Screening for PKU in New York State

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SINCE January 1965 New York State public health law has required that all newborn infants be tested for phenylketonuria in accordance with regulations of the State commissioner of health. These regulations prescribe the Guthrie inhibition assay procedure (*1*) as the only test currently fulfilling the legal requirement.

In New York State 99.2 percent of all live births occur in hospitals, and the statute and implementing regulations are hospital oriented. However, there is specific provision for testing an infant born outside a hospital and not subsequently admitted to one.

Infants must be tested early enough in life so that those with elevated blood phenylalanine levels can be investigated as rapidly as possible, but because the available tests require an adequate level of protein intake by the subject, they must be tested late enough to yield valid results. Infants are captive only for their immediate postnatal hospitalization, ordinarily 3–4 days.

The relative rarity of hyperphenylalanemia poses an additional problem because a laboratory may not find a positive result in less than 1,000 determinations. In a nationwide survey, only a few laboratories detected all of 75 true positive specimens submitted for evaluation by the Guthrie inhibition assay procedure. A subsequent evaluation revealed that only 16 of 36 laboratories were able to correctly detect all 25 positives in 100 specimens.

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This work pointed up the desirability of centralizing the laboratory phase of the program. Accordingly, the laboratory of the New York City health department; the division of laboratories and research of the State department of health, Albany; the laboratory of the Onondaga County health department, Syracuse; and the Erie County Laboratory, Buffalo, were designated to make the required tests.

Each of these laboratories processes from 2,000 to 10,000 specimens every month. Thus a presumptive positive, defined in our program as a specimen with 4 mg. per 100 ml. or greater, occurs often enough to keep the technical personnel acquainted with the appearance of such a test result.

In the 18 months preceding enactment of the law, more than 400,000 infants were screened for PKU using the Guthrie inhibition assay procedure in New York State and elsewhere (*2*). In addition to the blood test taken on the day of the infant's discharge from the hospital, each mother was asked to submit a piece of special filter paper saturated in the urine of the infant when he was 3 weeks old and mail it to the laboratory that analyzed the blood specimen. About 300,000 such urine specimens were examined. No case of PKU which had not been identified by the blood test was identified by the examination of the urine specimen. We did not therefore consider it necessary to require routine blood or urine tests in addition to the test of the specimen taken at discharge.

When the regulation was adopted, there were a number of additional methods for mass screening. The Guthrie method, however, was judged most suitable because specimens were readily and inexpensively transmitted to the

testing laboratory, and the test could be performed by technicians with less training and less expensive equipment than the other methods.

Other methods for screening are currently being evaluated, and the experiences of other States are being viewed with interest. Since the New York statute does not prescribe the method of testing, legislative action is not required to alter the method of testing. In fact, a number of changes in procedure have been instituted since the program's inception.

The Screening Program

To insure that the infant has as much opportunity as possible to ingest milk protein before the specimen is taken, the regulations prescribe than an infant be tested no earlier than the day of discharge from the institution in which initial newborn care was given. The specimen can be taken later if there is medical contraindication to testing on the day of discharge. Although only a test specimen taken on the day of discharge fulfills the legal requirement, additional tests done before discharge are, of course, accepted for screening. If an infant is less than 48 hours old when the specimen is obtained, a repeat specimen is requested by the testing laboratory.

The bureau of maternal and child health recommends that infants hospitalized because of low birth weight be tested on or about their 10th day provided they have had at least 24 hours of milk feeding. In addition, a test specimen taken the day of discharge must be submitted.

Infants who are not promptly discharged from the institutions in which they are born must be tested no later than their 14th day; those few infants born at home and not subsequently admitted to hospitals are also tested no later than the 14th day.

An elaborate procedure for obtaining and testing specimens and reporting of the Guthrie test results has been developed with the help of a department technical advisory committee appointed for this purpose.

The blood specimen is taken from the infant's heel as late as possible on the day of discharge, and the hospital is responsible for checking the blood specimen for its adequacy for testing before the infant's release. The legal burden of obtaining the test specimen is shared jointly by the attending physician and the hospital administrator, and cognizance of this joint responsibility has reduced the number of inadequate specimens to a minimum.

Specimens must be sent to the appropriate laboratory within 24 hours of collection. Here they are again screened for adequacy. If the specimen is inadequate and a repeat specimen is needed, the local health officer and an official of the State bureau of maternal and child health follow the case to insure prompt submission of the required specimen.

The results of all tests are reported in duplicate to the submitting hospital as less than 4 mg. (negative), 4 mg. or greater (positive), or inadequate. The original copy of the report is incorporated into the infant's hospital chart and the second copy forwarded to the attending physician. In addition, notification of each test result of 4 mg. or greater is sent to the appropriate local health officer and to the bureau of maternal and child health of the New York State or New York City health department.

When a test result of 4 mg. or greater is found, the testing laboratory sends to the physician who submitted the original Guthrie filter paper specimen a set of capillary tubes for collecting blood for microchemical analysis and a kit for collecting a second Guthrie filter paper specimen.

Infants whose initial Guthrie tests show levels of 20 mg. or greater are referred immediately for clinical evaluation. When the Guthrie test result is between 4 mg. and 20 mg., a retest of a Guthrie filter paper specimen and a confirmatory microchemical analysis by spectrofluorometry are performed. If these tests indicate a level of 6 mg. or greater, the physician is advised that the child be evaluated for possible phenylketonuria. The bureau of maternal and child health and the local health officer are notified of this action.

