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Thyroid Disorders Associated With Iodine Deficiency and Excess

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Epidemiology of iodine deficiency in Europe

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This subcommittee was established in the late seventies by Dr. A. Querido. After two preliminary reports to the ETA in Pisa (1981) and Brussels (1982) the final report of the committee is due to be presented at the forthcoming ETA-Meeting in Rotterdam, September 1984. It is hoped that the ETA committee will not object to my disclosing some of the information already available in advance.

In general, epidemiologic information in a strict sense is scanty in most European countries. There is much regional data available with relatively good information concerning the population sample studied as for age and sex. However it is frequently difficult to conclude which part of the whole population of a given area is represented by the sample studied, and what percentage of the total inhabitants of a country live in the area studied. The techniques for the study of endemic goiter (8) as recommended by WHO and PAHO (Pan American Health Organization) have not been fully applied. Despite the limitations of these studies the currently available information is still considerable.

In 1937, H. Pflüger published two maps depicting the goiter distribution in Central Europe, one of his own and one drawn by H. Bircher in 1883. D.A. Koutras (16) and P. Langer (20) and others reviewed the situation in Europe up to the late seventies in the book by J.B. Stanbury and B.S. Hetzel on Endemic Goiter and Endemic Cretinism (28). The data collected by the ETA-Subcommittee are shown in figures 1 and 2.



FIG. 1. Goiter Prevalence in Europe, Preliminary Map of the European Thyroid Association.



[] denotes regional values

FIG. 2. Urinary lodine Excretion in Europe, Preliminary Map of the European Thyroid Association.

REVIEW

The review of the situation in the individual European countries is necessarily incomplete and will be focussed on some points of general interest.

1. Endemic goiter in the country as a whole

The Federal Republic of Germany has an average goiter prevalence of 15% as observed in 5.4 million recruits and published in 1975 by Horster *et al.* (15) with 85% of the goitrous having stage I goiters. The mean iodine excretion was 20 µg/g creatinine in the south and 35 in the north as determined by Habermann *et al.* 1975 (16) in approximately 2000 school children and in more than

5000 adults from all over the country. There have been several more recent reports confirming the ongoing iodine deficiency. The goiter incidence may be even higher as demonstrated by Gutekunst *et al.* (12), using the technique of sonographic volumetry.

Likewise, goiter endemia and iodine deficiency in the country as a whole were well documented by Meng*et al.* (22) for the German Democratic Republic.

The available information permits to assume, but not to prove that ubiquitous endemic goiter and iodine deficiency still exist in the following countries: Poland, Hungary, Romania, and Bulgaria, some of which have definitely improved the situation.

2. Former iodine deficiency

A number of countries have convincingly shown that there is either no goitre, or that endemic goiter has been eliminated. This applies to Norway, Sweden, Finland and probably Denmark.

For Norway, Frey*et al.* (11) reported that the urinary iodine excretion varies in women and men between 165-364 μ g per day. The high iodine intake is mainly due to the feeding of cows with seaweed, whereas iodized salt which contains only 5 μ g KI per kg, contributes only negligible amounts of iodine.

Sweden has gradually increased the iodine content of table salt for mandatory use up to 50 mg per kg. The situation in Finland will be dealt with by A. Lamberg (18, 19), who reported that the average dietary iodine intake is now 340 μ g per day, so that the brackets in the figure 2 may be eliminated.

In Denmark a study by Munkner (23) of 6000 young men from all over the country showed that the population lives at a marginally low rate of iodine excretion of 41-68 μ g/day in Jutland and 68-139 μ g/day in Seeland. However no endemic goiter was detected in more than 350,000 children aged 7 to 17 years. The same contrasting observation of borderline iodine deficiency withouth proven endemic goiter was reported in Belgium by Beckers and Delange (3) and many others.

3. Regional iodine deficiency and goiter

A vast amount of information about the regional prevalence of endemic goiter, of iodine deficiency and sometimes even of cretinism was reported from almost all other European countries.

There is still some regional endemic goiter left in the eastern parts of the Netherlands. The most recent survey communicated personally by Elte, van der Heide, Goslings and Querido indicated that 26% of female school children in Doetichem have goiters of grade OB.

