Screening for congenital hypothyroidism in South Africa

Report on a national workshop (1992)

Following the first national workshop on congenital hypothyroidism held in Cape Town in May 1987, it was thought appropriate to again review the progress made in this field over recent years, and especially to exchange views and consider recommendations relating to the screening for congenital hypothyroidism in South Africa. For this purpose a follow-up workshop was arranged (23 June 1992, at Jan Smuts Airport) under the joint auspices of the National Pathologists Group of the Medical Association of South Africa and Genetic Services of the Department of National Health and Population Development.

The workshop was open to all those known to be directly involved with or interested in any aspect of congenital hypothyroidism. Following the greater participation of private chemical pathology laboratories in the screening of newborns for hypothyroidism over recent years, it was gratifying to also welcome several representatives of this professional group. In all, some 20 participants, representing all relevant specialties (laboratory, clinical, epidemiology, health services, etc.) and coming from Cape Town, Durban, Pietermaritzburg, Johannesburg and Pretoria, attended the workshop.

In his welcoming remarks the chairman of the workshop, Professor A. D. Rothberg, (Department of Paediatrics, Wits), recalled the conclusions reached at the previous workshop and which would serve as a point of departure for the present meeting. Delegates to the previous workshop had agreed that data were insufficient to justify universal screening in South Africa; screening programmes are unjustifiable unless they can guarantee adequate follow-up and intervention in positive cases; and that collaboration between the State and private laboratories regarding newborn hypothyroid screening requires investigation in the quest for cost-effective screening.

Professor W. J. Kalk (Department of Medicine, Wits) presented the introductory talk on 'Screening for congenital hypothyroidism' in which he provided the following overview:

There is good evidence that congenital hypothyroidism can be effectively treated in the majority of cases, so screening for this condition appears to be worth while. The reported incidence ranges from 1 in 3 000 in Holland, to 1 in 12 000 in US blacks, with a female preponderance (male:female = 2:1). The causes include thyroid dysgenesis (aplasia or hypoplasia) in 90% of cases; thyroid dyshormogenesis, with or without a goitre at birth (1 in 30 - 50 000 live births); and deficient TSH secretion (about 1 in 110 000 live births).

False-positive diagnoses, when total thyroxine is used to screen, can occur in babies with inherited deficiency of thyroxine-binding globulin, which is found in 10 - 14 000 births (M:F = 9:1). Prematurity, with low serum T_4 but normal TSH levels is another important cause (25% of cases in the USA) and is likely to be even more frequent in our African populations.

Transient neonatal hypothyroidism is said to occur in 1 in 6 000 births in the USA, but has a reported incidence of up to 5% in areas of iodine deficiency in Europe. Large areas of rural South Africa are iodine-deficient, so transient hypothyroidism may be a significant problem in local screening programmes. Iodine deficiency is an important cause of cretinism, which results from severe iodine deficiency early in intra-uterine life: many cretins with permanent hypothyroidism have circulating thyroid growth-blocking auto-antibodies. Recent evidence points to transplacental transfer of thyroid hormones in late pregnancy in humans, which explains the presence of detectable T_4 in the serum of athyreotic neonates, and may also explain why brain development is not severely delayed in many of these babies. This phenomenon, and the enhanced ability of brain tissue to convert T_4 to tri-iodothyronine (T_3) are probably important in protecting the brain from the deleterious effects of fetal hypothyroidism.

In developing screening programmes for the detection of neonatal hypothyroidism in South Africa several points must be borne in mind. Firstly, most babies are discharged from obstetric units on the day of delivery — later heel-prick blood sampling is not feasible. Secondly and most importantly, facilities for the tracing and follow-up of positive cases must be established. Thirdly, data from the USA suggest that the initiation of thyroxine therapy *per se* does not necessarily lead to optimal mental development in the hypothyroid infant: maternal education and frequent biochemical follow-up are a necessary part of the 'screening package'.

Dr H. W. Hitzeroth (Genetic Services, Pretoria) then put forward the proposed objectives of the workshop which he suggested should be addressed either by way of the individual presentations or during the panel discussion.

The self-explanatory titles highlight the contents of the remaining presentations and of the workshop in general, as follows: W. J. Zakolski (Department of Chemical Pathology, SAIMR, Johannesburg): 'Thyroid function tests using isotopic and non-isotopic methodological approaches'; C. Goldstone (Health and Housing Directorate, City Council of Johannesburg), G. N. Padayachee, A. D. Rothberg, L. Wagstaff and H. W. Hitzeroth: 'Results of a community-based congenital hypothyroid pilot screening programme'; F. Bonnici (Department of Paediatrics and Medicine, Groote Schuur Hospital, Cape Town), M. D. Mann, D. L. Woods and A. Philotheou: 'The Cape Town screening programme'; D. Wittenberg (Department of Paediatrics, University of Natal, Durban), T. Machattie and G. M. B. Berger: 'Screening for congenital hypothyroidism at R. K. Kahn Hospital in Durban'; J. J. Nel (Genetic Services, Department of National Health, Pretoria), P. Hurter, J. van Dyk and H. W. Hitzeroth: 'Congenital hypothyroidism screening programme in Pretoria: procedures and results'; representatives of private chemical pathology laboratories, Drs Ferguson, Roux and partners (Durban); Dr Pillay and partners (Durban); Dr Van Drimmelen and partners (Johannesburg); Drs Mauff, Zail and partners (Johannesburg): 'Congenital hypothyroidism screening in private practice: procedures and results'; J. van Dyk (Department of Paediatrics, HF Verwoerd Hospital, Pretoria) and C. W. Bredenkamp: 'Clinical follow-up of patients positive on TSH and T_4 testing (the Pretoria screening programme)'; F. Bonnici (Department of Paediatrics and Medicine, Groote Schuur Hospital, Cape Town), D. L. Woods and A. Philotheou: 'Unusual case situations'.

