



WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTE

WHO/HDP/CONS/88.3

ENGLISH ONLY

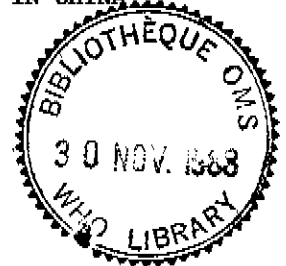
HEREDITARY DISEASES PROGRAMME  
DIVISION OF NONCOMMUNICABLE DISEASESBeijing and Tianjin, 23-29 September 1988

## THE PRESENT SITUATION WITH RESPECT TO INHERITED BLOOD DISEASES IN CHINA

Report on a Consultation

by

Dr Bernadette Modell  
Perinatal Centre  
Department of Obstetrics and Gynaecology  
University College and Middlesex School of Medicine  
London, England



The following report is based on a visit to the Institute of Basic Medical Sciences in Beijing, and the Institute of Haematology in Tianjin, China.

Alpha and  $\beta$  thalassaemia, and G6PD deficiency, are common enough to constitute a public health problem in South China, while haemophilia is an important genetic disease throughout the country. Since haemophilia can be prevented by family-studies and prenatal diagnosis and the major thalassaemias can be prevented by population-screening and prenatal diagnosis, these diseases are important both for the genetics programme in China, and the Hereditary Diseases Programme of WHO. Steps already taken to develop the technology for prevention in China, will form a suitable basis for future collaboration with WHO.

Thalassaemias

WHO recommends a two-stage strategy for preventing thalassaemia. Stage one involves developing appropriate methods for prenatal diagnosis, and applying them for retrospectively-detected couples at risk - i.e., those who have already had one affected infant. This ensures that the methodology is reliable, but makes little impact on the number of affected births. For this technology to be really useful, it is necessary to progress. Stage two involves population screening to identify and inform carriers and couples at risk; and the offer of prenatal diagnosis before they have had any affected children. This approach permits a major reduction in the numbers of affected infants born.

At the Institute of Basic Medical Sciences of the Chinese Academy of Medical Sciences (CAMS), there has already been strong emphasis on developing appropriate methods for the prenatal diagnosis of thalassaemia. Professor WU Guanyun of the Department of Biochemistry has developed methods for DNA-based diagnosis of haemoglobinopathies, and has arranged for her co-workers to be trained in advanced laboratories in the USA. She has established collaborations with centres in south China, especially in Guangxi Province, and has already transferred the technology for prenatal diagnosis of  $\alpha$ -thalassaemias to Guangxi Medical College. Professor LO Hwei-Yuen of the Department of Medical Genetics, with similarly trained colleagues, has also established a collaborative relationship with centres in Guangdong Province.

This document is not issued to the general public, and all rights are reserved by the World Health Organization (WHO). The document may not be reviewed, abstracted, quoted, reproduced or translated, in part or in whole, without the prior written permission of WHO. No part of this document may be stored in a retrieval system or transmitted in any form or by any means - electronic, mechanical or other without the prior written permission of WHO.

The views expressed in documents by named authors are solely the responsibility of those authors.

Ce document n'est pas destiné à être distribué au grand public et tous les droits y afférents sont réservés par l'Organisation mondiale de la Santé (OMS). Il ne peut être commenté, résumé, cité, reproduit ou traduit, partiellement ou en totalité, sans une autorisation préalable écrite de l'OMS. Aucune partie ne doit être chargée dans un système de recherche documentaire ou diffusée sous quelque forme ou par quelque moyen que ce soit - électronique, mécanique, ou autre - sans une autorisation préalable écrite de l'OMS.

Les opinions exprimées dans les documents par des auteurs cités nommément n'engagent que lesdits auteurs.

The development of methods for diagnosis of all forms of  $\alpha$  thalassaemia, and of  $\beta$  thalassaemias using the polymerase chain reaction (PCR) and oligonucleotide probes is progressing rapidly. In collaboration with Guangxi Medical College in Nanning, where samples are taken by chorionic villus sampling (CVS), 40 prenatal diagnoses were done in Beijing, and prenatal diagnosis is now done at Guangxi Medical College with back-up from Beijing. The same approach is now being developed for  $\beta$  thalassaemia, and a training course in PCR methods will be held in November 1988 to transfer this technology also, to the relevant provinces.

