

Genetic—Metabolic News*

This is the first in a series of newsletters designed to inform the Virginia medical community of recent advances in the area of GENETICS and METABOLISM and to provide information regarding a variety of services that are available at the Medical College of Virginia. The number, complexity and expense of tests that are now required in order to make precise diagnoses in many of the newly described genetic and metabolic disorders make it impossible for most clinical pathology laboratories to provide these services.

Accurate and meaningful genetic counseling *must* be based on *precise* diagnoses. Genetic counseling is imperative if we are to have some measure of success in reducing the familial transmission of these disorders. "An ounce of prevention is worth a pound of cure."

Diagnosis and continued therapy of many of the inborn errors of metabolism (i.e. phenylketonuria, galactosemia, glycogen storage disease, maple sugar urine disease, methylmalonic aciduria, etc.) require highly sophisticated biochemical tests and enzymatic analyses. Newer techniques for the detection of carrier states (i.e. Tay-Sachs disease, sickle-cell disease) have stimulated the development of several programs for mass screening for carriers. These screening programs have already been successful in identifying married couples where both husband and wife are carriers of a gene for an inborn error of metabolism and thus have a 25% likelihood of producing an affected child.

One of the more exciting developments in the past several years has been the ability to make chromosomal and metabolic diagnoses on cells in amniotic fluid obtained transabdominally (i.e. by amniocentesis) at 14–16 weeks of pregnancy. This procedure enables one to monitor certain "high risk" mothers for an affected fetus prior to the 20th week of gestation—a time sufficiently early to allow the therapeutic termination of pregnancy when indicated. Amniocentesis involves a very minimal risk to mother and fetus. Indications for this type of study performed in the Department of Obstetrics and Gynecology are noted in the following pages.

Beginning on Tuesday, January 8, 1974 the National Foundation—March of Dimes Genetic Coun-

seling Clinic will accept for investigation and counseling any families desiring these services. No charge will be made for the counseling services or for the services of the metabolic tissue culture laboratory. Where a precise diagnosis is not already well established, the family may be directed to various subspecialty areas, either as a private or general staff patient, where more definitive studies can be carried out on a fee-for-service basis. Charges for chromosomal studies are outlined in the following pages.

Medical personnel who desire further general information regarding the Counseling Clinic may write or call Dr. Peter Mamunes at (804) 770-3033 or 770-5076 or Dr. R. B. Young at (804) 770-4206 or 770-5076 in the Department of Pediatrics. A listing of the various genetic and metabolic services which are currently available at the Medical College of Virginia is provided in the following pages for your future reference. Where specific services are noted, direct contact should be made with the persons offering the services.

MEDICAL COLLEGE OF VIRGINIA GENETIC AND METABOLIC SERVICES

1. National Foundation—March of Dimes Genetic Counseling Clinic (Department of Pediatrics and Program in Human Genetics). The counseling services of this clinic are available at no charge to patients referred for genetic counseling. This clinic meets on the first and third Tuesday afternoons of each month. For inpatients and families where a precise diagnosis is not clearly established, appropriate referrals are made. Contact Dr. Peter Mamunes or Dr. R. B. Young.

2. National Foundation—March of Dimes Metabolic Tissue Culture Laboratory (Department of Pediatrics). This laboratory provides the definitive identification of certain metabolic defects which can be measured by enzyme analyses of white blood cells, red blood cells or fibroblasts from skin or amniotic fluid. Since these studies are complex and time consuming, they are performed only after preliminary screening studies have indicated the likelihood of a genetic defect.

Due to the very large number of genetic defects now recognized to occur, this laboratory performs tests only on a few specific disorders of carbohydrate,

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lipid and amino acid metabolism which have been recognized to occur with a reasonable incidence in this state. These include the glycogen storage diseases, defects in intermediary carbohydrate metabolism which lead to hypoglycemia or developmental delay, various problems which cause organic acidosis, the aminoacidopathies and a small number of abnormalities which are associated with abnormal lipid storage (especially Tay-Sachs disease). Where other diseases are suspected, specimens are sent to other laboratories in the U.S. that have specific interests in the particular disorder in question. Contact Dr. Robert Eanes or Dr. Peter Mamunes.

3. MCV Metabolic Service Laboratory (Department of Pediatrics. Contact Dr. Peter Mamunes).

A. Urine for Metabolic Screening. To screen for various inborn errors as a cause for psychomotor retardation, failure to thrive, recurrent acidosis, seizure disorder, etc., a battery of qualitative tests and high voltage electrophoretic separation of amino acids is performed on a random urine specimen (minimum 15 cc volume). After acidification to pH 1 (with a few drops of concentrated hydrochloric acid) the urine can be mailed to this laboratory at room temperature. Testing is performed once per week. More specific quantitative procedures are undertaken where the screening tests determine the need. The fee for preliminary metabolic screening tests on urine is \$20.00.

B. Measurement of Specific Metabolite or Enzyme. As a part of its research activities (in mitochondrial metabolism, pathophysiology of Reye's syndrome, organic acidemias and hypoglycemia) this laboratory has established a substantial number of quantitative procedures for metabolites and enzymes. When there is a need for a test not performed locally, referral to the appropriate source laboratory is made.

C. Treatment of Inborn Errors of Metabolism. Supervision of dietary and other treatment modalities for the inborn errors of metabolism is monitored by careful analysis of accumulating substrate or intermediary metabolites. This program is supported to a large extent by the Bureau of Child Health of the Virginia State Health Department.

