

RECOMMENDATIONS FOR FURTHER RESEARCH AND TRAINING ON ENDEMIC GOITER AND CRETINISM

Committee Members: E. GAITAN, Chairman; E. ALAVEZ, T. MAHMOUD AL-HITI, I. AMEMIYA HOSHI, M. C. A. de BLANCO, P. P. BOURDOUX, J. C. CARRILLO FONSECA, A. ERMANS, J. M. HERSHMAN, S. H. INGBAR, R. H. LINDSAY, J. MAISTERRENA, M. PAREDES-SUAREZ, G. PINEDA V., S. REFETOFF, AND F. E. VITERI

I. Research

There are many unanswered questions about the causes, effects, treatment, and prevention of endemic goiter and cretinism. Further research is recommended in the following areas:

A. Etiology

1. *Environmental Factors.* While iodine deficiency is clearly the major cause, there may be persistence of goiter after iodine supplementation, and uneven distribution of goiter among localities with equal iodine intake. Studies are necessary on:

- Environmental goitrogens.
- Role of bacterial pollution.
- Effect of nutritional state and nutrient interactions.

2. *Host Factors.* Under similar environmental conditions, only a segment of the population may develop goiter. Explanations for this should be sought among the following areas:

- Genetic variation.
- Immunologic factors.
- Sex and age as modifiers of expression.
- Growth factors (e.g., somatomedins).

B. *Physiopathology of Endemic Goiter and Mechanisms of Goitrogenesis*

1. Relative roles of TSH and autoregulation in goitrogenesis.

2. Pharmacokinetics of goitrogenic compounds.

3. Effects of etiological factors (iodine deficiency, goitrogens, host factors) in all stages of thyroid gland function, including synthesis, secretion, and peripheral metabolism of thyroid hormones.

4. Effect of nutritional status on goitrogenesis.

5. Influence of sex hormones on the thyroid.

6. Influence of growth factors on the thyroid.

7. Development of animal models more closely related to humans than the rat for study of special aspects of endemic goiter and cretinism.

C. *Disorders Related to Iodine Deficiency and Endemic Goiter*

1. *Endemic Cretinism*

a. Animal models for development of neurologic cretinism.

b. Iodine dependency and thyroid hormone dependency of brain development; e.g., the role of T_4 to T_3 conversion in the brain, the role of iodine in brain development, and the role of environmental goitrogens.

2. *Thyroid Cancer*

Incidence in endemic and nonendemic areas.

3. *Hyperthyroidism*

Incidence and types of hyperthyroidism before and after iodination measures.

4. *Lymphocytic Thyroiditis*

Relationship of iodine nutritional status to this condition.

5. *Subclinical Hypothyroidism*

Assessment and diagnosis in populations with endemic goiter.

6. *Suboptimal Performance in Neurological, Mental, Growth, and Other Functions*

Relationship of these to iodine deficiency and to various degrees of hypothyroidism, particularly in its mild and subclinical forms.

D. *Therapy and Prevention*

1. Alternatives to iodine supplementation other than by salt or parenteral iodized oil; oral iodized oil; other iodinated compounds; and water iodination.

2. Undesirable effects of preventive measures, such as hyperthyroidism (characterization of different forms) and lymphocytic thyroiditis.

3. Assessment of public health implications of goiter occurring while on iodine supplementation.

4. Operational research:

a. Cost-benefit and cost-effectiveness studies of prophylaxis.

b. Management strategies for communities in their effective use of preventive measures: anthropological, managerial, and the like.

c. Health systems research for efficiency of preventive measures.

E. *Economic and Social Impact*

To obtain data on the economic and social impact of endemic goiter, a multidisciplinary approach should be promoted, involving economists, sociologists, and educators. It should be adapted to each region and consider present conditions and resources. Similar data should be obtained to assess the economic and social benefit of control measures.

