Genetic Counseling for Pediatricians Dealing With Newborns L.B. Holmes, Genetics Unit, Mass. General Hospital, Boston.

We have assessed the frequency of hereditary disorders identified in the first 5 days of life among 12,000 newborn infants. There were no affected relatives in 84% of the families with infants with genetic disorders. This indicates that the pediatrician usually must evaluate and counsel for affected infants in the absence of a history of affected relatives. This experience underscores the necessity of recognizing in the affected infant alone those conditions that are due to single mutant genes, multifactorial inheritance and chromosome abnormalities.

Among these infants the most commonly recognized hereditary disorders were congenital malformations. Those due to multifactorial inheritance occurred in 0.5% of infants, the most common being neural tube defects, cardiac anomalies, hip dislocation, cleft lip and palate and club foot. 0.4% of newborns had malformations due to single mutant genes. 0.1% had chromosome abnormalities recognizable by physical examination.

In this study only 2 infants had recognizable metabolic disorders, both the adrenogenital syndrome.

Programs studying each newborn for unsuspected metabolic and chromosome abnormalities showed an additional 10 affected infants (0.1%).

Our experience has shown it is equally important to provide counseling for parents with an abnormal child for which no genetic cause is evident.

CHROMOSOMAL BREAKAGE AND SPRAY ADHESIVE EXPOSURE: E.B. Hook, P. Brinson, J.C. Feck, L. Fisher, P. Greenwald, N.H. Hatcher and O.J. Stanecky, Birth Defects Inst., Burns Care Inst., Cancer Control Bur., New York State Dept. of Health, and Dept. of Ped., Albany Med. Coll., Albany.

The recent claim of a 5 to 6 fold increase in cells with chromosomal damage in individuals in Oklahoma City exposed to spray adhesives, the resulting national warnings, and the questionable nature of the evidence offered in support of the association, prompted a local "blind-assessment" study of chromosome breakage in 11 exposed and 11 control individuals. PHA stimulated peripheral blood cultured for 72 hours (as in the Oklahoma study) was used. The cells were scored "blindly", i.e. without knowledge of their source, and only metaphase spreads with clear evidence for chromosome breakage, exclusive of gaps, were scored as "positive". Approximately 700 cells from each group were evaluated. The rate in the exposed was 1.3% and in the controls 1.0%; a non-significant difference which in fact excludes with 95% confidence a rate in the exposed 2½ times or greater that in the controls. In the entire study 3 cells with evidence for chromosomal *rearrangement* were seen: 2 dicentrics in the controls and 1 in the exposed. Thus this study does not confirm the Oklahoma report. It does raise more general questions as to what laboratory evidence of chromosome breakage warrants the nationwide emergency action that occurred with spray adhesives, and how scientific societies can provide immediate consultation for regulatory agencies in need of advice.

ADDITIONAL DATA RELATIVE TO PATERNAL AGE AND FRESH GENE MUTATION. Kenneth L. Jones, Mary Ann Harvey, Linda Quan, Bryan D. Hall and David W. Smith. Univ. of Washington Sch. of Med., Dept. of Ped., Seattle.

Older paternal age has been recognized as a factor in fresh gene mutations and has been documented in sporadic cases of 5 autosomal dominant conditions.

In this collaborative study, an older paternal age factor was additionally documented in sporadic cases of the Basal Cell Nevus syndrome, the Crouzon syndrome, and the Waardenburg syndrome, 3 conditions in which autosomal dominant inheritance has been implied; and in sporadic cases of Acrodysostosis and Progeria, suggesting a fresh mutant gene etiology for these 2 conditions in which the mode of inheritance has been unknown. Paternal age data from a number of other disorders showed inconclusive or no older paternal age factor.

Recognition that older paternal age is a major factor leading to fresh gene mutation in man should be incorporated into general recommendations relative to family planning.

CYTOGENETIC STUDIES OF COUPLES WITH FETAL WASTAGE: CONVENTIONAL VERSUS BANDING TECHNIQUES. Hyon J. Kim, Lillian Y. Hsu, and Kurt Hirschhorn. Mt. Sinai Sch. Med., Dept. Ped.,N.Y.C.

