

## Research from the South

# Glucose-6-phosphate dehydrogenase deficiency: a preventable cause of mental retardation

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### Abstract

Over two years cord blood from 27 879 babies was screened for glucose-6-phosphate dehydrogenase (G6PD) deficiency. The overall incidence was 3.1% in boys and 1.6% in girls. Sixty nine babies had severe jaundice (bilirubin concentration >380 mmol/l (20 mg/100 ml)), and exchange transfusion was performed. Parents were given written and verbal instructions to avoid herbs and drugs that trigger kernicterus, which reduced the incidence of kernicterus and thereby prevented mental retardation.

G6PD deficiency is common in all three ethnic groups (Malays, Chinese, and Indians) in Malaysia and screening is recommended.

### Introduction

Kernicterus is a well known cause of death in neonates, and survivors may suffer mental retardation and cerebral palsy with considerable loss of hearing. Early detection and appropriate management (phototherapy or exchange transfusion, or both) and avoidance of triggering factors will prevent brain damage due to kernicterus. Children with glucose-6-phosphate dehydrogenase (G6PD) deficiency are prone to develop acute haemolysis and kernicterus if exposed to triggers such as Chinese herbal medicines (San Chi and Chuan Lian), which are added to bath water and thus absorbed through the skin. Chinese herbs are also given to neonates as a tonic for jaundice. In addition, Chinese mothers take a lot of ginger and Chinese herbs as a tonic during the postpartum period, which can pass through their milk and cause haemolysis in babies with G6PD deficiency.

Mothballs containing naphthalene, which causes haemolysis in subjects with G6PD deficiency, are widely used in Asia to protect babies' clothes, and several drugs (table I) also cause haemolysis, as does diabetic ketoacidosis and certain bacterial and viral infections, such as pneumonia, hepatitis, and mononucleosis (although when G6PD deficient patients have received chemotherapy it may be difficult to establish whether the infection or the drug caused haemolysis).

The prevalence of G6PD deficiency in Malay, Chinese, and Indian populations in Malaysia is unknown, and this study was undertaken to investigate the prevalence in the state of Malacca.

### Subjects, methods, and results

From January 1983 to December 1984 cord blood was taken from all infants delivered in Malacca and tested for G6PD deficiency. The blood

was collected on filter paper and dried, and the enzyme was estimated using fluorescent ultraviolet light.

In 1983 blood was analysed from 12 579 babies, of whom 307 (2.3%) were found to be G6PD deficient. The incidence was high among the Chinese (3.2%) and Malays (2.3%) but low among the Indians (1.3%). Table II shows the results for 1984.

TABLE I—Drugs and agents that cause haemolysis in children with G6PD deficiency

<i>Antihistamines</i>	<i>Analgesics and antipyretics</i>
Antazoline phosphate	Aspirin
Diphenhydramine hydrochloride	Phenazone
Tripelennamine hydrochloride	Phenacetin
<i>Antimalarials</i>	Acetanilide
Chloroquine	Amidopyrine
Mepacrine hydrochloride	<i>Miscellaneous agents and drugs</i>
Primaquine phosphate	Dichloralphenazone
Pamaquin	Dimercaprol
Pentaquine phosphate	Methylene blue
<i>Antibiotics</i>	Naphthalene
Chloramphenicol	Probenecid
Nalidixic acid	Quinidine*
Niridazole	Ascorbic acid
Aminosalicylic acid	Phytomenadione
Nitrofurantoin	Naphthoquinones
Sulphonamides	Phenyhydrazine hydrochloride
Sulphones	Procainamide hydrochloride
Furazolidone	Fava beans*
Sulphacetamide	Chinese herbs (San Chi, Chuan Lian)
Sulfoxone sodium	
Co-trimoxazole	

\*Reported to cause haemolysis in G6PD deficient white and Chinese subjects but not in black subjects with the deficiency.

TABLE II—G6PD deficiency in Malacca in 1984

	No tested		No (%) positive	
	Male	Female	Male	Female
Malays	5528	5103	229 (4)	117 (2)
Chinese	1867	1911	104 (6)	39 (2)
Indians	449	442	6 (1)	7 (2)
Total	7844	7456	339 (4)	163 (2)

### Discussion

Kernicterus is a major cause of death during the neonatal period and of mental retardation and cerebral palsy with high tone deafness. It may occur in babies with G6PD deficiency who are exposed to haemolytic triggers. By educating parents and health professionals to protect children from exposure to trigger mechanisms the incidence of kernicterus may be reduced; to achieve this all children with G6PD deficiency should be identified.

