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THE X CHROMOSOME BENDING SITE IN THE HUMAN, GORILLA, AND CHIMPANZEE: LOCATION AND EVOLUTION OF THE X INACTIVATION CENTER. Daniel L. Van Dyke, Lester Weiss, Maria J. Worsham,

and Wendy L. Flejter, Henry Ford Hospital, Medical Genetics and Birth Defects Center, Detroit, Michigan.

Bands in midmetaphase chromosomes are not distributed randomly throughout the karyotype. A specific bend at Xq13.3 to Xq21.1 is evident in the lyonized X, clearly associated with the center for Barr body condensation (Flejter et al, Am J Hum Genet, in press). The relationship of the X chromosome bend with the X inactivation center makes it a useful marker for identifying the lyonized X and for locating the inactivation center in X chromosome rearrangements, including the X of other species.

In high-resolution G- and R-banded cells the bend site includes the entire region from Xq11.2 to Xq13.3. In some cells the X exhibits a 360° loop involving Xq11.2 to q13.3, or multiple loops which may extend further down Xq, but not into Xp. In many cells the X exhibits an apparent "synapsis" of sub-band Xq11.2 and Xq13.3, forming a distinctive omega-shaped curve beginning just below the centromere. We believe these behaviors represent visible manifestations of Barr body decondensation which will be useful in studies of X inactivation and chromosome structure.

Metaphase cells from a female gorilla fibroblast culture (provided by TC Hsu) had the bend in the same region as in the human X. Metaphase cells from a female chimpanzee (provided by DH Ledbetter) had the bend in the region Xq22 to Xq24. This suggests that the X inactivation center is located more distally in the chimpanzee than in the human or gorilla. Additional gorilla and chimpanzee subjects need to be examined, including midmetaphase and high-resolution karyotype studies. For the present, we postulate a pericentric inversion during primate evolution to explain our observations.

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AMNIOTIC EPITHELIAL CELL IMPLANTATION (AECI) IN LYSOSOMAL STORAGE DISEASES. Andrew M. Yeager, Hugo W. Moser, Harvey S. Singer, James R. Buck, Reuben Matalon, Susan O'D. O'Toole, and Carol Tiffany. The Johns Hopkins University School of Medicine and John F. Kennedy Institute, Departments of Oncology, Pediatrics, and Neurology, Baltimore, MD, and University of Chicago School of Medicine, Department of Pediatrics, Chicago, IL.

Human amniotic epithelium expresses very low levels of HLA antigens on the cell surface and is non-immunogenic when implanted subcutaneously into normal recipients (Nature 295: 325, 1982). Amniotic epithelial cells also produce several lysosomal hydrolases (Lancet 2: 1003, 1981). We performed AECI as possible enzyme replacement therapy in 5 patients, ages 22 mos-7 yrs, with heritable storage diseases. One patient had Gm₁ gangliosidosis, two had Farber's disease, one had metachromatic leukodystrophy, and one had mucopolysaccharidosis I Hurler-Scheie compound. Human amnion was obtained from elective caesarean deliveries and implanted subcutaneously into recipients within 6 hr after procurement. All patients tolerated the implantation well. In the post-AECI period, serum and leukocyte samples were obtained from recipients and assayed for enzyme activity. Most patients also had quantitation of urinary substrate at selected times after AECI. All patients have been followed for 3-6 mos post implant. We have not detected any increased enzyme activity or alterations in urinary excretion of substrate after AECI, and no patient has demonstrated objective clinical improvement. In our experience, AECI is well tolerated but fails to provide a source of replacement enzyme in selected storage diseases.

GENERAL PEDIATRICS, EDUCATION AND TRAINING

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THE VALUE OF PEAK FLOW AS AN INDICATOR OF TOTAL DISABILITY IN CHILDHOOD ASTHMA. M.D. Baker, S. Moore, P.H. Wise, (Spon. by M.D. Levine). Harvard Medical School, Children's Hospital, Dept. of Pediatrics, Boston.

This study examined the usefulness of peak flow rate (PFR) in identifying the total disability of the asthmatic child during an acute attack. 108 consecutive patients 5-18 years of age presenting to the Emergency Service of Children's Hospital with the diagnosis of asthma were studied. PFR's were measured throughout the course of a standard treatment. The decision for admission was not influenced by this study. Each patient was followed, and an assessment of intervening morbidity made. 16 patients were admitted, and 92 discharged. Our data revealed:

OUTCOME	PREDICTED PEAK FLOW RATE (PPFR) LESS THAN 60%		
	Initial (n=89)	1Hour (n=43)	Disposition (n=42)
Admitted	16%	28%	33%
Sick at Home	31%	63%	67%
Well at Home	53%	9%	0%

Children discharged with PPFR's prior to disposition of less than 60% averaged 7 days of subsequent disability at home. None of the discharged children with pre-disposition PPFR's greater than 59% experienced subsequent disability at home. Admitted patients remained hospitalized for an average of 2 days. None had additional home morbidity. We conclude that PPFR at the time of disposition in children with acute asthma is useful for identifying the need for admission, and that it is an excellent indicator of those at high risk of experiencing significant subsequent morbidity at home.