Since so much progress has been made with stage one of the prevention strategy, it is now reasonable to consider the requirements for progressing to stage two, prospective prevention, which requires considerable and coordinated effort in several new fields. It is therefore proposed to select one centre in one province for a feasibility study of prospective prevention. The province proposed is Guangxi, for the following reasons:

- There is good evidence that the incidence of  $\alpha^0$  thalassaemia trait, at 6-8%, is the highest in China. The birth incidence of  $\alpha$ -thalassaemia hydrops fetalis is estimated to be about 1.9/1000 and that of HbH disease about 3/1000, giving a total pathology due to  $\alpha$  thalassaemia of about 5/1000 births.  $\beta$  thalassaemia is also common, but its exact incidence is as yet uncertain.

- Professor LIANG Shie at Guangxi Medical College has considerable experience with thalassaemia, and methodology for prenatal diagnosis of  $\alpha$ -thalassaemia has already been transferred to his laboratory.

It is proposed in the first instance to define the incidence of  $\beta$  thalassaemia in Guangxi Province with a small survey of perhaps 300 adult males, using a one-tube osmotic fragility test as a primary screen. All positives would have HbA<sub>2</sub> estimated, and would also be re-investigated at Dr WU's laboratory in Beijing for the  $\beta$  thalassaemia mutations known to be common in Guangxi, using PCR and oligonucleotide probes. This survey should provide definitive information on  $\beta$  thalassaemia gene frequency in this area.

At the same time, it is recommended to use clinical methods for estimating the gene frequency, using existing data on the number of new cases of  $\beta$  thalassaemia, and of  $\alpha$  thalassaemia hydrops fetalis, diagnosed annually at the Guangxi Medical College. Starting the collection and analysis of this data will encourage the cooperation among different disciplines that is necessary for thalassaemia control, and will lay the foundation of a monitoring system that is necessary to measure the effect of prospective prenatal diagnosis.

It will be necessary to obtain additional resources to set up population-screening. As one step in this direction, it is proposed that Dr Modell should visit Guangdong and Guangxi in October 1989, to work with the local team and specialists from the CAMS, to report on epidemiology, the appropriate strategy in the Chinese setting, and the costs and benefits of the proposed service. This report may be used as a basis for obtaining further support for the programme.

The above work on prevention of the haemoglobinopathies is of interest to the WHO Hereditary Diseases Programme as it may become a model for prevention of  $\alpha$  and  $\beta$  thalassaemia in a developing country. Proposals for collaboration with WHO are given below.

#### Haemophilia

At the Institute of Haematology of the CAMS in Tianjin, under the direction of Professor CHEN Wen-Chieh, research is actively pursued on both thalassaemia and haemophilia, among many other topics. Professor YANG Xue-Yong and others have achieved

mapping of the distribution of abnormal haemoglobins, thalassaemias, and G6PD deficiency throughout China, and have held training courses in methodology for carrier diagnosis. More recently, they have turned attention to mapping the incidence of haemophilia in China. In addition, they have established a register of haemophilic cases born in part of Tianjin with a population of three million, and have carried out psychological and social studies of the patients and their families. They now have a management system that depends on treatment of bleeding episodes with cryoprecipitate or Factor VIII, and education and psychological and social support for the families. Family studies are performed to detect female carriers, and prenatal diagnosis by CVS and DNA diagnosis (using RFLPs) is being developed. The ultimate objective is to demonstrate the effect that the introduction of such a programme can have in reducing the birth rate of haemophilia, in order to promote its introduction in other areas in China. As far as we are aware, this is the first programme aimed explicitly at haemophilia prevention in any country.

The strategy necessary for preventing haemophilia differs from that for thalassaemia in the way that couples at risk are found. Since this is an X-linked disorder, many women at risk are identified through family studies of existing cases. An effective programme can therefore be largely run from a specialist centre, and the requirement for involvement of the Primary Health Care (PHC) System is less than for thalassaemia. From the operational point of view, it will therefore be of great interest to compare the feasibility of approaches for preventing these two disorders in a developing country.

Since haemophilia is one of the common and burdensome hereditary diseases, this project is of interest to the Hereditary Diseases Programme of WHO, and proposals for collaboration with WHO are given below.

#### RECOMMENDATIONS

##### Thalassaemias

1. Initiate joint action of WHO and the Institute of Basic Medical Sciences on control of the haemoglobinopathies in selected provinces of China.
2. Designate the Department of Molecular Biology and Biochemistry at the Institute of Basic Medical Sciences as a WHO Collaborating Centre for the Community Control of Thalassaemias with Dr WU Guanyun as Principal Investigator.
3. Plan a visit to China of WHO advisers experienced in the integration of genetics services into PHC, including Dr B. Modell, to assist in the further development of the community approach in prevention of hereditary diseases.

##### Haemophilia

4. Initiate joint action of WHO and the Institute of Haematology in Tianjin, on control of haemophilia in China.

\* \* \* \* \*