

● **1279** SPECIFICITY OF RAT YOLK SAC ANTIBODIES IN PRODUCING CONGENITAL MALFORMATIONS, EMBRYONIC MALNUTRITION AND REDUCED PINOCYTOSIS. Robert L. Brent, Steven

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In a series of experiments first published in 1961, we reported that antibodies prepared against rat kidney were potent teratogenic agents when administered to pregnant rats (Brent 1961). It was determined that antisera which were teratogenic localized in the developing yolk sac (Slotnick and Brent, 1966). Antisera prepared against VYS proved to be the most potent teratogens, and these teratogenic antisera reduced the endocytic uptake of proteins by the VYS (Brent et al, 1972, Freedman et al, 1983). Utilizing isoelectric focusing techniques, various proteins were isolated from the VYS and antisera were prepared against these individual proteins. A large number of antisera were not teratogenic and did not localize in the developing yolk sac. A smaller group of antisera were found to localize in the VYS. These antisera were studied with several techniques: Determination of the endocytic index utilizing (¹⁴C) sucrose, in vivo yolk sac localization utilizing fluorescent labelled antibody and teratogenic potency. It was found that yolk sac localization of antibody specific for yolk sac antigens does not prove that the antibodies have teratogenic potency. On the other hand, if the antibodies also reduce the endocytic index, then the antibodies will invariably have teratogenic potency. Thus, the reduction of endocytosis is the first method of accurately predicting teratogenic potential without having to perform time-consuming in vivo bioassays.

† **1280** THE ANOGENITAL INDEX: A WAY TO IDENTIFY ABNORMAL LABIOSCROTAL FUSION IN INFANTS? Carlos C. Callegari, Susan Everett, Susan Scott, Jo Anne Brasel. Department

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The clinical detection of virilized genitalia can be difficult in the preterm female since clitoral size is fully developed by the 27th wk gestation while the body as a whole is not. Absence of fat in the labia majora also makes the clitoris appear more prominent. Androgen-induced labioscrotal fusion will increase the anogenital distance, but we could find no published normal values. We have made 116 measurements of the following distances: anogenital or anus to fourchette (AF); fourchette to clitoris (FC); and anus to clitoris (AC) in infants of 27-42 wk gestational age. Not surprisingly all distances showed positive and significant correlations with body surface area, weight, length and gestational age ($p < 0.001$). The ratio of AF/FC and AF/AC follows a Gaussian distribution and does not correlate with any of the above anthropometric variables or gestational age. Mean values \pm SD for all subjects measured to date are: AF/FC = 0.582 ± 0.149 ; AF/AC = 0.373 ± 0.065 . An anogenital index (AF/AC) greater than 0.5 falls outside the 95% confidence limit. This suggests labioscrotal fusion and indicates a need for further evaluation. The anogenital index is not difficult to measure if proper care is taken. Since it is independent of body size and gestational age, it should be a useful tool in the diagnosis of abnormal genitalia in both premature and full term female infants. (Supported in part by GCRC grant RR00425.)

† **1281** EFFECTS OF ETHANOL ON NEURONAL PROCESS FORMATION AND NEUROTROPHIC FACTOR PRODUCTION IN VITRO. Kimberly E. Dow and Richard J. Riopelle. Queen's

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Ethanol may produce its toxicity during early neurogenesis by: 1. affecting the survival of neurons 2. preventing neuronal attachment to substrates of growth 3. inhibiting neuronal process formation 4. preventing neuronal interaction with neurotrophic materials or by 5. inhibiting neuronal production of neurotrophic materials.

We have previously described that ethanol produces dose-dependent inhibition of neurite outgrowth (Pediatr Res 18:1248, 1984). In the present studies ethanol was shown to inhibit process formation on a variety of biological substrates with no effect on neuronal survival or substrate attachment at the 50% toxic dose (TD_{50}) of ethanol for process formation. The binding of Nerve Growth Factor to its receptor on sensory neurons was not inhibited by ethanol at the TD_{50} . Ethanol did inhibit the production of autocrine neurotrophic material. The calcium channel antagonist diltiazem protected the neuron against the toxic effects of ethanol on process formation.

These data suggest that the interaction of neuronal surface receptors with ligands within the extracellular environment are not influenced by ethanol, but that this xenobiotic affects neuronal metabolism by a mechanism involving the biological handling of calcium.