Panel discussion and recommendations

All presentations, to a greater or lesser extent, centred on the proposed objectives of the workshop and on related questions. During the panel discussion the chairman again put these to the participants for more thorough discussion and evaluation. The most important viewpoints and recommendations that were put forward are as follows:

Incidences

The screening results confirm that the incidence of congenital hypothyroidism in South African whites is comparable to incidences in Europe and North America, i.e. about 1 in 4 000 newborns; tentative results for South African Indians suggest the incidence to be higher and for 'coloureds' probably lower than for whites. Whereas published data for blacks elsewhere show the incidence of hypothyroidism to be much lower than for whites, no adequate data can as yet be presented for South African blacks. This lack of epidemiological data is seen as a major shortcoming that should urgently be addressed. However, the abandonment of population classification and the difficulty of effective follow-up of black newborns after a positive screening test, make this increasingly problematic in present-day South Africa.

Clinical diagnosis

The participants were unanimous that diagnosis of congenital hypothyroidism by way of clinical signs/symptoms was generally inadequate and often too late to allow effective treatment which would prevent the permanent, serious sequelae.

Clinical screening of babies

Following programmes in Canada and Cape Town to routinely assess babies according to a schedule of selected clinical signs/symptoms (during a home visit at about 6 weeks of age) — to score them in terms of a risk figure and then to subject only high-risk cases to a laboratory investigation — a Johannesburg team tested the feasibility of such an alternative procedure under local conditions. After 1 year the results confirmed this to be neither a practical nor an effective alternative to routine newborn screening.

The need for newborn screening

The participants unanimously agreed that from a medical point of view, there are very good reasons to subject newborns of high-risk population groups to routine laboratory screening for hypothyroidism. There is no other effective way to make an early diagnosis and hence facilitate early preventive treatment. For this reason, the screening of newborns for congenital hypothyroidism should be encouraged and extended in high-risk population groups.

Private and/or state laboratory screening

The term 'state' in this context includes provincial and provincially funded academic laboratories. Note was taken of the fact that state health authorities can provide newborn screening only on a very limited scale. As far as state funds can be made available for such screening programmes these should primarily benefit people with inadequate financial means (e.g. with no medical aid insurance). In such cases the guidelines require that the laboratory work be put on public tender for all qualifying laboratories to participate (these will include private and academic/university laboratories).

However, the rapidly growing demand by private paediatricians and general practitioners for such laboratory tests is increasingly being met by private chemical pathology laboratories. These are then usually paid for by medical aid insurance schemes. Under the given circumstances this development is appropriate and welcomed, and needs to be extended. This will allow increasing numbers of affected babies to be identified and hence treated, thus preventing the permanent disability associated with this condition. However, concern was expressed by some participants regarding the discrepancy between the cost of the screening tests (about R30) in private laboratories in South Africa, when compared to the cost of mass screening in many overseas countries and in South Africa. It was felt that this needed to be addressed.

Among the difficulties experienced by the private laboratories with screening for congenital hypothyroidism are that the quality of the blood-spots is not always of the required standard, since the specimen collections (by heel-prick on filter paper) are done by staff members not under their control; and that very little feed-back is received on the follow-up and final diagnosis of cases identified with the screening tests (which lessens opportunities for quality control).

Laboratory technology

From the various presentations it appeared that a variety of testing procedures and technologies are currently in use for the detection of congenital hypothyroidism in South Africa. These include the heel-prick (mainly applied to cases referred by private doctors to private laboratories), and the cord blood collection method — thus requiring different laboratory methodologies. Techniques highly divergent in sensitivity are also being used, which entail differences in cut-off levels. Measuring the TSH level was accepted as the most effective screening test and the combination of TSH and T_4 as the most effective diagnostic test. Whereas it is the prerogative of each laboratory to apply the laboratory technology of its choice, the participants were adamant that the laboratories should use the most accurate and up-to-date methods currently available; this should include acceptable quality control procedures.

Treatment by specialised centres

The participants at the workshop strongly recommended that babies affected by congenital hypothyroidism should be referred to recognised, specialist treatment centres. The unanimous feeling was that only in this way will it be possible to ensure effective long-term treatment/management of the baby. This should include regular evaluations, checks on compliance and continuous counselling.