In Malacca in 1982, 77 exchange transfusions were performed in infants in whom G6PD deficiency was detected late (bilirubin concentration greater than 380 mmol/l (20 mg/100 ml)); seven of these infants died of kernicterus. In 1983 and 1984 a noticeable

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reduction occurred in the numbers of exchange transfusions (46 in 1983 and 23 in 1984) and deaths due to kernicterus (two in 1983 and one in 1984). Thus this study shows that early detection reduces the incidence of exchange transfusion, kernicterus, and death due to kernicterus.

In our survey the incidence of G6PD deficiency was unexpectedly high among the Malays. The incidence is known to be high among the Chinese; results similar to ours (3%) have been recorded for Singapore Chinese.<sup>1</sup> The incidence among the Indians was 1.3%. This could have resulted from intermarriage between the Indians and other ethnic groups, as could the higher incidence among the Malays. Thus it seems that we need to continue screening all ethnic groups in Malacca and perhaps in Malaysia. Early detection of

G6PD deficiency with appropriate management can prevent mental handicap and related developmental disabilities.

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## *Philosophical Medical Ethics*

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### “The patient’s interests always come first”? Doctors and society

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That doctors have a special moral obligation to their patients has been a recurrent theme in this series, and one to which I shall return in the next article. In this article I wish to pursue briefly some implications for medical ethics of the social context in which doctors practise. Such implications often contradict a common and absolutist medicomoral cliché that “the patient’s interests always come first.”

In earlier articles I have indicated how even if doctors are interested only in the welfare of their own patients there may be times when moral obligations to others supersede their moral obligations to a particular patient. The most obvious example is when a doctor can satisfy one patient’s requirements only at the expense of another’s. Such examples multiply when the interests of one doctor’s, specialty’s, hospital’s, or health authority’s patients are incompatible with the interests of some other group of patients, and some principle of justice is needed to decide which patients’ interests are to come first, and which are not. Given the vigorous disagreement among doctors and within our society generally about how to resolve such conflicts, given that doctors have no special skill in the matter, and given that most of the resources for satisfying the interests of any patients are being provided by a democratic society, there seems little doubt that society’s representatives should be closely concerned with making these decisions, and indeed the structures for such decision making increasingly ensure this.

Similar considerations apply when we look at the potential medicomoral gap between the medical profession’s obligations to its (collective) patients and the interests of sick people in general. The profession has long asserted in its official ethical codes that a doctor’s primary moral obligation is to his patients,<sup>1,2</sup> and although it avows a principle of “service to humanity”<sup>3</sup> and even that “it is the mission of the medical doctor to safeguard the health of the people,”<sup>4</sup> it is clear that “the health of my patient will be my first

consideration.”<sup>2</sup> Although such medicomoral priority for our patients is laudable, it tends to leave people who are not patients out in the cold, often literally, and societies have become increasingly concerned to develop systems to ensure that all sick people can become patients and thus obtain the special moral concern of the medical profession. Nevertheless, vast areas of the world remain virtually without doctors, and in others, including our own, the distribution of medical services is uneven and the medical care of “the people” suffers accordingly.<sup>5</sup> Even if it is unrealistic to expect the medical profession to take seriously the sort of transnational moral obligation to all sick people extolled by Sir Theodore Fox in his Harveian oration<sup>6</sup> (which would certainly demand a radical restructuring of our attitudes, including perhaps some sort of compulsory international medical service during professional training to meet such an obligation to the otherwise undoctored sick) we should at least acknowledge sympathetically a legitimate area of social concern to achieve equitable distribution of medical care.

#### Society versus obligations to patients

In practice the medical profession accepts, at least implicitly, a broad range of social obligations that may override the interests of individual patients. The British Medical Association groups doctors’ professional relationships into three categories: therapeutic, impartial expert, and (non-therapeutic) medical researcher. The category of the medical researcher is implicitly justified by allowing medical obligations to non-existent patients of the future to take priority over medical obligations to existing patients. Preventative medicine (regarded by the BMA as an aspect of “impartial expert” medical work) implicitly acknowledges that medical concern for potentially sick people may in some circumstances take priority over therapeutic medicine. If the profession really believed that the patient’s interests always come first then it presumably would not allow medical time and effort to be diverted away from direct therapeutic activity.

Quite apart from acknowledging that obligations to other patients, sick people, sick people in the future, and even merely potentially sick people may conflict with obligations to current patients,

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