

MASS NEWBORN SCREENING IN SINGAPORE

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Abstract. Births in Singapore are almost exclusively in hospitals and this is conducive to mass newborn screening. Mass newborn screening began in 1965 for G6PD deficiency and has led to successful eradication of the complicating kernicterus. Screening has also identified the distinct ethnic and sex linked variations in incidence. The predominant molecular abnormality is the Canton variant. Congenital hypothyroidism screening was started as a pilot project in 1981, then became institution-based in 1985 and nationwide in 1990. The screening is carried out on the cord blood and is now a primary TSH screen. An incidence of about 1 in 3000 is being obtained and treatment has been started within 2 weeks of birth in almost all babies. A pilot Newborn Screening for hearing impairment started in 1999. It uses the measurement of Transient Evoked Oto-Acoustic Emissions, is hospital based and covers about 10% of the newborn population. The program has identified hearing impairment requiring intervention at a rate of about 1:1000 births. A program covering about 50% of the national births has been commissioned by the Ministry of Health to establish epidemiologic data and to document the outcome of early intervention. Mass newborn screening for inborn errors of metabolism is being considered.

INTRODUCTION

Mass newborn screening in Singapore has evolved in a manner that enabled customisation to meet societal needs, exploiting local geography, demographic and cultural characteristics, national health and economic strategies and policies. Universal screening is presently carried out for Glucose-6-Phosphate Dehydrogenase Deficiency (G6PDD) and Congenital Hypothyroidism (CH) (Joseph *et al*, 1999). More than 99% of the approximately 45,000 annual births occur within hospitals, with slightly under half being in the public sector hospitals. Almost a third of babies return home within 24 hours of birth and only 40% remain beyond 48 hours. Each hospital including the ones in the public sector is a corporate entity and is financially responsible for its services. The State approves of and recommends mass newborn screening for G6PDD and CH. However, it does not legislate or mandate the screening. There is no central screening laboratory and screening programs are hospital based and physician driven. Current state financing of mass newborn G6PDD and CH screening is confined to meeting about 40-60% of the screening charges for the "subsidized patients" within the public sector hospitals. In the case of CH screening, the State funded a pilot project (S\$50,000) and later a feasibility study (S\$250,000) to establish CH screening as part of basic newborn care.

SCREENING FOR G6PD DEFICIENCY

The objective is to identify those affected within a day of birth. This is vital as preventive measures and

counseling need to be instituted early to prevent exposure to triggers and consequent sudden and severe hyperbilirubinemia. Screening on the cord blood is thus the best and this has been our strategy. Details of the screening tests have been previously reported (Wong, 1964;1975). The incidence obtained is about 1.62% of all newborns, 3.15% in males and 0.11% in females. The Chinese and Malay male have a distinctly higher - 3.94% and 2.95% incidence respectively when compared to the Indian male with only a 0.66% incidence. Intermediate deficiency is present in the Chinese female at a rate of 1.83% (Joseph *et al*, 1999). Parents of those affected are counseled on the nature of the disease, its consequences and heritability, and the common triggers that produce hemolysis. The most common trigger was the naphthalene balls used for protecting stored clothes. G6PD deficient babies are physically protected from environmental triggers by keeping them in hospital for a variable period of time. Initially it was for a period of 3 weeks. More recently the period has been reduced to 1-2 weeks. The application of the preventive measures described has resulted in the eradication of kernicterus secondary to G6PD deficiency. No cases have been reported in the last two decades. There is demand from parents for the discharge of their G6PDD babies within a few days of birth just like all other babies. The challenge will be to meet this demand without increasing the risk for a hemolytic crisis and or kernicterus. Under investigation now is the use of early bilirubin and haematologic values to predict the G6PDD baby who may be at a higher risk.

SCREENING FOR CONGENITAL HYPOTHYROIDISM

Screening is by the measurement of TSH in the cord serum. Screening rates that approximate 100% are obtained. Details of the program have been previously reported (Joseph *et al*, 1999; Yeo *et al*, 1983; Joseph *et al*, 1991). In view of the very short turnaround time of the assay, screening results are obtained well within twenty four hours of birth. This ensures early evaluation and onset of treatment within a week of life. Over 500,000 newborns have been screened and the screening rate has been about 99.95%. Recall rates are close to 1%. It has been shown that this rate can be reduced to about 0.7% if a supplemental cord free thyroxine (fT₄) below 1 standard deviation above the mean is used to determine recall (Joseph *et al*, 1993). More recently, recall rates can be directly reduced to about 0.4% by having a two stage protocol. Under investigation is the value of reevaluating before the hospital discharge (usually as early as 18-30 hours), all babies who had screened positive on the cord specimen.

SCREENING FOR HEARING IMPAIRMENT

Since early 1999, newborns were being screened using Transient Evoked Oto Acoustic emissions (Joseph *et al*, 2001). Screening rates of about 97% have been obtained. A significant number of parents elect not to return in the newborn period for a hearing screen, usually citing behavioural responses of the baby to environmental sounds as an indicator of hearing sufficiency. A final referral rate stands at about 7%. Significant impairment (at least moderate impairment in one ear) has been detected in 1 in 548 births and severe impairment in 1 in 1096 births. Three quarters of those identified were not known to be at higher risk for hearing impairment. In the majority, intervention has been instituted within 6 months of age. We are working on screening 7 days a week to obtain a 100% screening rate and introducing a screening Auditory Brainstem Responses in those initially testing positive. This is expected to reduce the referral rates to about 2%. The State has funded a study that will broaden the coverage to all births in the public sector hospitals.

CONCLUSION

In a small country with limited human resources, maximizing the potential of every newborn is critical. The challenge is to continue to identify efficient, effective, safe and affordable newborn screening programs. A research proposal for mass newborn screening with gas chromatography and tandem mass spectrometry is being evaluated.

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