II. *Training, Communications, Assistance, and Teaching*

A. Scientists need to be trained in the areas of thyroid pathology, thyroid function, methodology for goiter surveys, and follow-up studies. This will improve the overall quality of research and care in endemic goiter areas. The Brussels group is willing to undertake this effort, and proposes to organize biennially an accelerated training course for physicians who are directly involved in the control of endemic goiter in their countries. The course would include two weeks of theoretical and practical work and an optional additional two weeks of laboratory training. It would be given by the staff of the Brussels "Thyroid Unit" and other recognized experts. Sponsorship and partial support should be sought from the World Health Organization.

B. There should also be research into the most effective means of promoting in the community the understanding of goiter, hypothyroidism, and cretinism, and the awareness of prevention and control measures.

C. There is need for assistance, in the form of information and dissemination of available studies and methods, for ongoing and future research in endemic goiter areas. WHO could act as clearinghouse for this activity.

D. To improve communication among researchers concerned with endemic goiter and between researchers and public health officials, a communication coordinator should be nominated. He should select, publish, and disseminate quarterly a bibliography of endemic goiter, through the facilities of the PAHO/WHO Regional Library of Medicine.

III. *Financing of Research*

PAHO/WHO should contact member countries, urging financial support for research projects designed to answer the questions posed above. To facilitate this procedure, investigators should send a copy of their research proposals to PAHO/WHO.

DISCUSSION

Ermans: The course in Brussels would allow persons from developing countries to receive intensive training in the methodologic and basic aspects of endemic goiter. We propose it because we perceive a gap between knowledge of the problem's existence and access to the more sophisticated techniques that are available to deal with it. We plan for such a course to provide two weeks of background material and theory, which would include 20 to 25 formal lectures covering all the principal topics of epidemiology and laboratory techniques, followed by two weeks of laboratory and methodological training. Such a course might be given every two years with six to ten experts assisting in the instruction. We hope to have WHO support for this course. Initially, it would probably be given in English, but courses in other languages would be considered later.

Muzzo: When we talk about research in endemic goiter, we are frequently speaking about the more severe forms. I believe it is important to stress that there is need for research into the milder forms as well.

Delange: I think it would be valuable to have a statement about the need for research on the significance of neonatal impairment of thyroid function in areas of endemic goiter even when there are no major problems in the general population. This would be one of the facets of what you call "subclinical hypothyroidism."

Kontras: I believe you should stress the importance of support for endemic goiter research in all countries having an endemic goiter problem. This is justified because in the long run it is vital to a country's welfare to control this problem. Such research is not only valuable for science *per se*, but it also has the practical value of producing experts in endemic goiter, who will be a valuable resource in controlling it.

Delange: I would like to see the report include a statement that we explore the proposition that neonatal thyroid screening in areas of moderate iodine deficiency could be used as a sensitive marker for the possibility of impaired brain function.

Thilly: This point was included specifically in the recommendation of the committee on technical conduct of goiter programs.

C. Daza: PAHO is now taking an active role in field studies to develop indicators for high-risk pregnancies. Since we are talking about hypothyroidism, countries that are developing markers for high-risk pregnancies should include this important element in their assessment. On another topic, Dr. Erman's suggestion of a training course is very interesting. Sometimes it is difficult for people from this hemisphere to go abroad. To complement his proposal, I would suggest that we consider the possibility of organizing supplementary courses using available scientific resources. For example, we might have training courses for the Andean countries, using the expertise of international authorities. More specifically, in terms of PAHO we have the Institute for Nutritional Research for Central America, and this should be considered as a resource for training programs.

DeBlanco: Many developing countries simply do not have the resources to send workers to Brussels for the type of course proposed by Dr. Ermans. I believe there is need for the type of regional training proposed by Dr. Daza.

Gaitan: The two types of training proposed do not cancel each other out. The course proposed by Dr. Ermans is for persons scientifically trained and these will not only help with needed prophylaxis, but will also improve knowledge of the problems and their complications for the region as well.

Viteri: In regard to the regional courses, our concept was that the course in Brussels should be tried initially; it would then serve as a model for the future development of regional courses.

DeMaeyer: There are many precedents by which WHO and PAHO have offered fellowships for such courses so that the economy of a country is not drained. I think these would enable people to take such courses.