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EVALUATING A CORE CURRICULUM IN THE PEDIATRIC CLERKSHIP. Angela Bennett and Laurence Finberg, SUNY, Downstate Medical Center, Department of Pediatrics, Brooklyn, New York

For the year 1982-83, the cognitive portion of our required pediatric clerkship was defined as having only seven components: Nutrition, physical and behavioral development through adolescence; neonatology (excluding NICU); fluid and electrolytes; infectious diseases and immunization; accidents and poisonings; and selected genetic disorders. The evaluation instrument used was the subject test of the NBME part II (4 versions were used in 8 clerkships). Security of the examination was not breached. Core questions, as defined by us, formed 45-48% of the examination. Our experimental design tested the hypothesis that the total mean score would rise over the eight successive clerkship modules, while the "core" score would be constant. The hypothesis was refuted; both scores were reasonably stable. The core questions however were answered correctly consistently better than the non-core; 66% vs. 56% p<.01 a reassurance that emphasis in teaching may influence cognitive outcome. The mean normative NBME score ranged from 449 to 519 (i.e., -0.61 to +0.19 S.D. of the national reference group when the test is taken for licensure). Given only an average pediatric clerkship in the U.S. of 7 weeks (ours, 6 weeks) we suggest that a consensus core be defined in U.S. schools and that the NBME part II committee, mirroring the schools, tailor the evaluation instrument to reflect that core.

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THE EFFECT OF REDUNDANT CUES, SEVERITY OF THE DIAGNOSIS, AND PSYCHOSOCIAL INFORMATION ON MEDICAL DECISION MAKING. David A. Bergman (Spon. by Melvin M. Grumbach) Dept. of Pediatrics, University of California SF, San Francisco.

In an effort to understand how clinical information is utilized in medical decision making, we presented 60 pediatricians 6 clinical vignettes each of which included a possible diagnosis. Each of the vignettes took two forms. One form had 3 diagnostic cues with known predictivity for the given diagnosis; the other form had these 3 cues and 3 additional cues that did not change the predictivity. One group of physicians responded to the 3 cue form and the other group responded to the 6 cue form. The vignettes also varied according to the severity of the given diagnosis and the psychosocial nature of the cues. The predictivity for the target diagnosis in all 6 vignettes was approximately the same. Physicians were asked to estimate the probability for each given diagnosis and a range of estimates around this probability, what additional information they would acquire, and how they would manage the patient. The results showed: 1) probability estimates were higher in the 6 cue than 3 cue vignettes (p .05), 2) probability estimates were higher for those vignettes where the diagnosis was more serious (p=.05), 3) both probability estimates and the range around those estimates were lower for those vignettes with psychosocial cues (p=.01), 4) for 5/6 vignettes probability estimates were significantly correlated with the decision to initiate therapy. The results did not vary with physician experience. This study has shown that the addition of redundant cues, the severity of the diagnosis, and the psychosocial nature of the cues affect the accuracy of physicians' assessment of diagnostic likelihood.

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HALF DOSE DPT VACCINE INADEQUATE FOR PRETERM INFANTS. J. Bernbaum, A. Daft, J. Samuelson, S. Douglas, R.A. Polin, University of PA School of Medicine & Dept. of Pediatrics, Children's Hosp of Phila., Phila. PA.

The Am. Acad. of Peds. currently recommends primary immunization in preterm infants with full dose FD (0.5ml) DPT vaccine at 2, 4 & 6 mos. after birth. Pediatricians, in an attempt to lessen side effects in preterm infants, often administer this vaccine in reduced dosage. No data exist to support this practice. This study was designed to quantitate the immune response of preterm infants immunized with half dose HD (0.25ml) vaccine and to determine the nature and extent of side effects. 10 study infants (mean±SD BW 1.4±.3 kg, GA 31±2 weeks) were immunized with HD vaccine IM at 2, 4, & 6 mos. after birth. 22 preterm infants of similar BW & GA immunized with FD vaccine at the same time intervals served as controls. Prior to each immunization & 2 mos. after the 3rd, DPT specific antibodies were quantitated. Side effects were determined by parental report. The table demonstrates the % of preterm infants receiving HD & (in parenthesis those receiving FD) who had D & T protective antibodies, and % conversion for P at each time interval.

	Pre-immun.	Post-immun.#1	Post-immun.#2	Post-immun.#3
D	88 (73)	75 (86)	100 (100)	100 (100)
T	100 (91)	100 (77)	100 (100)	100 (100)
P	63 (14)*	38 (18)	38 (91)*	63 (95)* *p<05

D & T antibody titers were protective after DPT #2 in both groups, but the immune response to P antigen was inadequate in the HD group even after DPT#3. There were no significant differences in incidence or severity of side effects between treatment groups. Therefore, we strongly recommend that preterm infants receive full dose vaccine at the routine time intervals to insure adequate protection.