Most of the population of Portugal lives near the coast, where there is no endemic goiter (Sobrinho and Limbert, personal communication). However, several regions of the interior are severely affected. In one region of the district of Castelo Branco nearly 16,000 school children and adults were studied in the early 60s. Prophylaxis with iodized salt (20 mg KI per kg) was started in 1971 and reduced the goiter prevalence from 51% to 9.3% by 1977 (21). In another region, also in the district of Castelo Branco, the prevalence of goiter in school children approached 40%. Here the mean urinary iodine from school children lacking iodine prophylaxis was only 12 μ g/g creatinine. Two further regions, Baixo Alentejo and Algarve and Portalagre, were recently shown to house goiter endemia up to 54% locally and also some endemic cretinism!

There is insufficient space to discuss the information provided recently by Escobar del Rey (10) in detail. The situation in adjacent Spanish provinces is not yet shown in fig. 1 and 2 and is comparable to that shown for Portugal. Ongoing studies in Spain revealed other regions of endemic goiter and iodine deficiency in Guadalajara, Cataluna and in Galicia.

As for Italy it is impossible to review in this context the vast number of detailed studies published by Italian authors; some of them are pioneers in the field. Detailed surveys exist for the Valle D'Aosta by Costa, for the Alto Adige by Cabassa, for Tuscany by Fenzi and Pinchera, and for Sicily by Vigneri, to name but a few. The picture may be summarized in that some densely populated areas are apparently free of endemic goiter, whereas regionally severe goiter endemias and iodine deficiency were shown particularly in the mountain districts (1, 2, 4, 5, 6, 7, 27, 30).

The situation in Greece was studied by Koutras *et al.* (17), and the situation in Turkey resembles that in Italy (29). With regard to central Europe we have to mention Switzerland and the CSSR, where there are remnants of endemic goiter particularly in the older age groups (9). As for the CSSR, Podoba and Langer on the basis of excellent surveys coverning 2% of the whole population reported that endemic goiter is decreasing below 10% and that iodine excretion was successfully raised to 100 μ g/g creatinine and will be raised further (20, 25).

Further important nations not yet mentioned will be dealt with in the forthcoming ETA-Report.

4. Iodine prophylaxis

The mandatory prophylaxis in Sweden and the contribution by the iodine content of milk in Norway and in Finland has already been mentioned. In the Netherlands all salt used for baking bread has to be iodized. The report of the Ministry of Health published in 1981 and forwarded by G. Hennemann, proposed "that struma prophylaxis be improved by raising the KI content of bread and salt, so that one slice of bread would contain 20 μ g iodine. It also proposes making the addition of KI to household salt compulsory, so that 1 g salt would contain 20 μ g iodine".

In Switzerland, the potassium iodide content of salt was raised from 5 to 10 mg/kg in 1962 and to 20 mg/kg in 1980. The high goiter prevalence in the elderly is probably due to the fact that they suffered from iodine deficiency

before the salt was adequately iodinated (9). Further countries considering an increase in the iodine content of their salt are Austria, CSSR, Hungary, Poland and The Netherlands.

It has been shown by Habermann *et al.* (13) that potassium iodide was not sufficiently stable in iodized salt from several European countries. Therefore in the Federal Republic of Germany the iodination of salt to be used on a voluntary basis was altered in 1981, so that potassium iodate is added to give an iodine content of 20 mg per kg salt.

CONCLUSIONS

Bearing in mind the limitations of this review, due largely to the incompleteness of information obtained, the results of the inquiries performed by the ETA subcommittee for the study of endemic goiter and iodine intake in Europe allow some conclusions to be made:

1. There are some European countries where either endemic goiter used to be prevalent within the country as a whole, or where areas of endemic goiter (and cretinism) were formerly well described. Iodine prophylaxis either mandatory or voluntary, but accepted by more than 90% of the population was introduced in these countries but had and still has to be intensified in some cases, since it was shown to be formerly insufficient. Nevertheless, eradication of endemic cretinism and a marked reduction of goiter prevalence have been reported particularly for the younger age groups. This description would probably apply to Austria (?), Bulgaria, Switzerland, CSSR, Hungary (?), The Netherlands (?), and Finland.

