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MOLECULAR DIAGNOSIS OF PRESYMPTOMATIC. Wilson's disease. Philippe Labrune *, Micheline Misrahi **, Michèle Hadchouel **, Olivier Bernard **, Edwin Milgrom **, Michel Odièvre*
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Wilson's disease (WND) is an autosomal recessive disorder of copper metabolism. The metabolic defect is still unknown, but the locus of the disease has been mapped to chromosome 13q14-q21. Using polymorphic DNA markers in affected families, we are now able to recognize WND before the onset of clinical manifestations.
PATIENTS AND METHODS 121 subjects have been studied. They belonged to 31 families having at least one affected member. Genomic DNA was analyzed by Southern blots. Four different probes were used for the analysis of RFLPs : D13 S 31 (polymorphism with TaqI), D13 S 59 (polymorphism with BamII), D13 S 26 (polymorphism with HphI) and RB (retinoblastoma gene, polymorphism with RSaI).
RESULTS Using these four probes, 80% of the families were informative, and allowed to distinguish between heterozygotes and homozygotes. In some cases, the use of probes localized on both sides of the WND locus, yielded a 95% informativity.
CONCLUSION
RFLP analysis is a simple method to study the sibship of a patient with WND. It allows to avoid other investigations such as serum caeruloplasmin, urinary copper, liver needle biopsy. Furthermore DNA analysis allows presymptomatic diagnosis of WND and thus an early treatment with D-penicillamin.

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IMPAIRED SYNTHESIS OF CYSTEINYL LEUKOTRIENES IN GLUTATHIONE SYNTHETASE DEFICIENCY. Ertan Mayatepek, Georg F. Hoffmann, Birgit Carlsson*, Agne Larsson*, and Katja Becker. University Children's Hospital, Heidelberg, Germany and *Uppsala, Sweden.

Glutathione synthetase deficiency (GSD) is an inborn error of glutathione (GSH) metabolism leading to a generalized intracellular GSH defiency. Leukotriene (LT)C_4 is derived from the unstable epoxid LTA_4 by conjugation with GSH. In the circulation LTC_4 is rapidly metabolized to LTE_4 which is excreted into the urine. In this study, LT metabolites were separated in a patient with biochemically established GSD by reversed-phase HPLC and quantified by enzyme immunoassays. Results: Our investigations revealed that in GSD LTC_4 synthesis is significantly decreased in calcium ionophore activated monocytes as well as in neutrophils (11-14% and 7-10%, respectively, of the levels detected in the parents or controls). Endogenous urinary LTE_4 relative to creatinine (nmol/mol) was also found to be abnormally low in GSD (0.4 compared to 15-46 in parents and controls). Conclusions: GSD represents the first described disorder with decreased synthesis of LTs and may serve as a unique model for the linkage between LT synthesis and GSH metabolism *in vivo*. Since cysteinyl LTs may be important for cellular functions in the central nervous system, their impaired synthesis might be involved in the pathophysiology of GSD.

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11-beta-KETOTHIOLASE DEFICIENCY WITH OBSTRUCTIVE CARDIOMYOPATHY AND SPECIFIC MORPHOLOGICAL BRAIN DESTRUCTION. Volker Hesse, Hans-Josef Bohles, Adrian C. Sewell, Heike Forster, Werner Janisch, Druce Middleton, Holgar Haberland. Department of Pediatrics Hospital Lichtenberg, Berlin, and Univ. of Frankfurt/Main, Dept. of Pathology, Hospital Lichtenberg and Charite Berlin, Dept. of Biochemistry, University of Nottingham.
11-beta-ketothiolase deficiency is a rare metabolic disorder, which requires further investigation. We report two brothers, 6 9/12 years (pat. 1) and 4 years (pat. 2), who suffered from a 11-B-Ketothiolase deficiency (EG 2.3.1.9) which was confirmed by an elevated 2-methyl-3-hydroxybutyric acid and triglyglycine excretion in the urine. Measurements of ketolytic enzyme activities in fibroblast extracts from mother and pat. 2 showed a low activity of the short chain specific mitochondrial thiolase (C_5/C_4) rates = 0.54 and 0.44 rsp.). Both patients had delayed development, neurological features (appallic syndrome, pat. 1, and tetraparesis, pat. 2 respectively), seizures and amaurosis with opticus atrophy and died in a metabolic acidotic crisis after development of an obstructive cardiomyopathy. Destruction in the brain included the parietal and occipital cortex, visual cortex, putamen, caput nuclei caudati and claustrum.
It is assumed that in this family there is a severe specific form of 11-beta-Ketothiolase deficiency which affected also the heart metabolism of the children.

