born, 21 were born alive. Treatment and support aiming at sobriety could be started at different stages of pregnancy and with varying response. Early sobriety resulted in average size at birth, sobriety from mid-pregnancy gave a mean suppression of size at birth of 1 SD from the mean Swedish growth charts, and abuse throughout pregnancy a mean suppression of 1.7 SD. Pathological evoked response electroencephalograms (ER) were found in all three groups at birth. Only 1 of 14 investigated infants had a normal ER.

The incidence of the complete alcohol syndrome was 1/600 deliveries. In children born 1975-77 in Göteborg every sixth case of cerebral palsy was associated with an alcoholic pregnancy.

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THEOPHYLLINE (T) METABOLISM IN THE PREMATURE NEONATE.

The recent use of methylxanthines in the treatment of apnea of prematurity and their possible efficacy in the prevention of hyaline membrane disease has underlined the need for detailed investigation of their disposition in the premature neonate. The metabolism of T was studied in 10 premature newborns(g.a. 27-35 wks) during the first month of life and in 3 adult volunteers for comparison. T was injected i.v. and blood and urine assayed for T, Caffeine (C) and their metabolites by HPLC. T was found to be methylated to C only in the preterm group. 1 Methyluric (1-MU) and 1-3 Dimethyluric (1,3-DMU) acids were the major metabolites of T in the newborn. Demethylation to 3 Methylxanthine (3-MX) was seen only in the adults. The molar ratios of the metabolites in urine are reported in the table:

	3-MX	1-MU	1,3-DMU	T	C
Premature neonates	-	.11	.40	.43	.04
Adults	.19	.28	.41	.12	-

This study confirms the possibility of a methylative pathway from T to C in the newborn, but not in the adult. Hydroxylation accounted for about 90% of T metabolism in the premature neonate, while N-demethylation was absent at birth. This finding is in contrast to what seen for other drugs (e.g. diazepam).

66 F.F.RUBALTELLI,E.ROSSI* and G.JORI*. Dept. Pediatrics and CNR Center for Physiology and Biochemistry of Hemocyanins. Univ. of Padova, Padova, Italy. Evidence for visible light-induced covalent binding between bilirubin and serum albumin "in vitro" and "in vivo".

Acetone-induced precipitation of the 1:1 serum albumin-bilirubin complex, followed by treatment with 7M guanidine, allows complete removal of bilirubin from albumin by gel filtration. After illumination in the 440-470nm wavelength region (300 µW/sq.cm/nm), bilirubin or its photoproduct(s) cannot be removed any more from albumin. This was also confirmed by gel filtration on Sephadex G-75 (30% acetic acid as eluant) of BrCN-treated albumin, after 30 min. irradiation. This suggests the formation of a covalent binding which was detected also "in vivo" in the sera of jaundiced newborns. After 7 hrs.phototherapy with 4 F20T12/BB Westinghouse lamps (irradiation intensity at the infant level = 22 µW/sq.cm/nm, in the range of 440-470 nm), the covalent adduct began to appear. The quantity of the adduct was dependent upon the amount of light energy received during treatment. The adduct disappeared at 15 to 20 days after treatment.

67 H.T.VERSMOLD, G.LISTER*, P.R.DALLMAN*, A.M.RUDOLPH*. Department of Pediatrics, Univ.of Munich, Germany, and the Cardiovascular Research Institute, Univ.of California, San Francisco, U.S.A. Limits of O_2 Delivery during Propanolol-Induced Reduction of Cardiac Output in Lambs after Birth: A Longitudinal Study.

To test the ability to increase O_2 extraction when cardiac output is decreased, we assessed total body O_2 delivery before and after ß adrenergic blockade during the early postnatal period. 8 lambs were studied chronically over the first 2 month of life. Cardiac output (CO), heart rate (HR), hemoglobin (Hb), Hb O_2 affinity and 2,3-DPG, oxygen consumption (VO_2), systemic O_2 transport (SOT), and arteriovenous O_2 content difference were measured while the lambs were resting and unsedated, and again after intravenous propanolol (PROP), 1mg/kg. After birth CO, HR and VO_2 at rest decreased steadily while fractional O_2 extraction (VO_2/SOT) remained constant. After PROP CO was consistently reduced by 1o - 2o %, and there were no significant differences with age. Most of the decrease in CO was explained by the reduction in HR.Upon this decline in CO there were significant decreases in VO_2 after PROP during the first postnatal week, and at 4 weeks. This was when O_2Hb affinity was greatest (≤1 wk) or Hb was lowest (3-4 wk). Moreover, only when resting mixed venous Po_2 was less than 29 torr was VO_2 consistently and predictably decreased after PROP.

Compared to the lamb in human infants P_{50} after birth is lower, and Hb is decreasing relatively more. We conclude that in the human infant like in the lamb there is very little reserve to increase O_2 extraction or arterialvenous O_2 content difference early in infancy when P_{50} or Hb is low.

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Raised hepatic copper in Indian Childhood Cirrhosis.