Approved Evaluation and Treatment Centers

New York State law recognizes phenylketonuria as a physically handicapping condition. The commissioner's rules and regulations for the medical rehabilitation program allow State-aid reimbursement to the local community

for the initial evaluation and recommendations for treatment of children with diagnosed or suspected phenylketonuria when these services are performed at centers previously approved to give this service by the commissioner of health.

There are currently four such centers in New York State—at Bellevue Hospital Medical Center, New York City; Albany Medical Center Hospital; State University Hospital, Syracuse; and Children's Hospital, Buffalo.

An approved center must be based in a hospital and have a qualified pediatrician as director. The hospital must have an approved house officership, the laboratory director must be appropriately qualified, consultation in all specialties related to the care of the patient must be available, and a qualified neurologist must be available for consultation.

The center has to have medical-social services and psychological services on a continuing basis, a dietary department directed by a qualified dietitian, facilities for evaluating the patient on an inpatient or outpatient basis according to his needs, and facilities for standard clinical pathological studies.

Centers are approved after evaluation by a team from the bureau of maternal and child health and the bureau of nutrition. The organization of a center is checked, as is its ability to provide referring physicians and sponsoring agencies with adequate reports on clinical evaluations, recommendations for treatment and followup, and other necessary records, and to provide the necessary mechanisms for the continuity of care.

State-aid reimbursement can be made available for followup outside the center, but only when performed by a qualified pediatrician or internist with the understanding that there will be close contact between the attending specialist and the evaluation center.

In both implementation of the screening program and flow of referrals to treatment and evaluation centers, there is continual contact between the testing laboratories, evaluation centers, bureau of maternal and child health, and local health departments. Additional telephone and written contact occurs when there is a delay in obtaining a second specimen. Copies of all reports are routinely sent to the bureau of maternal and child health from the evaluation centers and laboratories, and the local health departments are kept informed about infants with suspected or diagnosed cases within their jurisdictions.

Discussion

Since phenylketonuria is genetically determined, a fairly large number of cases can be expected among families of persons previously diagnosed. For the patient, little is accomplished unless dietary management is begun very early in life, but the family's awareness that the condition could occur in future progeny can be expected to be a very effective means of preventing the mental retardation which might be associated with the birth of future children not brought under immediate surveillance.

During the first year of the screening program a junior public health intern visited the families of 24 infants with known cases of phenylketonuria and had 158 of their relatives tested. In so doing, he discovered two cases of phenylketonuria which had previously gone unrecognized. At the same time he gave the families information on the relationship of mental deficiency to the lack of appropriate dietary management and on the genetic basis underlying the disorder. This work has been reported elsewhere (*3*).

During the first 3 years of the program there were 968,346 live births, and 77 newborn infants were diagnosed as having phenylketonuria, an apparent incidence of approximately one in 13,000 live births. Spot checking hospital records and comparing the number of Guthrie test specimens submitted with the number of reported births shows that all newborn infants in New York are now being tested as required.

The total cost of the screening program is $227,000 per year, which means that it costs nearly $10,000 to detect a case of PKU in an infant. Since the number of births in New York State is somewhat in excess of 300,000 a year, the cost for each determination performed is roughly 66 cents.

Summary

Since January 1965 New York State law has required all newborn infants to be tested for phenylketonuria. Regulations prescribe the

Guthrie inhibition assay procedure as the only test currently fulfilling the legal requirement.

Results of all tests are reported in duplicate to the submitting hospital as less than 4 mg. (negative), 4 mg. or greater (positive), or inadequate. Infants whose initial Guthrie tests show levels of 20 mg. or greater are referred for immediate clinical evaluation; those with levels between 4 mg. and 20 mg. are retested.

Since the inception of the mandatory testing program, 77 infants have been diagnosed as having phenylketonuria, yielding an apparent incidence of approximately one in 13,000 live births. All newborn infants in New York are now being tested as required.

The total cost of the program is $227,000 per year. It costs approximately $10,000 to detect a case of PKU in an infant. The cost of each determination performed is roughly 66 cents.

REFERENCES

(*1*) Guthrie, R., and Susi, A.: A simple blood phenylalanine method for detecting phenylketonuria in large populations. Pediatrics 32: 338–343, September 1963.

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National Survey of Use of Lasers

The National Center for Urban and Industrial Health in Cincinnati, Ohio, and the National Center for Radiological Health of the Public Health Service and State officials are conducting a national survey to determine how widely lasers are used in industry and medicine.

The intense beam generated by lasers is such that a worker looking at it without goggles for even a fraction of a second can have his eyes permanently damaged. The survey will determine how often lasers injure the eyes, cause burns, or severely damage the skin of the workers who use them.

Lasers are used for melting metals, crushing rocks, and drilling diamonds. In medicine, they are used in eye surgery and experimentally against cancer. The value of lasers as a communications and military tool is being investigated.

The occupational health program of the National Center for Urban and Industrial Health has completed a detailed study of the use of lasers in Massachusetts, chosen as the first State to be surveyed, because it is one of five States in which about half of the lasers in the country are located. The other States are California, New York, New Jersey, and Ohio.

Connecticut, Illinois, and New York have legislation pending to register, certify, or establish standards to control industrial and medical exposures. Similar legislation has been introduced in Congress.