PKU screening–Is it worth it?

The Advisory Committee on Inborn Errors of Metabolism to the Ministry of Health*

Summary: Ontario's program for PKU screening of newborn infants reached 94.5% of the newborn population from 1966 to 1971. There were 70 infants identified by the program, 47 of whom were classical cases and 23 atypical cases of phenylketonuria. The incidence was 1:16,700 live births for classical cases and 1:34,000 live births for atypical cases. Since the beginning of the program 44 children have been identified in infancy as having PKU and have been treated successfully. Retardation has become evident in only three infants, two of whom were missed by the screening program.

The cost of identification and care of one child for five years is about $7000, much less than the $250,000 needed to provide lifetime institutional care for one severely retarded individual.

The prime objective of screening the newborn population for phenylketonuria is clearly the prevention of mental retardation.

In 1965 many states in the United States were passing legislation requiring the testing of all newborns for phenylketonuria. Ontario set up a voluntary program urging all hospitals caring for mothers and newborn infants to institute a program using the Guthrie test. The Minister of Health left it to the hospitals to carry out the test themselves or to use the facilities of the Provincial Laboratories. The response to this recommendation was very favourable and by 1966 a high proportion of all infants were being tested in the newborn period.

Ontario experience up to 1968 of screening, assessment and management of cases of phenylketonuria has been reported previously[1]

This is a report of Ontario screening experience from 1966 to 1971 and of the cost effectiveness of early diagnosis and treatment. The screening and treatment program is administered by the Maternal and Child Health Service. At the outset an Advisory Committee was set up to guide the program, and included representatives from three university pediatric departments, the Provincial Laboratory Service, and the Maternal and Child Health Service. Criteria for inclusion of metabolic disease in the program are as follows:

1. That a test appropriate for screening be available.
2. That an effective method of treatment be known.
3. That the treatment result in the prevention of retardation.

In this six-year period 785,554 live births occurred and 742,262 Guthrie tests were performed, which represented 94.5% of the total newborn population. Among these, 47 cases of classical PKU and 23 cases of atypical PKU were identified. The latter cases are characterized by lower initial serum phenylalanine levels than in classical cases, and negative or weak reactions in urine tests with ferric chloride or Phenistix® (Ames), compared with classical cases. The atypical cases are probably not at risk for mental retardation but do require assessment and observation for a period to establish their atypical nature. A review of atypical cases and their management has been prepared.[2]

On the basis of this experience the incidence of classical PKU is 1:16,700 live births and of atypical PKU 1:34,000 live births. In the early years of screening programs, the incidence was thought to be 1:10,000. The incidence of classical cases requiring dietary treatment is now lower because of the recognition of atypical cases.

The benefits of the program are evident (Table I). Of 203 known cases in Ontario 79 children, cared for in institutions because of mental retardation, were born before 1966, the first full year of the program. Of the 50 mentally retarded children being cared for at home, only three were born after the provincial program was started; two were considered screening program failures, having been missed in hospital screening, and the third developed retardation in spite of treatment. The criterion for normality was an estimated I.Q. of 90 or more when formal testing was carried out.

Of the 47 classical PKU cases identified from 1966 to 1971, 44 children are within the range of normal intelligence, while three are retarded. Obviously the program has identified and treated a high proportion of PKU patients successfully.

Table II
Estimated cost of identification and care of one PKU patient for five years

Identification	$4000
Hospitalization	1225
Medical care	270
Laboratory tests	235
Diet (Lofenalac®)	1070
Total	$6800

Table I
Cases of classical phenylketonuria in Ontario

Place of residence	Born before 1966	Born 1966 to 1971	Total
Institution	79	0	79
Home: mentally retarded	47	3	50
normal	25	44	69
Unknown	5	0	5
Total	156	47	203

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What has this cost? Estimates only are possible, because costs of laboratory procedures, hospital care, medical care and special diets have all changed over the period of study. It has not been possible to include any estimate of the cost of the hospitals' part in the program, i.e. staff time and mailing charges to the laboratory (Table II).

