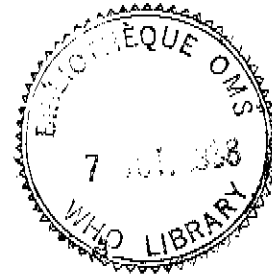




HEREDITARY DISEASES PROGRAMME
DIVISION OF NONCOMMUNICABLE DISEASES

Sydney, 8 March 1988



REPORT OF A JOINT WHO/ICF(M)A MEETING
ON PREVENTION AND CONTROL OF CYSTIC FIBROSIS

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1. INTRODUCTION

This report should be seen as a sequel to three earlier reports of joint meetings of the two Organizations^{1,2,3}. Despite increasing awareness of cystic fibrosis (CF) throughout the world, there are still many countries where it is often, perhaps usually, misdiagnosed. It had therefore been proposed that limited neonatal screening projects should be carried out in target countries in order to: (a) estimate the incidence of CF; and, (b) identify those countries with a high gene frequency so that they could benefit from the strategies for control of CF which could be expected to emerge during the next few years. At the meeting in Cyprus, it was proposed that participating centres should send duplicate dried blood spots collected for neonatal screening (for phenylketonuria and hypothyroidism) to a single international laboratory which would screen for CF using the immunoreactive trypsin method². This policy was reconsidered in 1987, but delayed implementation in view of the considerable logistic difficulties and the possibility that new methods of heterozygote detection would be available in the near future, which could be utilized to reach the objective of determining the gene frequency more cheaply and more quickly³.

This meeting was convened on the occasion of the 10th International Cystic Fibrosis Congress in Sydney, in order to review policy and to consider further proposals.

2. PROCEEDINGS

The original objective of identifying the CF gene frequency in selected, representative populations in various parts of the world was agreed to be the major objective, and the optimum method is clearly one which would identify heterozygotes. Not only would this involve screening of a much smaller number of individuals than homozygote detection, but it would also avoid the ethical problem of identification of affected infants for whom no appropriate or adequate medical services were available. Neonatal screening may nevertheless be an appropriate strategy for some countries, for the following reasons:

(a) The time-scale for development of a heterozygote detection test is still uncertain, although it is hoped that such a test will be available within one to two years;

(b) Case identification is a powerful means of increasing medical and population awareness of CF;

(c) Case identification through screening may be justifiable for its own sake in countries where CF is recognized but seriously under-diagnosed; and,

(d) The availability of a possible test using non-radioactive methods and applicable within the country of study would avoid the cumbersome machinery of transporting samples to a central international laboratory, and the cost and complexity of communication between the screening laboratory and participating centres. A recently developed enzyme-linked assay for trypsinogen (Trypsinogen EIA kit, Agen Inc.) has been shown to produce results comparable with the more widely used radioimmunoassay for trypsinogen, and may meet the requirements for a test to be used in selected countries.

It was agreed that any country or city (collaborating centres) wishing to participate in the project must have the following criteria:

(a) A neonatal screening programme using dried blood spots (e.g., for phenylketonuria and/or hypothyroidism) already in operation;

(b) A laboratory capable of performing reliable sweat tests; and,

(c) A clinician in charge of the study and a system of medical care able to provide adequate clinical care and genetic counselling.

3. SUGGESTED LOCATIONS

Three countries represented at the meeting were identified as meeting the criteria outlined above, and in each case a significant under-diagnosis of CF is believed to occur. It was proposed that Leningrad in the USSR with 70,000 births a year participate. In Argentina, about 60,000 infants are born annually in Buenos Aires and screening of up to 100,000 babies per year was thought to be possible. The city of Oporto in Portugal was identified as the best location for testing, and about 120,000 screening tests per year could be expected.

4. METHODOLOGY

The recommended procedure uses a monoclonal antibody-based amplified sandwich immunoassay for human trypsinogen which can be performed in microwell trays. It has been subjected to a clinical trial in Brisbane, Australia, and performed well in comparison with a standard radioimmunoassay^{4,5}. It would therefore appear to be suitable for a WHO/ICF(M)A programme, provided funds would be available.

Ms Janet Caffin, representing Agen Inc. (Biomedical Ltd, Durbell Street, Acacia Ridge, Queensland 4110, Australia), at the meeting, agreed to report back to her company, which would then prepare a financial proposal to be considered by WHO and the ICF(M)A. Dr Bulyzhenkov (WHO) and Professor Dodge (ICF(M)A) agreed to consider the Agen proposal in the first instance and to report back to their respective Organizations in due course.

5. LIST OF PARTICIPANTS

WHO

Dr V. Bulyzhenkov, Responsible Officer, Hereditary Diseases Programme, Division of Noncommunicable Diseases, 1211 Geneva 27, Switzerland

ICF(M)A

Professor V.S. Baranov, Laboratory for Prenatal Diagnosis, Institute of Obstetrics and Gynaecology, Academy of Medical Sciences of the USSR, Mendeleevskaya line 3, Leningrad 199064, USSR

Dr F. Caldera Reis, Universidade Federale Minas Gerais, 30000 Belo Horizonte, Brazil

Professor J.A. Dodge, Secretary of the Medical/Scientific Advisory Committee, The Queen's University of Belfast, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ, Northern Ireland

Dr R. Gonzales Pineda, Clinica Naciones Unidas, Arda 2, Calles 20-22, San José, Costa Rica

Dr L. Marques Pinto, Associacao Portuguesa de Fibrose Quistica, Hospital de Santa Maria, Av. Egas Moniz, 1900 Lisbon, Portugal

Dr O. Pivetta, Uriarte 1957, 1414 Buenos Aires, Argentina

Dr E. Tempany, President of the Medical/Scientific Advisory Committee, Our Lady's Hospital for Sick Children, Crumlin, Dublin 2, Ireland

Dr Y. Yamashiro, Department of Paediatrics, Juntendo University, Tokyo, Japan

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- (2) Report of a WHO/ICF(M)A Meeting on the Distribution of Cystic Fibrosis. Publication of the WHO Hereditary Diseases Programme, Division of Noncommunicable Diseases, Geneva, Switzerland (Nicosia, Cyprus, April/May 1985, HMG/ICF(M)A/85.2).
- (3) Report of a Joint WHO/ICF(M)A Meeting on Prevention and Control of Cystic Fibrosis. Publication of the WHO Hereditary Diseases Programme, Division of Noncommunicable Diseases, Geneva, Switzerland (Oslo, June 1987, HDP/ICF(M)A/WG/87.3).
- (4) Bowling, F.G., Watson, A.R.A., Rylatt, D.B., Elliott, J.E., Bunch, R.J., and Bundesen, P.G. "Monoclonal antibody-based enzyme immunoassay for trypsinogen in neonatal screening for cystic fibrosis". Lancet 1987 - 1: 826-827.
- (5) Bowling, F.G., and Brown, A.R.D. "Newborn screening for cystic fibrosis using an enzyme-linked immunoabsorbent (ELISA) technique". Clin. Chim. Acta. 1988 - (in press).

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