anomaly has not been proven in man. The detection of position effects might be possible in man by the analysis of apparently balanced translocations and a search for correlations between specific breakpoints and phenotypic abnormalities. A dysmorphic and mentally retarded boy has been found presumably carrying a *de novo* balanced translocation which involves the long arms of chromosomes 13 and 18. Breakpoint mapping the long arms of the chromosomes 13 and 18 has revealed presumptive evidence for a position effect in 18q21.

## Possible Evidence of Y Chromosome in Testicular Tissue of Patients with True Hermaphroditism and Karyotype 46,XX

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It is widely accepted that male determinant genes must be present, at least in primordial germinal cells, in order to determine testicular differentiation. However, exceptions have been reported, such as the existence of XX in apparently normal males and in the majority of true hermaphrodites. Several theories have been advanced to explain the existence of testicular tissue in the absence of a Y chromosome, but they have not been confirmed cytologically. The present work attempts to detect the presence of a Y chromosome by the quinacrine fluorescence technique in histologic sections of gonads from three patients with true hermaphroditism and somatic cell karyotypes 46,XX. Typical fluorescence of the Y chromosome was found in the testicular tissue from the three patients, indicating the existence of the Y chromosome in gonadal tissue. These findings strongly support the hypothesis that a Y chromosome is necessary for testicular differentiation.

## Partial Trisomies and Deletions of Chromosome 13

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With the advent of new banding techniques there have been increasing numbers of patients with trisomies and deletions for specific portions of chromosome 13 discovered. Some authors have suggested a preliminary phenotypic mapping of chromosome 13. We have studied five patients with trisomies and deletion of parts of chromosome 13 using banding techniques and we have attempted a karyotype-phenotype correlation. 1) *Deletion 13q31 → 13qter:* karyotype 46,XX,del(13) (13pter→ 13q31:) is associated with mental retardation, craniofacial asymmetry, microcephaly, wide forehead, short philtrum, large mouth with protruding and wide spaced superior incisors, prominent and wide nasal bridge, large ears, hypertelorism, retinoblastoma of left eye, and kyphoscoliosis. 2) *Deletion 13q31/13q32/13q33 → 13qter:* karyotype 46,XY,13r is associated with growth and mental retardation, large eyes, epicanthus, hypertelorism, frontal bossing, high arched palate, short philtrum, protruding and wide spaced superior incisors, simple low set ears, hypoplastic fingernails, posterior prominence of heel, deep crease of hallux, dorsiflexed first toe, and a third toe longer than the other toes in both feet. 3) *Trisomy 13q12--13qter:* karyotype 46,X,+t(Y;13)(q11:q12)(Ypter → Yq11:13q12 → 13qter:) is associated with trigonocephaly, craniostenosis with prominent metopic suture, epicanthus, colobomata of left iris, high arched palate, dysplastic low set ears, postaxial symmetric polydactyly, abnormal flexion of fingers, hypoplastic fingernails, and bilateral club feet. 4) *Trisomy 13q13 → 13qter:* karyotype 46,XX,t(5;13)(p14;q13)(13qter → 13q13::5p14 → 5qter)pat. is associated with growth retardation, microcephaly, craniostenosis, sloping and prominent forehead, protruding nasal bridge, short palpebral fissures, bilateral cleft lip, cleft palate, short neck, abnormal flexion of fingers, simian crease, clinodactyly of fifth fingers, bilateral club feet, and duplication of fifth toe with syndactyly in the right foot. 5) *Trisomy 13pter → 13q12:* karyotype 47,XX,+del(13)(13pter → 13q12:) is associated with mental retardation, microophthalmy, enophthalmy, colobomata of iris and glaucoma of left eye, bilateral preauricular dimples, imperforate anus, rectovulvar fistual, and double left calyceal system.

These observations permitted phenotypic mapping of the partial trisomic and monosomic segments in cases 1, 2, 3, and 5, which was not possible in case 4 because the patient also had a partial monosomy of chromosome 5. The deletions of the short arm of chromosome 13 (case 2) and long arm of chromosome Y (case 3) were considered to have no significant functional effect.

## Tay-Sachs Disease Heterozygote Selection

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The authors determined the serum hexosaminidase A levels in 197 subjects (106 males and 91 females); 174 were adults and 23 were children aged from 20 days to 15 years; 13 of the children were of Jewish origin, the other 10 children were non-Jewish. Of the total 197 subjects, 94 (51 males and 43 females) were Jews whose ancestors lived in Western and Central Europe (Ashkenazi). The other 103 subjects (53 males and 50 females) had no Jewish ancestors.