Percutaneous liver biopsies from 19 children with liver disease were studied. Indian Childhood Cirrhosis was diagnosed in 5, and in these orcein staining demonstrated widespread granular deposits within hepatocytes The hepatic copper content in these 5 cases was greatly increased at 1389 ± 525 µg/g dry weight (range 1045 - 2303 µg/g, normal range 15 - 55 µg/g) The other 14 children had various hepatic disorders. None had widespread granular orcein staining Hepatic copper concentrations were normal in 12, and slightly elevated in 2 (170 and 292 µg/g). The absence of prolonged jaundice, histological cholestasis, or serum lipoprotein X in the cases of ICC indicated that hepatic copper accumulation was not secondary to cholestasis Serum ceruloplasmin concentrations were greater than 20 mg/dl in all 19 cases. A survey failed to detect any cases of ICC in Asian children born in the UK, so implicating environmental factors. We suggest that copper is implicated in the aetiology of ICC, that early treatment with penicillamine may be effective,and that reduction of copper intake may be preventative.

69 B. STEINMANN*, L. TUDERMAN*, G.R. MARTIN* AND D.J. PROCKOP* (intr. by R. GITZELMANN). Dept. Pediatrics, University of Zurich, CH-8032 Switzerland.

FIRST DEMONSTRATION OF A STRUCTURAL MUTATION OF PROCOLLAGEN IN A PATIENT WITH EHLERS-DANLOS SYNDROME (EDS).

Three patients with severe hypermobility of the joints but only mild hyperelasticity of the skin were previously reported (Science *182*,298-300,1973) to have partial deficiency of procollagen N-protease, one of the two enzymes necessary for the conversion of procollagen to collagen. One 9 year old patient was reinvestigated. In a biopsy sample of her skin, collagen was more extractable in neutral 0.5 M NaCl containing protease inhibitors. In addition to the normally occurring α1- and α2-chains, α2-precursor chains (pNα2), but no pNα1 were detected by SDS-PAGE. Digestion of the collagen with animal collagenase generated the three N-terminal fragments $\alpha1^A$, $\alpha2^A$ and $pN\alpha2^A$ but only the two normally occurring C-terminal fragments $\alpha1^B$ and $\alpha2^B$. Digestion of the extracts with purified procollagen N-protease did not remove the N-propeptide from the pNα2 chains. This excluded the possibility of incomplete conversion of pN-collagen owing to partial procollagen N-protease deficiency. The findings were corroborated by the study of radioactive procollagen produced by cultured skin fibroblasts. The latter had normal N-protease. Results suggested that the proα2-chains had a structural defect near the N-protease cleavage site preventing the enzymatic removal of the N-propeptide. Since equal amounts of pNα2- and α2-chains were produced, gene dosage was evidenced in this sporadic case of EDS probably caused by a new mutation.

70 I. SIPILÄ*, O. SIMELL* and P. ARJOMAA* (Intr. by K. Raivio). Children's Hospital, University of Helsinki, Finland. Guanidinoacetate (GAA) excretion and plasma amino acids after an arginine load in patients with hyperornithinemia and gyrate atrophy of the choroid and retina (GA).

GA is an autosomal recessive disease characterized by progressive atrophy of the choroid and retina starting by age 5-9 years, and atrophy and formation of tubular aggregates in type I muscle fibers. Plasma ornithine concentration is 10-20 times increased. To quantitate in GA the efficiency of the first reaction in creatine production from arginine, we gave a 5 min i.v. load of arginine-HCl, 1.1 mmoles/kg, to 7 patients and 4 controls. Urinary excretion of GAA was measured in 15-60 min collections for 6 hours, and plasma amino acids at 15-60 min intervals. The plasma arginine values increased similarly in patients and controls. Plasma ornithine concentrations at 0 and 30 min (peak value) were 757±134 µM (mean ±SD) and 1600±279 µM in the patients and 43±9 µM and 209±64 µM in the controls, respectively. In the patients, only the 15 min arginine value exceeded that of ornithine; the controls always had higher arginine. The basal GAA excretion by the patients was only 10% of that of the controls. In the patients, the excretion was increased for the first 30 min after the load, but returned then to the low levels. In the controls, excretion was increased throughout the collections. Thus, the high ornithine concentration may inhibit GAA formation and subsequently creatine and phosphocreatine synthesis; the resulting lack of high energy phosphagens may be a mediator in the muscle and eye atrophies in GA.

71 H.P. SCHWARZ*, K. ZUPPINGER, T. SCHAEFER*, H.P. SIEGRIST*, U. WIESMANN and N. HERSCHKOWITZ. Department of Pediatrics, University of Bern, Switzerland. Galactose enhances sulfatide synthesis in glucose-deprived cultured mouse brain cells.

Glucose-deprived brain cell cultures have a markedly reduced sulfatide synthesis (SfS). As SfS is glucose dependent, galactose (gal) was studied to delineate its role as a substitute for glucose (glu). SfS is a mandatory step in the formation of myelin. Gal is necessary to form cerebroside which is converted to sulfatide by incorporation of sulfate. Neonatal mouse brains were dissociated and cultured for 10 days. Cell cultures