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REYES' SYNDROME: EVIDENCE FOR ABNORMAL POLYAMINE (PA) METABOLISM. Robert A. Campbell, John B. Isom, Dagmar Bartos and Frantisek Bartos. (Spon. by Robert C. Neerhout), University of Oregon Health Sciences Center, Doernbecher Memorial Hospital, Department of Pediatrics, Portland, Oregon.

Four children, ages 1-16, were admitted with a history of a prodrome viral illness and, after an interval, pernicious vomiting and the onset of disordered psychomotor activity. Abnormal liver function tests including blood ammonia were present in all during the course of their illness. Patients sampled for PAs were staged with respect to CNS status, I-IV, after Huttenlocher. Serial serum-free PAs, namely spermine (SPM) and spermidine (SPD) were determined from serum sample aliquots by radioimmunoassay. All patients had elevated SPD values (mean peak value of 2.06 nanomol/ml) which declined rapidly to a post-admission value of 0.45 nanomol/ml in the 3 surviving children. Highest SPD value (4.20 nanomol/ml) was observed in the patient with the most severe neurological score (III) on admission. SPM levels, by contrast, were much lower and there was a 1-2 day delay in SPM peak development in the 3 surviving children. Clinical improvement paralleled the decline in serum PAs. PA administered I.V. to man causes prompt and persistent vomiting. Specific PA binding sites have been identified on animal brain cell membranes. SPM has been demonstrated to markedly reduce oxygen consumption by brain tissue. In vitro Na, K-ATPase activity is also depressed by PA addition. Parenteral PA doses to experimental animals may cause somnolence, ataxia, coma and death.

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DYSTONIA ASSOCIATED WITH CARBAMAZEPINE USE. Carl Crosley & Phillip Swender (Spon. by Frank A. Oski) Dept. of Peds., SUNY Upstate Med. Ctr., Syr., N.Y.

Carbamazepine (Tegretol[®]) is used effectively in the treatment of seizure disorders and trigeminal neuralgia. Reported side effects are primarily neurological, occur infrequently and rarely require discontinuation of the drug. We have cared for 3 children in whom 4 episodes of dystonia and opisthotonus occurred in association with carbamazepine use. The patients, a 2 yr. old with microcephaly, a 3 yr. old with cerebral dysgenesis and a 5 yr. old with spastic quadriplegia; all had seizures requiring multiple anticonvulsants. In all 3 patients carbamazepine was introduced and gradually increased to a maximum of 25 mg/kg/d. Symptoms began 2-3 weeks after introduction of therapy and subsided within 3 weeks after discontinuation. In one case a 2nd course of carbamazepine resulted in a return of the dystonia. No hematologic or hepatic abnormalities were noted. Blood levels of concurrently administered anticonvulsants, including phenytoin, were within therapeutic range. A single carbamazepine blood level obtained during one of the episodes was also therapeutic (5.1 mcg/ml). Early reports of carbamazepine's beneficial effect in some dystonic syndromes have not been supported by further clinical trials. It has also been reported to enhance the release of ADH. Our observation of incapacitating but reversible dystonia raises further question about the effects of carbamazepine on the central nervous system. The need exists for an awareness of this complication in physicians caring for neurologically handicapped children.

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INTRAUTERINE DIET FORTIFICATION AND OFFSPRING BRAIN DEVELOPMENT. H. Peter Chase and Linda S. Crnic. Univ. of Colo. Med. Ctr., Dept. of Ped & Psych, Denver.

Vegetable protein, providing 80% of protein requirements in Third World Countries, can be quantitatively adequate but qualitatively inadequate in protein content. Supplementation with limiting amino acids (AA's) is possible and might aid intrauterine offspring development. In the present experiments 21 Sprague Dawley rats were impregnated and groups of 7 begun on one of 3 diets: A) bread, B) bread + lysine and threonine, or C) lab chow. Weights of all offspring at birth were lower ($p < .001$) in group A ($5.64 \pm 0.52g$) compared to groups B ($6.39 \pm 0.88g$) or C ($6.49 \pm 0.34g$). Two newborns from each of the 7 litters in each of the 3 groups were randomly selected for further brain studies. Total brain weights were lower for group A pups ($.239 \pm .019$) compared to groups B ($.279 \pm .022$, $p < .05$) or C ($.258 \pm .026$, $p < .001$).

Total DNA, representing total cell number, was higher in the cortices of AA supplemented (group B) offspring ($.562 \pm .019$) compared to group A neonates ($.537 \pm .029$, $p < .01$). DNA was also higher in the cerebellum-brain stem of group B animals ($.169 \pm .010$) compared to group A animals ($.158 \pm .014$, $p < .05$). There were no significant differences in DNA between the AA supplemented and the chow fed offspring. Total cortex protein was lower in group A animals compared to groups B ($p < .001$) or C ($p < .02$). These experiments demonstrate that amino acid fortification of a maternal vegetable protein diet results in improved intrauterine brain development.