The serum hexosaminidase A levels were determined following the method of O'Brien *et al.* (1970) modified by Kaback (Methods Enzymol., *28:* 862 (1973)). In those cases where the results were doubtful, especially in the pregnant women (6), the hexosaminidase A levels were also tested in the leukocyte, according to the method described by Kaback and Zeiger (Advan. Exp. Med. Biol., *19:* 13 (1972)). The results are presented in Table 1.

Table 1. *Serum hexosaminidase A in Jews and non-Jews*

| Hexosaminidase A serum (% A of total) | Children (23) | | Adults (174)[1] | |
|---|---|---|---|---|
| | Jewish (13) | Non-Jewish (10) | Jewish (81) | Non-Jewish (93) |
| >40% (normal homozygotes) | 9 | 8 | 57 | 83 |
| 30–40% ("doubtful" cases) | 5 | 1 | 14 | 9 |
| <30% (heterozygotes) | 0 | 1 | 10 | 1 |

[1] In the pregnant women in which results from 15.6–35.0% of serum hexosaminidase A were found, the leukocyte tests showed levels within the limits of normal homozygotes.

**Comments:** The high incidence of heterozygote carriers of Tay-Sachs disease in Ashkenazi Jews (1:30), emphasized once more by this investigation, justifies the population screening for these heterozygotes, particularly among Jews, in order to offer genetic counseling and try to prevent further cases of Tay-Sachs disease.

## Anti-Human Growth Hormone (HGH) Antibody Determination in HGH-treated Patients

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Determinations of anti-HGH antibody were performed by radioimmunoassay in 57 patients with pituitary insufficiency who had been treated with human growth hormone (HGH). Antibodies were not detected in 38 patients, 10 had low antibody titers (1:15–1:120), 4 medium titers (1:120–1:960), and 5 high titers (of 1:960). In 42 patients, antibody titers could be correlated with growth velocity during HGH treatment. An adequate growth velocity was observed in 25 of 27 patients with negative titers, 5 of 7 with low titers, 3 of 4 with medium titers, and 1 of 4 with high

titers. The 3 patients with high titers and a decrease in growth velocity all had an isolated hereditary growth hormone deficiency.

In conclusion, most patients with negative, low, or medium anti-HGH antibody titers grow adequately. The presence of high level titers inhibited the growth response to HGH administration.

## High Affinity Estrogen Receptors in Uterus of Early Malnourished Rats

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We have found that marasmic malnutrition in rats permanently decreases uterine cell number. On the other hand, a decrease of total plasma estrogen levels in mothers of small for gestational age newborns has been demonstrated. We have found, also, decreased levels of sex hormone binding globulin in these mothers, suggesting lower levels of free plasma estrogens. As an index of hormone action upon the target cells, we studied uterine estradiol receptors of early malnourished rats. Malnutrition was induced in rats by increasing litter size to 18 pups per dam from birth until weaning. These offspring received a 22% protein diet from days 21–90 of life. Control dams nursed 6 pups, which were fed the normal diet after weaning; all animals were killed at 90 days. Uterine estradiol receptors were measured according to the technique of Feherty *et al.*, recovering bound estradiol with DEAE-cellulose filters instead of dextran-charcoal. Estradiol binding capacity of the uteri of marasmic rats was decreased compared to normal, age-matched controls expressed as picomoles per mg tissue ($8.26 \pm 2.76 \times 10^{-4}$ *vs.* $5.16 \pm 1.96 \times 10^{-4}$, respectively, $P < 0.025$), picomoles per mg protein ($0.262 \pm 0.0055$ *vs.* $0.0153 \pm 0.0054$, respectively, $P < 0.001$), or picomoles per DNA ($1.96 \pm 0.80 \times 10^{-4}$ *vs.* $1.10 \pm 0.28 \times 10^{-4}$, respectively, $P < 0.025$). These results show that the number of estradiol receptors in the uterus of rats malnourished early in life is decreased. This is more evidence that early malnutrition produces damage in the uterus of the rat.

