EDITORIAL

# Inherited metabolic disease in Hong Kong

From having been considered paediatric rarities only a few decades ago, inborn errors of metabolism (IEM) can now be diagnosed in many clinical situations. Globally, there are hundreds of conditions caused by single gene defects that have been identified (McKusick register, :http://gdbwww.gdb.org/omim/docs/omimtop.html). The incidence of the individual defects varies considerably, e.g. from 400 million people with a deficiency of glucose 6-phosphate dehydrogenase (distributed on 400 different variants) to four cases of porphyria due to δ-aminolevulinic acid dehydratase deficiency.[1] However, the incidence of IEMs as a group is substantial and in many countries affect up to 0.5% of all newborns (excluding sickle cell disease and other IEMs with a high incidence). The incidence of the 15 to 20 most common IEMs among neonates in North Carolina, the United States, has been estimated to be approximately 1:3000.[2] If the incidence were similar in Hong Kong, approximately 30 babies would be born with an IEM each year.

What is the actual situation in Hong Kong? Neonatal screening for congenital hypothyroidism (a hereditary cause of this condition remains to be established) and glucose 6-phosphate dehydrogenase deficiency began in 1983. The incidence for congenital hypothyroidism is approximately 1:3200 and that of glucose 6-phosphate dehydrogenase deficiency is 1:22 in boys and 1:300 in girls.[3-5]

Most cases of IEM present during the neonatal period, when the baby assumes full metabolic responsibility, after having relied on the mother during intrauterine life to cover for potential metabolic defects. There are also later-presenting forms of IEM, some appearing in adult life.[6] In Hong Kong, investigations of children in homes for the mentally retarded have established that mental debility in some of these children could be due to inherited conditions such as maple syrup urine disease, pyruvate carboxylase deficiency, proprionic acidaemia, and multiple carboxylase deficiency.[7] These findings indicate that IEMs can be expected to be present in Hong Kong.

Interestingly, not a single child has clinically been diagnosed with phenylketonuria (PKU) in Hong Kong. The outcome of a pilot project conducted from 1977 to 1980 to screen for the condition among neonates was also negative[8] (19 152 babies were screened on the fifth day by collecting blood onto Guthrie cards). Recently, pilot projects have been carried out in several cities in mainland China including Beijing, Shanghai, and Guangzhou, aimed at establishing the incidence of PKU in these areas and based on numbers of screened neonates in excess of 50 000 in each region.[9] The investigations were carried out on blood spots from Guthrie cards collected on the fifth day after delivery, according to internationally accepted recommendations for neonatal screening. An incidence of approximately 5 to 8:100 000 was found in two northern provinces.[10] In Guangzhou, the incidence was estimated to be approximately 5:100 000, and included one neonate with classical PKU, two with hyperphenylalaninaemia, and one with tetrahydrobiopterin deficiency among the 60 000 neonates screened. All positive cases were born to parents from the province of Guangdong and the family tree did not contain members born in the north.[11]

It cannot be excluded that some of the neonates with raised blood phenylalanine in Beijing and Shanghai represented hyperphenylalaninaemia and not classical PKU, as positive cases could not be followed up. Still, it seems that a north-south gradient may be present, with a higher incidence in the north. There is also evidence that the pattern of mutations in the PKU gene differs in southern and northern China.[12] Even with this caveat, it is puzzling that not a single neonate with PKU has been diagnosed in Hong Kong. At least one neonate should be born here with classical PKU each year, assuming that the incidence is the same as in Guangdong, from where the majority of the Hong Kong population has come.

The clinical expression of PKU in the Chinese population is the same as in Caucasian children, including fair hair, blue eyes, and mental retardation (Chen RG, personal communication). Hence, children with this condition in Hong Kong should be detected at school age, but there are no reports of school teach-

ers taking action. The situation therefore remains a paradox, and may require another neonatal screening pilot project that screens more neonates than did the previous study.[8]

What about other hereditary disorders in Hong Kong? By comparison with data from other parts of the world,[2] it seems that only a fraction of the expected cases have been identified. One reason is that serious neonatal illness is more likely to be caused by other pathological conditions such as sepsis and organ immaturity. A high level of suspicion and 24-hour specialist laboratory facilities with short turn-around-times for establishing the correct biochemical diagnosis are needed to increase the rate of diagnosed cases of IEM. The requirements for such a laboratory service are discussed elsewhere in this issue of the journal.[13]

However, more epidemiological information is needed about the incidence of the most frequent inherited metabolic disorders in Hong Kong, to estimate the resource implications both with regard to laboratory facilities and clinical care. To obtain this information, an epidemiological study of all neonates could be begun, collecting blood after each child is seven days old. This would need to be continued for several years to provide adequate data for statistical analysis. Such a study may not be easily conducted in Hong Kong, as blood would have to be collected from neonates after they have left the maternity unit. Alternatively, the results of planned neonatal screening for a series of IEMs in Guangdong and other Chinese provinces could be used for local planning. More detailed post-mortem biochemical investigations in paediatric cases of sudden death in Hong Kong could be performed, which would reveal the presence of at least some cases of inherited metabolic disorder.[14]

A simple register of all known cases of IEM in Hong Kong would help to focus attention on this group of disorders and provide some basic information about clinical outcome, including survival rates. Such information would also help in considering the resource implications for providing prenatal diagnosis of IEM.[15]

NM Hjelm, MD, FRCPath
Department of Chemical Pathology
The Prince of Wales Hospital
Faculty of Medicine
The Chinese University of Hong Kong
Shatin, Hong Kong

Whatever the approach, additional resources are needed to improve the diagnostic record (estimated to cost HK$1.30 for each child born in Hong Kong) and to provide the basis for treatment of IEMs, where good results can be obtained if treatment is started immediately, within hours of clinical presentation.

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