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WAR-RELATED POST-TRAUMATIC STRESS DISORDER
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Post-Traumatic Stress Disorder (PTSD) follows a psychologically distressing event outside the usual human experience. Characteristic symptoms: re-experiencing the traumatic event, avoidance of stimuli associated with the event or numbing of general responsiveness and increased arousal. Using semi-structured questionnaires, we studied background, war traumas and physical/psycho-emotional reactions in 163 Bosnian and 30 Croatian refugees (mainly mothers & children) in an Italian Red Cross camp. Results. Adults: PTSD in most, with psychiatric relevance in 16. Infants: esp. physical ailments (poor appetite; vomiting; colic; diarrhoea; constipation; alterations in sleep wake cycle, mood, and development), all worsening when psychological disturbances in mothers increased. Children >3 yrs: frequent PTSD with insomnia, restlessness, repetitive play, moodiness, psychosomatic symptoms. Adolescents: PTSD with defence mechanisms against anxiety (rationalisation and idealisation). Conclusions: infants better defended from traumas providing mothers act as a protective shield. Releasing tension through play is often ineffective in protecting Children. Adolescents' idealisation process tends to exasperate the contrapposition between friends and enemies, undermining their sense of reality and their personal identity.

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CHANGES IN APNEA AND AUTORESUSCITATION IN PIGLETS AFTER INTRAVENOUS AND INTRATECHAL INTERLEUKIN-1ß INJECTION.
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Recent research indicates that hypoxia precedes death in approximately 80% of the SIDS cases and that SIDS infants have a stimulated immune system at time of death. It has been shown in infants as well as in several experimental animal models, that CNS-maturity affects the effectiveness of autoresuscitation. It has been postulated that Il-1ß may be the intermediary causing prolonged sleep apnea and SIDS during respiratory infections. To test this, 5-10 days old piglets were given Il-1ß intravenously (n=8) or intratechally (n=9) prior to laryngeal stimulation with NH_3, an agent known to cause apnea. The procedure was also tested in a control group (n=7). The duration of the apnea was recorded as well as the number of respirations in 2 min following apnea. Values are given as median and interquartile range.

	Duration of apnea (sec)	Resp/2 min
Ctr.	12 (10 - 13)	109 (39 - 150)
I.V.	38 (27 - 52)*	21 (7 - 40)*
I.Th.	26 (24 - 36)*	42 (27 - 58)

*p<0.01 vs. Ctr.
We conclude that i.v. and i.Th. injection of Il-1ß effects the length of apnea and the quality of autoresuscitation.

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HOW SHOULD WE ESTIMATE LIVER SIZE CLINICALLY?

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Paediatricians often estimate liver size by palpating and percussing the liver edge in the right mid-clavicular line (RMCL). This measure is awkward in children, as determination of the RMCL is difficult - is measurement of the liver edge more accurate in the midline? 20 children aged between 6 months and 5 years were examined 'blind' by 5 practising clinicians on 3 separate occasions. We observed poor repeatablity in measuring the RMCL between observers (15%>2standard deviations, SD), although the length of the sternum, with defined, bony anatomical points, showed less variability (0.5%>2SD). Measurement in the midline showed greater repeatability between observers than in the RMCL (4%>2SD vs 8%>2SD). Estimation of the upper edge of the liver by percussion showed greatest variabilitiy (15%>2SD). Intra-observer variation followed the same pattern. Two children with exacerbations of asthma were followed by the examiners over 30 days: changes in the liver position were more accurately documented by measures made in the midline. We conclude that manual measurement of the hepar in the midline in children under 5 is more accurate than that in the RMCL.