Identification costs include the cost of the screening procedure per case. Hospitalization is the cost of hospital care during diagnostic assessment and initiation of dietary treatment. Medical care includes medical care during hospitalization as well as follow-up care for five years. Laboratory tests are those performed on an out-patient basis during five years of follow-up. Diet consists of a synthetic food which is low in phenylalanine and is provided by the program. The diagnosis and special care of the child with PKU therefore costs $6800 or about $7000 more than the care of a normal child. Most of these costs are carried by the province as insured health services. In contrast is the estimated cost of $250,000 of caring for an untreated severely retarded child in an institution. It would be impossible to put a price on the benefits to the child and his family of the prevention of retardation.

Résumé

Le dépistage de la phénylcétonurie en vaut-il la peine?

Le plan de dépistage de la phénylcétonurie (PCU) chez les nouveaunés mis sur pied par les autorités ontariennes a permis de toucher 94.5% des nouveau-nés entre 1966 et 1971. Il a permis d'identifier 70 nourrissons, dont 47 étaient des cas classiques et 23 étaient des cas atypiques de PCU. La fréquence était de 1 cas par 16,700 naissances d'enfants vivants pour les cas classiques et de 1 cas sur 34,000 naissances d'enfants vivants pour les cas atypiques. Depuis le début du programme, un diagnostic de PCU a été posé chez 44 enfants durant la première enfance de le traitement qui leur a été appliqué a été couronnée de succès. Trois nourrissons seulement ont subi une arriération mentale, dont deux avaient échappé au cours du plan de dépistage.

Le coût de l'identification et du traitement pour un enfant durant cinq ans est d'environ $7000, se qui est évidemment très inférieur à la somme de $250,000 nécessaire pour couvrir les soins hospitaliers, la vie durant, d'un individu dont l'arriération mentale est sévère.

References

1. PKU Advisory Committee to the Ontario Department of Health: The newborn phenylketonuria screening program in Ontario. *Can Med Assoc J* 101:185, 1969
2. Advisory Committee on Inborn Errors of Metabolism: Atypical PKU in Ontario, July, 1965 — December, 1971 (in press)

Cutaneous infections due to Corynebacterium diphtheriae

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Summary: Toxigenic *Corynebacterium diphtheriae* was grown from skin lesions of 44 indigent patients seen at the emergency or out-patient departments of this hospital, 43 of them within the last 16 months of the study period. In all cases staphylococci or hemolytic streptococci were also present in the wounds. An increase in the incidence of clinical diphtheria occurred in the few months preceding and overlapping the period of recognition of the cutaneous infections. The *gravis* strains, which accounted for the majority of the infections, were sensitive to erythromycin and to penicillin, but were relatively resistant to cloxacillin.

Cutaneous diphtheria is not uncommonly seen in tropical countries[1, 2] and extensive outbreaks occurred in some prisoner-of-war camps during World War II,[3] but in North America diphtheritic skin infections have been recorded infrequently.[4-6] In Vancouver diphtheria has been very uncommon in recent years: no cases were seen in the Vancouver General Hospital during the years 1963 to 1967, nor were any toxigenic strains isolated in the hospital laboratory during that period. However, in June 1968 a patient with a septic lesion on the foot due to *C. diphtheriae* was seen in the out-patient department. Between that time and April 1972, 43 other patients, most of whom live in the skid-row area of Vancouver, have been treated for similar cutaneous lesions infected with toxigenic strains of *C. diphtheriae*. All 43 additional cases were seen in the last 16 months of this period. Since 1968 the number of cases of faucial diphtheria seen in this hospital has also increased sharply.

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Patients and methods

The patients, for the most part, were unemployed adults who presented themselves to the out-patient or emergency departments of the hospital for the treatment of septic lesions. Most lived in small hotels or rooming houses in a restricted area of the older part of the city. Many had no fixed address and a history of alcoholism was common. Swabs from the cutaneous lesions were sent to the hospital laboratory for culture. The clinical records of all patients whose wounds yielded toxigenic organisms were reviewed.

In the laboratory, blood-agar, mannitol salt agar and trypticase soy broth containing 0.1% agar were the media used routinely. If diphtheroids were seen in the gram-stained smear of the exudate, tellurite blood-agar was also used as a