4. MCV Chromosome Service Laboratory (Department of Pediatrics and Program in Human

Genetics). Chromosomal analysis is performed on a fee-for-service basis on patients with: 1) multiple congenital anomalies; 2) sex anomalies not fully identified by sex chromatin (buccal smear) studies; 3) suspected chronic myeloid leukemia for identification of the Philadelphia-1 (Ph¹) chromosome. Blood specimens can be collected in micro capillary tubes (heparinized) and mailed in special culture tubes which are available on request. Culture and analysis require approximately two weeks. Charge for complete culture and photographic karyotyping on peripheral blood leukocytes or bone marrow will vary from \$75.00 to \$150.00 according to complexity. Special arrangements are necessary for the scheduling of this test. Charge for routine buccal smear for sex chromatin (Barr body) is \$10.00 or by fluorescent technique for identification of the double Y bodies in the XYY syndrome is \$20.00. Contact Dr. Andrew Chen or Dr. R. B. Young.

5. MCV Amniocentesis Laboratory for Intra-uterine Study of Chromosomal Anomalies (Department of Obstetrics and Gynecology). Patients may be referred by their obstetrician or family physician to be considered for amniocentesis and chromosomal analysis. Parents in certain high risk situations should be referred for counseling *before conception when possible* or as early in pregnancy as possible. Arrangements could then be made for the amniocentesis to be performed around the 14th–16th week of pregnancy primarily in the following *high risk* situations:

- A. one parent a known carrier of a chromosomal translocation (i.e. 14/21 translocation in mongolism) which carries a *one-in-three* to *one-in-five* chance of having another affected child;
- B. any family with a prior mongoloid child (recurrence risk is approximately 1:200);
- C. any mother 40 years of age or older (occurrence risk is approximately 1:100);
- D. any family where parents are known to be carriers of a sex-linked recessive condition such as hemophilia (occurrence risk is 50% in *male* children);

- E. any family where both parents are known carriers of a biochemical disorder that is capable of being detected in amniotic fluid (now some 20 or more disorders). Most of these disorders have autosomal recessive transmission with a 25% recurrence risk.

Amniocentesis will be performed on an outpatient basis in the Department of Obstetrics and Gynecology. In most cases amniocentesis will be preceded by placental localization by diagnostic ultrasound. Referred specimens of amniotic fluid may be accepted if prior arrangements are made. Total charges will range from \$200 to \$250. The time required for tissue culture and photographic karyotyping of the chromosome is approximately three weeks. It is anticipated that almost all parents will elect early termination of pregnancy if the fetus is found to be affected. Immediate consultations between referring physician and the Department of Obstetrics and Gynecology will be imperative in these situations. Contact Dr. Fay Redwine, Dr. Edward Davis or Dr. Leo Dunn, Chairman.

6. Consultation and Evaluation Clinic Chromosomal Laboratory—Bureau of Child Health and Department of Pediatrics. Children being evaluated for psychomotor retardation in any of the C&E clinics throughout the state are eligible for chromosome analysis without charge when these studies are clinically indicated. Any mongoloid (Down's syndrome) patient may also be referred by his physician for chromosome analysis without charge. Further family studies will be carried out when indicated.

7. Special Study Project of Multiple Spontaneous Abortions—Sponsored by Developmental Disabilities Study Grant and Program in Human Genetics. Chromosomal studies will be performed

free of charge for the next six months (December 1, 1973 to June 31, 1974) on parents who have had two or more spontaneous abortions to search for possible translocations which may then indicate high risk of recurrence. Amniocentesis might then be considered if a translocation is identified in either parent. Contact Dr. Andrew Chen or Dr. R. B. Young.

8. Tay-Sachs Screening Program—Supported by the Department of Pediatrics, the Department of Pathology, the Virginia State Health Department and voluntary contributions from individuals and organizations. A Tay-Sachs carrier detection program has been established. Over 1,800 adult Jews in the state have thus far been screened after an intensive educational campaign in the greater Richmond area. Each of the 60 identified carriers has been appropriately counseled. Presently, we are advising and supporting other Virginia communities in their efforts to educate, test and counsel for this lethal, inherited metabolic disorder of the central nervous system which affects primarily Jews. Because the test (done on one milliliter of serum) measures enzyme (hexosaminidase A) activity, special handling of the specimen is required. All married Jews in the childbearing age should *definitely* be tested. Charge is a voluntary contribution. Contact Dr. Peter Mamunes.

9. Sickie Cell Testing and Counseling. The Virginia Sickie-Cell Anemia Awareness Program (VASCAP) tests for carriers of sickle trait in the *childbearing age* and provides genetic counseling. Blood samples may be sent by the patient's physician (mailing tubes can be provided) or the patient may go to the testing clinic at 1008 East Clay Street in Richmond. Call (804) 770-7797 for information.

For Specific Information in the Above Areas Contact:

<u>Name</u>	<u>Department</u>	<u>Telephone (804)</u>
Dr. Andrew Chen	Program in Human Genetics	770-4646 or 770-4645
Dr. Edward Davis	Department of Obstet.-Gynecol.	770-4111
Dr. Leo Dunn	Department of Obstet.-Gynecol.	770-4111
Dr. Peter Mamunes	Department of Pediatrics	770-3033 or 770-5076
Dr. Fay Redwine	Department of Obstet.-Gynecol.	770-4111
Dr. R. B. Young	Department of Pediatrics	770-4206 or 770-5076
Dr. Robert Eanes	Department of Pediatrics	770-7610 or 770-5076