It has been shown that both numerical and structural chromosome aberrations are significant etiologic factors in fetal wastage. The estimated frequency of finding a balanced structural aberration in couples with fetal wastage is 1 in 26. Since 1968, we have studied a total of 123 parents including 56 couples and 11 single parents with history of two or more spontaneous abortions, still birth(s) and/or live born(s) with multiple anomalies. 53 parents (24 couples and 5 single parents) studied with the conventional method, yielded two mothers with 45,X/46,XX/47,XXX mosaicism and one couple with abnormal chromosomes in both (mother-46,XX,inv 3(p-q+); father-46,XY/47,XY,+D). Since the introduction of the current banding techniques, 70 parents (32 couples and 6 single parents) were studied. In this group, two mothers were found to have a reciprocal translocation which was not detectable by conventional karyotyping (1 mother-46,XX,t(17;19)(q23;p13); 1 mother-46,XX,t(4;11)(q25;q13)); 1 mother was mosaic for 45,X/46,XX/47,XXX; 3 fathers had an increased frequency of chromosome breaks and 1 father showed mitotic instability. Recently, we studied a couple with infertility and found a balanced translocation, 45,XX,t(14q;22q) in the wife. Couples with fetal wastage, subfertility or infertility must be studied with the new banding techniques. This will provide more accurate genetic counselling and guide prenatal monitoring by prenatal diagnosis.

GENETIC HETEROGENEITY IN FUCOSIDOSIS. Boris G. Kousseff, Nicholas G. Beratis, Cesare Danesino, Kurt Hirschhorn, Mount Sinai School of Medicine of the City University of New York, Department of Pediatrics, Division of Medical Genetics, New York. Fucosidosis is an autosomal recessive lysosomal disorder resulting from the deficient activity of the enzyme alpha-L-fucosidase. The originally described cases were characterized clinically by progressive psychomotor retardation, severe neurologic signs, coarsening of facial features, variable skeletal abnormalities, and fatal outcome in childhood. Three cases of fucosidosis with a different clinical picture have been described. We are reporting two brothers, 4½ and 9 years old, affected by a variant form of fucosidosis indicating genetic heterogeneity of this storage disease. A marked deficiency of alpha-L-fucosidase was demonstrated in cultured skin fibroblasts of both patients (0.0 to 3.5 n moles of p-nitrocatechol/mg protein/hour). The enzymatic activity in the parents (32.0) was approximately 28% of the activity of control fibroblasts (111.2). This new form of fucosidosis (fucosidosis type 2) is characterized by angiokeratoma corporis diffusum, spondyloepiphyseal dysplasia, as well as a milder course of psychomotor retardation, milder neurologic findings, and a longer survival than the originally described cases of the disease. Because of similarities of type 2 fucosidosis with mucopolysaccharidosis and Fabry's disease, the differential diagnosis of these disorders should include alpha-L-fucosidase determination.

REDUCTION OF THE FREE-CYSTINE CONTENT OF CYSTINOTIC FIBROBLASTS BY ASCORBIC ACID AND DEHYDROASCORBIC ACID. Wolfgang A. Kroll and Jerry A. Schneider. Univ. of Calif., San Diego, Sch. of Med., Dept. of Ped., La Jolla.

Ascorbic acid (0.57 mM) caused a slow decline in the free (acid-soluble) cystine content of skin fibroblasts from 6 cystinotic patients of 58.6% (range 48-75%) over a 3 day period. The cystine content then remained at this level as long as ascorbic acid was added every 24 hours. When ascorbic acid was removed, the cystine content returned to its original value in 2-3 days. Dehydroascorbic acid, the oxidation product of ascorbic acid, caused a similar reduction in cystine content of cystinotic fibroblasts. Thus, the effect of ascorbic acid is not related to its reducing properties.

Cystinotic fibroblasts preloaded with ^{35}S-cystine rapidly released ^{35}S when treated with dithiothreitol (DTT) but not when treated with ascorbic acid. When cystinotic fibroblasts were depleted of cystine with DTT, the cystine reaccumulated 20% more slowly with dehydroascorbic acid (0.57 mM) in the media. Thus, ascorbic acid and dehydroascorbic acid appear to act by slowing the entry of cystine into the cystine pool of cystinotic fibroblasts and not by increasing the release of cystine from this pool.