National record-keeping

Following the example set in the USA and elsewhere, it was felt that efforts to implement a national database for congenital hypothyroidism screening should continue. The minimum objective would be to compile data on the overall numbers screened and positive cases identified. This would obviously require the voluntary co-operation of all the screening laboratories. A more ambitious objective would be to keep records of all patients diagnosed and under treatment (together with some appropriate clinical data). However, some participants expressed concern about the practical feasibility and desirability of such a detailed level of record-keeping.

Improved education and level of awareness

The participants at the workshop expressed unreserved support for the promotion of newborn screening for congenital hypothyroidism by appropriate educational campaigns, directed at medical target groups (laboratories, paediatricians, etc.). In addition, the lay public should also be alerted to the option of newborn screening and the benefits which these tests can hold. In particular, it was felt that the families with an affected baby urgently needed practical information on congenital hypothyroidism and its treatment/prevention in order to complement and support the medical intervention. It was suggested that the Genetic Services of the Department of National Health should address this need, in consultation with all interested parties.

Follow-up workshop

To keep up the momentum and to evaluate progress, everybody agreed that a follow-up workshop in 2 - 3 years' time with appropriate report-back and exchange of experiences, would be highly desirable. A very significant feature of this workshop was the fact that private pathology laboratories were represented and contributed substantially to its success. It was felt that this momentum of co-operation should be maintained so that screening for congenital hypothyroidism in South Africa could become as effective and comprehensive as possible.

Participants

F. Bonnici (Cape Town), A. S. Botha (Pretoria), J. D. Cartwright (Johannesburg), C. A. Goldstone (Johannesburg), H. W. Hitzeroth (Pretoria), P. Hurter (Pretoria), M. Jordaan (Johannesburg), W. J. Kalk (Johannesburg), M. A. King (Durban), J. J. Nel (Pretoria), C. E. Niehaus (Pretoria), T. Padayachi (Durban), A. Price (Johannesburg), A. D. Rothberg (Johannesburg), L. A. van der Walt (Johannesburg), J. C. van Dyk (Pretoria), D. F. Wittenberg (Durban), S. Zail (Johannesburg), W. J. Zakolski (Johannesburg).

The workshop was sponsored by Diagnostic Products and the Weil Organisation. Convened and reported by H. W. Hitzeroth, Department of National Health (Genetic Services).

TABLE I.
Congenital hypothyroidism screening data for 1990, 1991 and 1992

Population group	Screened	Positive on screen	Confirmed positive	No feed-back
1990				
Blacks	514	3	0	0
Whites	9 426	332	3	0
Asians	1 396	8	1	0
Coloureds	919	19	0	0
Not specified	1 704	0	0	0
Total	13 959	362	4	0
1991				
Blacks	1 763	24	0	0
Whites	9 000	262	3	0
Asians	2 835	10	0	0
Coloureds	470	7	0	0
Not specified	8 372	70	2	5
Total	22 440	373	5	5
1992				
Blacks	2 003	42	0	0
Whites	7 883	308	3	0
Asians	930	3	0	0
Coloureds	380	8	0	0
Not specified	17 950	91	0	83
Total	29 146	452	3	83

Notes

1. The data are based on screening tests done by the following laboratories/departments, and are compiled and presented here with due acknowledgement to these: Department of Chemical Pathology, University of Pretoria, and Dr Du Buisson and partners (Pretoria), both on behalf of Genetics Services, Department of National Health (Pretoria); Department of Chemical Pathology, and of Paediatrics and Child Health, University of Natal (Durban), on behalf of Genetic Services, Department of National Health (Pretoria); Drs Ferguson, Bouwer and partners (Durban); Dr Pillay and partners (Johannesburg); Drs Mauff, Zail and partners (Johannesburg); Dr Van Drimmelen and partners (Johannesburg); Drs Penman, Kock and Knight (Cape Town); Drs Dietrich and Street (Cape Town). Data on the screening programme conducted by the Department of Chemical Pathology, Red Cross Children's Hospital (Cape Town) is not included in the present compilation.
2. The following qualifications need to be considered when evaluating the statistical data: some laboratories only began screening in the course of 1990; in the course of 1991 two more laboratories began with screening tests; in 1992 two more laboratories began screening. The recorded figures for 1992 cover only part of that year.
3. The varying numbers shown as 'positive on screen' largely reflect different laboratory technologies and levels of sensitivity (cut-off levels for TSH, etc.) as used by the respective laboratories.
4. The numbers shown as 'population group not specified' follow from the fact that this criterion of recording is being phased out.
5. Two of the 3 white 'confirmed positive' cases in 1991 are newborns who initially were part of a 'population group not specified' screening cohort, on recall and retesting they were identified as white babies.
6. For the 'no feed-back' group no final diagnosis could be provided, mainly because the private chemical pathology laboratories are not always explicitly involved with the follow-up or informed of the final diagnosis.