## 41

Hepatic Hypertrophic Osteoarthropathy (HHO) - An apparent high prevalence in a developing country.
Dr. M. Zuckerman, Dept Paediatrics, Baragwanath Hospital, University of Witwatersrand, South Africa.

HHO in association with chronic liver disease is a rare syndrome reported in only 4 paediatric cases to date. A retrospective study in children with chronic liver disease due to neonatal hepatitis (NH) or biliary atresia (BA) at Baragwanath Hospital was performed. The prevalence of HHO, age of onset of its various components as well as predisposing factors were noted.

Of 40 patients studied, 19 (47%) had ongoing jaundice (3 with NH, 16 with BA). Seven infants had evidence of HHO (clubbing and arthropathy and/or periosteal reactions) and a further 3 had clubbing only. The earliest manifestation in all cases was clubbing (20 ± 10 months). Clinical joint involvement developed later, while bone thickening was the last sign to be elicited, although radiological periosteal reactions were evident much earlier. The mean age of patients with HHO is 33.5 ± 11 months and those without HHO is 13.6 ± 8 months.

HHO in children occurs more frequently than described in the literature. Its pathogenesis is unknown, although several mechanisms have been postulated including failure of degradation of humoral substances. In view of the high prevalence of NH and BA at this hospital and the unavailability of liver transplantation, these infants are an ideal study population. A prospective study is in progress.

## 42

RANITIDINE TREATMENT OF STRESS-INDUCED GASTRIC LESIONS IN NEWBORNS
Anna-Leena T Kuusela, Tarja H Ruuska, Martti Janas, Markku J Mäki
(spn. by Jarmo K Visakorpi)
Department of Clinical Medicine, Tampere University, Finland

Stress-induced gastric mucosal lesions are a common complication in preterms and term newborns treated in intensive care. These lesions appear before any symptoms have occured. For adult patients in the intensive care ranitidine has been used as a profylactic treatment. We have now performed a double-blind randomized controlled study where 48 newborn infants were enrolled (mean gestational age 32 weeks, range 24-41 and mean birth weight 1830g, range 620-4550). All infants were mechanically ventilated from birth mostly because of prematurity. 23 of the infants received profylactic ranitidine 5 mg/kg body weght/day divided in three doses during four days starting at the day of birth. 25 of the infants received no medication. Gastroscopy was performed with Olympus GIF 5.2 baby gastroscope at the day 3 to 7 to all of the neonates in both groups. Those receiving ranitidine were free of ulcers, 2 had gastritis, 7 had mucosal haemorrhage and 14 had normal mucosa: In contrast, ulcers were seen in 8 of the neonates without profylactic treatment, gastritis in 8, haemorrhage in 4 and only 5 had normal appearing mucosa (p=0.004). Between the groups there was no difference in occurence of nosocomial infections. No side-effects of the short-term ranitidine treatment was observed. This study shows that a four-day profylactic ranitidine treatment reduces the occurence of gastric lesions in preterm and term infants under stress.

## 43

PARVOVIRUS B19 AND NECROTIZING ENTEROCOLITIS (NEC)
Orsolya Genzel-Boroviczeny, Gundula Jager, Ludwig-Maximilians-Universitat Munchen

Necrotizing enterocolitis can occur in epidemics. Various infectious agents have been associated with these clusters, but so far there has been no report of Parvovirus B19 infection and NEC in previously healthy premature infants.
We report here an epidemic of NEC linked to Parvo B19 infection. Within 10 days 8 premature infants developed the clinical picture of NEC, 6 of them within 24 hours. Their GA ranged from 27 - 32 weeks, their postnatal age from 4 days to 6 weeks. Prior to the onset of severe abdominal pain with bloody stools all infants had tolerated their enteral feedings well. Three infants required exploratory laparatomy. The entire small and large intestines were intraoperatively found to be cyanotic with no focal lesion or focal necrosis. Stool and blood cultures were negative for enteric pathogens and Rotavirus. Parvo B19 DNA was found in stool and serum samples of 3 infants by the Polymerase-Chain-Reaction (PCR), 3 infants were negative and 2 infants were not studied. Primers were selected from the VP1 region, so they bracketed a 240 base pair fragment of the Parvovirus B19 genome. Sequence analysis of the PCR-products revealed characteristics typical of Parvo B19 in all investigated positive cases.
There were 2 isolated cases of Parvo B19 pos. NEC 4 month later.
Summary: Parvovirus B19 could be detected with PCR in 5 of 10 infants with NEC, but only in 2 of 19 healthy control infants. Since 2 sick infants were not examined no definite statement can be made, but we believe that there is now some evidence that Parvovirus B19 infection can cause necrotizing enterocolitis in neonates. Further prospective studies are needed to elucidate this association.