## Bioavailability of Heme-Iron Preparations Derived from Bovine Red Blood Cells

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In the past, milk has been fortified with inorganic iron compounds. The bioavailability of these compounds for absorption is altered according to the properties of the vehicle. The purpose of this work was to study the possibility of fortifying whole milk with organic iron obtained from fresh bovine red blood cells. The organic iron preparations used in this study were: 1) hemoglobin with stroma, 2) hemoglobin without stroma, 3) hemin. These compounds are soluble in milk and water (with the exception of hemin), do not alter the flavor of the milk, and give the milk a chocolate color. The absorption of these preparations was studied using both whole milk and aqueous solutions as vehicles by a double isotope technique. Seventy healthy infants from 6–18 months old were distributed into five groups: 1) hemoglobin with stroma in whole milk, 2) hemoglobin without stroma in whole milk, 3) hemin in whole milk, 4) hemoglobin with stroma in water, 5) hemin in water.

On day 1 each group was given 150 ml milk or water to which were added 2 mg Fe in the form of the heme-iron being studied (hemoglobin with stroma, hemoglobin without stroma, or hemin) and the same product prepared from calf red blood cells that were biologically marked with $^{55}Fe$ (0.5 $\mu$Ci/kg). On day 2, the infants received 50 ml of a ferrous-ascorbate solution that contained 2 mg iron ($FeSO_4$) marked with $^{59}Fe$ (0.1 $\mu$Ci/kg). Absorption was calculated 14 days later according to circulating radioactivity. The heme-iron preparations in milk showed a geometric mean absorption of 20%. The ratios among the formulas of day 1 in milk and day 2 did not show statistically significant differences. No difference between the absorption of hemoglobin in milk or in aqueous solution was observed; however, the hemin showed a lower absorption value ($P < 0.01$) in aqueous solution. It can be concluded that fortification of whole milk with hemoglobin preparations is feasible. The addition of hemoglobin preparations to milk appears to be an excellent combination because of the organoleptic characteristics and high bioavailability of iron.

## Study of the La Brosse Spot Test for 3-Methoxy-4-hydroxymandelic Acid (VMA)

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The object of this paper is to compare the La Brosse test with the quantitative urinary VMA measurement (Pisano's technique). Substances whose breakdown products appear in the urine and give false positive results were eliminated from the diet. Seven hundred 24-hr urine samples belonging to 580 patients were studied. Fifty-six patients had sympathoblastomas, 15 pheochromocytomas; the remaining several pathologies were not related to a catecholamine increase. Four hundred twelve negative, 132 intermediate, and 156 positive reactions were obtained. The negative tests had normal VMA in all cases except in five urine samples (false negative) belonging to three patients with pheochromocytoma who had increased VMA (between 15.4 and 38.6 mg/24 hr). The intermediate results had normal VMA in all cases except one patient with pheochromocytoma (VMA 18.4 mg/24 hr). Among the positive tests, 70 showed increased VMA and 86 normal VMA (false positive FP). The former results belonged to 55 samples from sympathoblastoma patients and to 15 from pheochromocytoma patients. The FP occurred in 15 patients treated for sympathoblastoma and in 71 patients without any pathology associated with a catecholamine increase. Of the sympathoblastoma patients, 30 were studied before any treatment (group I) and 26 after treatment (group II). In group I, all but 1 yielded positive tests: 28 had increased VMA and 2 had normal VMA. From this group, 16 patients were followed during treatment: 11 continued with positive tests and increased VMA excretions and 5 converted to negative tests and normal VMA. In group II, 19 were negative, 4 were intermediate, and 3, all with normal VMA, were positive. Only one patient persisted with positive tests in the subsequent evaluations.

In conclusion, the La Brosse test is a practical screening test to detect and follow the course of treatment in patients with sympathoblastoma who initially had positive tests and increased VMA. All these results must be interpreted with caution because there are false positive results and a 15% of sympathoblastoma patients have normal VMA. The false negative results (1.2%) were observed in 17% of pheochromocytoma patients. The intermediate reactions were associated with normal VMA excretions except in one pheochromocytoma patient.

## Pathology of "Uninvolved" Renal Parenchyma in Nephroblastoma

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Two hundred twenty-five primary renal tumors in children were histologically examined; 191 of these were nephroblastomas (Nbl) (Wilms' tumor). In 61, sufficient residual parenchyma was available for study. In a 5-month-old girl admitted with corticoid-resistant nephrotic syndrome, an Nbl was found and a nephrectomy was performed. In the uninvolved renal tissue a severe diffuse glomerular mesangial sclerosis was present; it led to her death in renal failure 6 months after onset. In 12 other specimens nephroblastomatosis was present. The most common lesions were subcapsular metanophric hamartomata (either as discrete nodules or as diffuse involvement of the superficial cortex). They were frequently associated with nodular renal blastema and occasion-