38 B. KREMPIEN* and J. LUCKEY*, Department of Pathology, University of Heidelberg, F.R. Germany. Functional structure and strenght of the growth apparatus in normal and in uremic rats.

Epiphyseolysis is a rare condition in healthy children, but it is a common finding in children with chronic uremia.

We therefore tried to analyse the tensile strenght and the functional structure of the proximal epiphyseal cartilage in normal and uremic rats.

Material and methods
Tibiae of Wistar rats (250g, uremia of four weeks duration, sham operated controls) were excised and freed from the surrounding soft tissue. In order to measure the tensile strenght of the growth apparatus, we prepared two bore wholes within the epiphyseal and diaphyseal bone, which served as a suspension in a ZWICK material testing machine.

Non mineralized surfaces of cartilage, which were exposed by the final rupture, were prepared by the critical point drying method. Mineralized structures of cartilage and bone were exposed by digestion of unmineralized organic material by sodium hypochlorite. The specimens were analysed by scanning electron microscopy. Collagen fiber systems were either studied in serial sections using transmission electron microscopy, or by scanning electron microscopy after a dissolution procedure of the cartilage matrix by a papain treatment.

Results
Tensile strenght of normal rats was 56,73 +/-6,03 N. In uremic rats we found a significant reduction of tensile strenght of 39,90 +/- 4,96 N.

Electron microscopical studies: Epiphyseal cartilage and epiphyseal bone are connected by numerous plugs of cartilage, which insert in holes of the epiphyseal bone plate. This structure prevents a sliding of the epiphysis.

In columnar cartilage several columns are bound together to bundle pillars by collagen fibers. Longitudinally arranged fiber systems and a lattice system of shearing fibers can be identified in between these columns. Each pillar is connected with the epiphyseal bone plate by a radially orientated fiber system which resembles a system of shrouds. Neighbouring cells within the columns are bound together by a densely packed wickerwork of crossing fibers.

In the zone of mineralization longitudinal septa of cartilage show globiform mineral deposits. These globiform surface structures enlarge the interface between the chondrocytes and the mineralized matrix, increasing the adhaesive strenght in this region.Longitudinal septa are gradually transformed into metaphyseal bone by enchondral ossification. Thus a continuous functional system of epiphyseal bone, growth cartilage and metaphyseal bone is formed.

39 O. SIMELL, Children's Hospital, University of Helsinki, Helsinki, Finland. Serum and tissue alkaline phosphatases and electron microscopy of the bone lesions in the juvenile hypophosphatasia syndrome

Abstract not received

40 ELEANOR DAFFORN-IERODIAKONOU*, A. MORAKIS*, C.VRETOS* and P. LAPATSANIS*, Paediatric and Orthopaedic Unit "Aghia Sophia" Children's Hospital, Athens, Greece. Hyperphosphaturia producing collapse of vertebral body.

A child age 9 years complained of pains in both legs from November 1975 and was unable to walk 1 month later. On clinical examination he had pain on pressure over L3 and L4 lumbar vertebrae, but no other abnormal clinical findings. Body height 142 cm (90th percentile).The following tests were abnormal: serum phosphorus (P) 3.6-4.0mg/dl, $\frac{UP}{UCr}$ 0.88-1.1. X-ray showed a collapse of L4. The patient was put in a plaster jacket and started on 2g of phosphorus daily by mouth. 3 months later he was able to walk again and in another 7 months painfree and the plaster was removed. His height was 145 cm (90th percentile), serum Ca 11 mg/dl, serum P 3.7 mg/dl $\frac{UCa}{UCr}$ 0,07, $\frac{UP}{UCr}$ 1.15:x-ray of spine showed a marked improvement of L4. The treatment with oral administration of phosphate was continued and the patient reviewed 12 months after removal of his plaster in September 1977. X-ray showed a continuing improvement of L4, serum Ca 9.9 mg/dl, serum P 4.3 mg/dl, urinary Ca and P excretion in 24 hours 73 and 1385 mg respectively. One year later in September 1978 whilst still on phosphate therapy his results were serum Ca 9.7 mg/dl, serum P 4.3 mg/dl and x-ray improvement in shape of L4. This condition seems to be due to a renal tubular handicap for handling P resulting in phosphaturia but producing only an isolated bone lesion without rickets. Since there is healing with phosphate alone and his father also has abnormal phosphaturia but no bone lesions it could be an atypical form of vitamin D dependent rickets.

41 R. STEENDIJK*, Department of Paediatrics, University Hospital, Binnengasthuis, Amsterdam, The Netherlands. Statural growth and serum-P in hypophosphataemic rickets.