1282 IN-UTERO EXPOSURE TO NICOTINE: EFFECTS ON THE NEWBORN, Loretta P. Finnegan, Francoise LeBrun, Catherine Nessman, Sandra Ehrlich and Claudine Amiel-Tison, Clinique Baudelocque, University of

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As a result of the popularity and social acceptability of nicotine, in-utero exposure is common. To study the effects of prenatal smoking, 74 infants were evaluated. Group 1 consisted of 32 infants born to women who had smoked 10 to 20 cigarettes per day throughout pregnancy. Group 2 included 42 infants born to non-smokers. Infants were examined at 2 to 5 days of age. Dependent variables included: gestational age, birth weight, Apgar scores, physical and neurological status (evaluated by the Amiel Score-Journal of Anesthesiology, 56:340, 1982), occurrence of abstinence (evaluated by the Neonatal Abstinence Score-Pediatric Research, 17:1678, 1983) and, the infant's special care needs and ability to feed (Casear et al. Early Human Development, 7:331, 1982). Results revealed no differences in duration of labor, use of analgesia/anesthesia in labor and delivery, gestational age, length, head circumference, Apgar scores, morbidity or physical abnormalities. No significant symptoms of abstinence were noted in Group 1. Although there were no significant differences in Amiel Scores, smokers' infants were more apt to show deficiencies in sucking, automatic walking, and alertness. In non-smokers, there was a higher incidence of prolonged rupture of membranes and breech presentation. Evaluation of the infant's ability to feed revealed that infants of non-smokers were twice as likely to experience an overall well-being as reflected by a strong, contented infant during feedings. The infants of smokers had lower birth weights and an increased need for resuscitation and special care. A trend of increased maternal complications in pregnancy and delivery was also noted. These findings supplement existing information which advises pregnant women to stop smoking as early as possible during pregnancy in order to prevent untoward consequences.

1283 ROLE OF EPIDERMAL GROWTH FACTOR IN THE PHENOTYPIC EXPRESSION OF LEPRECHAUNISM. J. Paul Frindik, Wojciech Zawada, Pat Walker, Stephen F. Kemp,

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Epidermal growth factor (EGF) is a polypeptide hormone important in growth and differentiation of multiple cell types. It has a wide range of biological activities including precocious eruption of teeth, gut mucosa hyperplasia, and proliferation of epidermal cells in mice. Despite multiple known biological functions and presence in several body fluids, no disease state has been identified in which there is either a deficiency or excess of EGF. Leprechaunism (L) has many of the characteristics expected in EGF hypersecretion, i.e., severe acanthosis nigricans, hirsutism, pachyderma, precocious breast development and hypertrophy of gut and genitals. We have measured urinary EGF excretion in an 8-year-old patient with L over several years and found a mean concentration to be $151.9 \pm 50.4 \mu\text{g}/\text{gm cr}$. In comparison we have measured urinary EGF concentrations in normal children and children with various disease states. EGF excretion was linear with creatinine excretion and not influenced by age. The mean EGF excretion is $26.7 \pm 4.3 \mu\text{g}/\text{gm cr}$ in control children as compared to 29.6 ± 1.1 and $39.8 \pm 1.6 \mu\text{g}/\text{gm cr}$ in normal adult males and females respectively. Blood EGF levels in our patient were increased above normal. Measurement of other gut hormones were normal. We conclude that many of the phenotypic manifestations of L are secondary to excessive EGF, thus providing a disease for this well characterized but otherwise orphan hormone.

1284 PHOCOMELIA OF LEFT LOWER LEG IN AN INFANT WHOSE MOTHER TOOK LARGE DOSES OF PYRIDOXINE (B-6): ? DÉJÀ VU OF THE THALIDOMIDE DISASTER? Lytt I. Gardner, Jannell Welsh-Sloan and Robert B. Cady. SUNY Upstate Medical Center, Depts. of Pediatrics and Orthopedics, Syracuse.

This girl, now age 2½ mos, has nearly total amelia of her left leg at the knee. There is a rudimentary foot (? just the 5th toe). X-ray shows no knee joint or tibia. Femora are normal length. Examination is otherwise normal. Pregnancy was full-term normal vaginal delivery. Birth wt 3.2+ kg. Megavitamin preparations of B-6, B-12, A, E and C were ingested by the mother, who weighs only 47 kg. At least 54 mg/day of B-6 was taken in mos 1-4 of pregnancy, and possibly more, since over-the-counter B-6 tablets are shelved together in 50, 100, 500 and 1000 mg sizes.

Recent reports describe sensory neuropathy in adults with megavitaminosis B-6 (NEJMed 309:445, 1983; ibid. 311:986, 1984). This neuropathy shows striking clinical similarities to that of thalidomide: stocking glove numbness first in feet and later in hands, and ataxia. A late sign with thalidomide was weakness; not yet seen in B-6. Lenz' suspicions were aroused by a woman who took thalidomide during pregnancy and developed "polyneuritis", delivering a phocomelic baby. We face the same dilemma with B-6 that Lenz did when he stated in Nov. 1961: "From a scientific point of view it seems premature to discuss it [thalidomide as teratogen]. But as a human being and as a citizen, I cannot remain silent..." (see review "The Saga of Thalidomide: Neuro-pathology to Embryopathy", NEJMed 267:1184 and 1238, 1962).