## 44

**FIBROBLAST-DERIVED HUMAN PROTEINS ARE TARGETS FOR GENETICALLY DETERMINED RETICULIN AND ENDOMYSIUM AUTOANTIBODIES**
Markku J Mäki and Aulis Marttinen (spn. by Jarmo K. Visakorpi). Department of Clinical Medicine, University of Tampere, Finland.
Healthy reticulin- and endomysium-antibody-positive first-degree relatives of coeliac disease (CD) patients, irrespective of the appearance of the small-bowel mucosa, are genetically similar to known CD patients (Lancet 1991;338:1350-53). Recently we identified human noncollagenous extracellular matrix proteins to be targets for these antibodies (Lancet 1991;338:724-25). We now hypothesised fibroblasts to synthesise and secrete CD-specific autoantigens. A human embryonic fibroblast cell line, found to stain positively with CD patient sera IgA, was cultured for 4 days with tritiated amino acids. The fibroblasts synthesised and secreted a large-molecular-weight protein complex reacting with the IgA. The protein complex, separated using HPLC gel filtration, was decomposed and nine different protein molecules (17-39 kD) with $^{3}H$ activity was detected, four of which reacted with CD patient sera IgA. In affinity chromatography these molecules bound to reticulin and endomysium antibodies but not to gliadin antibodies. The fibroblast-derived proteins and the formed autoantibodies may be important in the pathogenesis of CD. We hypothesise a gliadin-triggered autoimmune mechanism to be operative.

# GENETICS

## 45

### Validity of metacarpal-index in children with Marfan-syndrome and children with constitutional tall stature

M Nelle [1], Tröger J [3], Rupprath G.[2] and Bettendorf M.[1]
*[1]From the Departments of Pediatrics and [3]Pediatric Radiology, University Childrens Hospital of Heidelberg, FRG, [2]Municipal Childrens Hospital, Kaiserslautern, FRG*

Aim of our study was to compare the metacarpal indices in children with Marfan syndrome and constitutional tall stature and to find out whether this index discriminates the clinical impression of arachnodactyly in children with constitutional tall stature. In a posterior-anterior X-ray of the left hand in 55 children with constitutional tall stature and 54 children with Marfan syndrome the metacarpal-index was evaluated as the ratio of the maximal axial length of the second, third, fourth and fifth metacarpals to the width of the same metacarpals at their midpoints. Metacarpal indices in children with Marfan syndrome were 9.15± 0.93 (mean±SD) and in children with constitutional tall stature 8.65± 0.83. Indices in both groups were significantly different but they differ from indices found in normal individuals (less than 7.9), showing clearly arachnodactyly in both groups. We conclude that the MCI distinguish between children with Marfan syndrome and children with constitutional tall stature but there is a considerable overlap making the MCI a poor discriminator between them. Therefore all patients with tall stature or clinical signs of arachnodactyly should be carefully examined for additional signs of Marfan syndrome or other hereditary disorders of the connective tissue.

## 46

"STIFF-BABY-LIKE" SYNDROME WITH SEVERELY DIMINISHED GABA IN CSF - A DEFECT OF GLUTAMIC ACID DECARBOXYLASE?
G.F. Hoffmann, C. Jakobs, H.-M. Meinck and D. Rating. Univ. Heidelberg, [1]Dept. Pediatrics, [2]Dept. Neurology and [3]Free Univ. Hospital Amsterdam

The dominantly inherited stiff-baby syndrome is characterized by marked muscle rigidity from birth. The symptoms ameliorate with time. The long-term outcome is good. Clinically similar is the stiff-man syndrome, which occurs sporadically in adults and is caused by autoimmune antibodies against glutamic acid decarboxylase in the majority of patients.
A baby girl, born to consanguineous healthy parents, presented with permanent muscle stiffness, fixed stare, flexion of forearms and legs, closed fists and myoclonic jerks heightened by the slightest physical stimulus. The child did not respond to sounds. Rigidity did not decrease over time. Neurophysiological investigations revealed sensory deafness and severely disturbed peripheral sensory pathways. Neuroradiological investigations including NMR were unremarkable. Investigations for neurometabolic disorders in urine, plasma and CSF repeatedly revealed severely diminished levels of free GABA in CSF (0 to 3, controls 30-140 nmol/l) as the only abnormality. Antibodies against glutamic acid decarboxylase were not detectable (Dr. Küpsch, Munich, FRG). Different neuopharmacological attempts to reduce hypertonia by potentiating GABA transmission had no effect. Spells of hypoxia occured; and the child died at the age of 8 months. We propose that this child suffered from a recessively inherited defect of glutamic acid decarboxylase. Appropriate molecular studies are in progress.