In cross-sectional studies the average height of 37 untreated boys and girls with X-linked hypophosphataemic rickets (X-LH) between 1 and 13 years of age was 2 standard deviations below the normal mean, but there was no relation between height and serum-P in single determinations (Steendijk and Latham, Helv Paed Acta 26: 179, 1971). Sustained increased growth rates have only rarely been observed during therapy with high doses of vitamin D or dihydrotachysterol, and it is not known whether those occurred following a sustained rise in serum-P. Catch-up growth during treatment with oral phosphate supplements, causing a rise in serum-P, has more often been seen, but only in short-term studies. To establish a relation between the level of serum-P during childhood and adolescence, and adult height in a long-term longitudinal study 8 patients with X-LH were followed for periods of 12 to 17 years until adult height had been reached. The patients were treated with dihydrotachysterol in high doses but did not receive phosphate supplements. Since serum-P was not constant during the years of treatment it was necessary in every patient to derive an average value from the serum-P determinations. This was done in the following manner: serum-P was determined at least 4 times per year in each patient, and the average serum-P value per year of age was calculated. From these mean values, the average serum-P (av. serum-P) for the whole period of observation was determined. This final value was correlated with adult height, expressed as standard deviation score (SDS). The coefficient of correlation (r) was 0.789 ($p < 0.05$) and the regression equation was:

$$\text{Height (SDS)} = 7.64 \times \text{av.serum-P} - 24.51$$

Av. serum-P ranged from 2.77 to 3.17 mg/100ml and adult height ranged from 0.04 to -3.34 SDS. Within this range of values a reduction of av.serum-P by as little as 0.1 mg/100ml would entail a reduction of adult height by 0.77 SDS (1 SDS equals 6.8 cm in men and 6.2 cm in women). This relatively large effect of a small change in serum-P may help to explain why a relation between serum-P and height has not been found before.

42 I. McKINLAY*, J.D. CROMBIE*, N.R. BELTON* and D.G.D.BARR*, Royal Hospital for Sick Children, Department of Child Life & Health, University of Edinburgh, Edinburgh, United Kingdom. Effects of calcitonin in a case of congenital hypophosphatasia.

A female infant with congenital limb deformities developed craniotabes and x-ray revealed rachitic metaphyses. Initial biochemistry showed serum calcium 11.6 mg%, phosphate 7.8 mg%, alkaline phosphatase 6 King Armstrong units. Subsequent alkaline phosphatase values were persistently low (range 0.9-2.7 K.A.Units) and a diagnosis of the severe form of congenital hypophosphatasia was made supported by levels of alkaline phosphatase in cultured cells and tissues. Family studies showed a pattern consistent with autosomal recessive inheritance.

At the age of three months she was irritable, feeding poorly and failing to thrive. Porcine calcitonin 50 M.R.C. Units/day was given intramuscularly for three weeks. Within two weeks hardening of the skull bones was noted with disappearance of craniotabes which recurred, however, six weeks later. X-rays over the following months showed increased mineralisation and periosteal new bone. Metabolic balance studies for calcium, phosphorus and magnesium before, during and after calcitonin therapy showed an alteration from an average positive calcium balance of 15 mg/day to 103 mg/day with treatment. No consistent change in phosphate or magnesium balance was evident. At the time of calcitonin treatment evidence of craniosynostosis developed. The child died of chest infection at 14 months of age.

In this case of severe congenital hypophosphatasia there is evidence of clinical, radiological and biochemical response to calcitonin. Treatment may have precipitated craniosynostosis and failed to alter the grave prognosis. It is possible that smaller doses of calcitonin over a longer period of time would be safer and more effective.

43 H.W. KRETH* (Intr. by V. ter Meulen). Institute of Virology and Immunbiology, University of Würzburg, W-Germany, Cell-mediated immunity in acute and chronic measles virus infections.

While the etiology of subacute sclerosing panencephalitis (SSPE) by a measles-like virus is now firmly established, the pathogenesis of SSPE is not understood. It has been suggested that the disease might be due to a specific unresponsiveness at the level of T cells (Burnet, Lancet ii,610,1968). To test this hypothesis specific T cell functions were measured by direct lymphocyte-mediated cytotoxicity in vitro using measles virus-infected lymphoblasts as target cells in 4- hr Cr-51 release assays. Results: Cells with the properties of cytotoxic T lymphocytes (CTL) were only present in children with acute measles and could be found among peripheral blood lymphocytes for up to 7 days after onset of measles rash. These cells were functionally restricted by the HLA system and belonged to the FcRγ negative pool of lymphocytes. Such cells could neither be detected in measles convalescents nor in patients with SSPE. It is proposed that in order to assess specific T cell immunity in donors beyond the acute stage of measles, memory T cells must first be restimulated in vitro into secondary populations of CTL before testing direct lymphocyte-mediated cytotoxicity.

44 H.SIEMES*, M. SIEGERT*, and F.HANEFELD. Kinderklinik der Freien Universität Berlin, F.R.G.
Determination of Oligoclonal Gammaglobulin in the CSF of Children with Subacute and Chronic CNS-Infections by Quantitative Agarosegel Electrophoresis.

CSF-proteins of 1300 children and adolescents with different neurologic diseases and of 75 normal controls were examined by zone electrophoresis in agarosegel and by immunologic techniques. The quantitative evaluation of the phoretogramms by an analog computer revealed in 68 patients who suffered from subacute or chronic CNS-infections marked changes of the γ-globulin profile. 32 out of