Helsinki, Finland. ACTH test and insulin test in the prediction of clinical course in Idiopathic Nephrotic Syndrome (INS).

25 children with "minimal change" INS were given ACTH and insulin tests before, during and after prednisone medication to explore the influence of hypothalamus-pituitary-adrenal (HPA) axis suppression to the subsequent clinical course. A significant suppression of the axis was seen in all subjects after 6-28 days of prednisone 60 mg/m^2 daily in 3 doses. In most, the axis had recovered at the end of the subsequent 28-day period of "intermittent" medication (40 mg/m^2 in 3 daily doses on 3 consecutive days of the week). Three groups of different prognosis could be separated on the basis of the axis function. (1) Children with subnormal test responses both before and after medication had a new relapse in 0.5 year. (2) Children with subnormal pretreatment response, but normalized posttreatment response had an intermediate 0.5-1.0 year duration of remission. (3) Children with normal response both before and after treatment remained healthy longer than 1.0 year. In addition, 14 subjects were followed with pre- and posttreatment ACTH tests over a total of 44 relapses. A change of axis function from subnormal to normal, or vice versa, at consecutive relapses was followed by concordant change in the duration of remission in half of the cases (from <0.5 year to >0.5 year, or vice versa, respectively). Evidently the HPA axis function of children with "minimal change" INS is a significant determinant of the subsequent course of the disease.