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MOYA-MOYA IN AMERICAN CHILDREN. Carl Crosley (Spon. by Frank A. Oski) Dept. of Peds. and Neurol., SUNY Upstate Med. Ctr., Syr., N.Y.

Recurring cerebrovascular disease is extremely rare in children. Moya-moya (supraclinoid carotid stenosis with multiple cerebral telangiectasias) may be the vascular pathology underlying many such instances. Initially described as a congenital anomaly in the Japanese literature, it is uncommonly recognized in occidentals. We have cared for two Caucasian children in whom several factors strongly suggest moya-moya can be an acquired process and in whom the course was much more benign than commonly described. A 4½ year old boy with transposition of the great vessels developed a right hemiparesis after a total corrective operation. Six and one-half years later he had a subarachnoid hemorrhage (SAH). Computed tomography and cerebral angiography demonstrated a left frontal intracerebral hematoma and subadjacent brain atrophy and moya-moya. He has been well for 2½ years. A girl with sickle cell disease had a right hemiparesis at age 8. Six years later she had a SAH. Computed tomography and cerebral angiography demonstrated left parietal atrophy, intracerebral hematoma, and moya-moya. She has been normal for 2 years. Presentation of moya-moya in children as SAH has been noted only once previously. Moreover, our two children had a basic disease process not associated with cerebral telangiectasia but occasionally associated with cerebrovascular occlusive disease. The demonstration of moya-moya six years after a single presumably vascular occlusive event strongly suggests moya-moya can be a tenuous physiologic compensation to an acquired phenomenon.

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HANDICAP IN THE PRETERM SMALL-FOR-GESTATION (SGA) INFANT. Joseph O. O. Comney, Stanley A. Ashby, Pamela M. Fitzhardinge. Univ. of Toronto, Hosp. for Sick Children, Research Inst. Toronto.

Reports on incidence of central nervous system (CNS) sequelae in term SGA infants have been generally encouraging. This paper presents results of a follow-up study of preterm SGA infants (birthweight $\geq 2SD$ below mean) born at 33-36 wk. gestation. 41 infants meeting these criteria were admitted to the neonatal unit in 1974, 75. 30/35 survivors were followed for at least 2 yrs and were tested by the Bayley Developmental Scales at 18 mo from term. The Bayley scores were low - mean 83 ± 15 - with 12 (40%) scoring ≤ 80 . Cerebral palsy occurred in 6 children, 5 of whom were diplegic. 4 of the 6 scored ≤ 80 on the Bayley.

Bayley scores were not related to either the degree of intrauterine head growth restriction or the rate of early postnatal head growth. They did not correlate with gestation, complications of pregnancy/delivery, asphyxia or hypoglycemia. However, 6 of the 12 with Bayley ≤ 80 had asphyxia or hypoglycemia that was accompanied by seizures or apnea. Only 1/18 with Bayley ≥ 80 was so affected ($p < .02$).

The results show that, unlike the full term SGA, the preterm SGA is at a high risk for serious CNS handicap and that this risk increases if asphyxia or hypoglycemia is accompanied by seizures or apnea.

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VALPROIC ACID IN THE TREATMENT OF INTRACTABLE SEIZURES

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45 patients with intractable seizures are being treated with a new anticonvulsant, valproic acid (VPA). Two separate protocols are being followed. VPA was initially added to previous drugs.

The first protocol involves 19 patients with simple or complex absence seizures. Maximum VPA dose is 60 mgm/Kgm/day. 6 hr EEGs were obtained initially, after two weeks of placebo and after 10 weeks of VPA. EEG analysis included the number and duration of electrical seizures. All patients show clinical improvement. 14 have a 75-100% reduction in clinical seizures. 5 are seizure free; none on less than 60 mgm/Kgm/day. In 6, clinical improvement cannot be correlated with the degree of EEG improvement.

The second protocol involves 26 patients with mixed seizure types. Maximum VPA dose is 30 mgm/Kgm/day. Routine EEGs were done initially and after reaching stable maximum dosage, 13 patients are improved. 7 have a 75-100% reduction in clinical seizure frequency and 6 a 33-74% reduction. 3 patients are not improved. EEGs show no significant change. No patient is seizure free at a 30 mgm/Kgm/day dosage.

VPA was effective against a variety of intractable seizure types. There was no consistent correlation between clinical and EEG improvement. No serious side effects or exacerbations of seizures occurred.