Other countries with sufficient iodine intake and probably no endemic goiter are Great Britain (?), Ireland (?), Norway, and Sweden. A third group of countries have documented borderline low or insufficient alimentary iodine intake but fail to report even regional endemic goiter as in Denmark and Belgium (?).

It is notable that the eradication of goiter has not only been achieved through iodine prophylaxis but in some countries is also due to a change in dietary habits, e.g. feeding of seaweed to cows and use of iodine containing disinfectants in dairy hygiene. This resembles the situation seen in the United States and in Tasmania.

In the group of previously iodine deficient countries, some questions and continuing tasks remain including:

— monitoring of iodine prophylaxis, which needs to be continued with repetition of goiter prevalence surveys and monitoring of the urinary iodine excretion,

- studies on prevalence of residual goiter and goitrogenic mechanisms other than iodine deficiency, and

- longitudinal studies on the question, whether the sequelae of iodine

deficiency and endemic goiter, as nodular goiter in the elder age groups, or increased frequency of single toxic autonomous adenomas and disseminated autonomy will gradually subside.

All efforts aimed at these problems have to be recommended for this group of countries.

2. There are some European countries where endemic goiter is still prevalent, when the country is regarded as a whole. The two parts of Germany, Federal Republic of Germany and German Democratic Republic, have convincingly demonstrated endemic goiter and iodine deficiency. Other countries may have to be added. An effective general iodine prophylaxis is recommended strongly for these countries.

3. There are some European countries, where only regional prevalence of endemic goiter and iodine deficiency have been documented, the remainder of the country being free of endemic goiter. The information received up to now does not always allow conclusions as to the epidemiological situation within the country as a whole. Therefore either general iodine prophylaxis or regional measures are an alternative for these countries. The list of such countries may have to include Spain, France, Greece, Italy, Portugal, Poland (?), Romania, Turkey, and Yugoslavia. Possibly, one will have to add some of the following countries: Belgium, Denmark (?), Great Britain (?), Ireland (?), and the Soviet Union (?).

Further epidemiological studies are strongly recommended for some of these countries, since either general or regional iodine prophylaxis appears desirable.

This short review may be adequately summarized by quoting Dr. A. Querido, Pisa (1981): "The scientific community of the ETA has the obligation to contribute to the eradication of endemic goiter and iodine deficiency in Europe. With the available knowledge it seems an anachronism that endemic goiter in Europe still prevailes".

REFERENCES

- 1. Bartalena, L., Baschieri, L., Ceccarelli, C., Fenzi, G.F., Giani, C., Lippi, F., Macchia, E., Monzani, G., Pinchera, A., and Siclari, C. (1982): Il gozzo endemico in Toscana. *Salute e Territorio*, n. 24:18-21.
- 2. Baschieri, L., Costa, A., and Basile, A., eds. (1978): *Il gozzo*. Pozzi Publication, Roma, pp. 80-87.
- 3. Beckers, C., and Delange, F. (1980): Iodine deficiency. In: *Endemic goiter and endemic cretinism*, edited by J.B. Stanbury and B.S. Hetzel, pp. 199-217. J. Wiley and Sons Inc., New York.
- Belfiore, A., Sava, L., Runello, F., Tomaselli, L., and Vigneri, R. (1983): Solitary autonomously functioning thyroid nodules and iodine deficiency. J. Clin. Endocrinol. Metab., 56:283-287.

- 5. Costa, A., and Mortara, M. (1981): Goitre. Panminerva Medica, 23: 141-156.
- 6. Delange, F., Vigneri, R., Trimarchi, F., Filetti, S., Pezzino, V., Squatrito, S., Bourdoux. P. and Ermans, A.M. (1978): Etiological factors of endemic goiter in north-eastern Sicily. J. Endocrinol. Invest., 2:137-142.
- 7. Doveri, F., Fenzi, G.F., Siclari, C., Bartalena, L., Ceccarelli, C., Chiovato, L., Macchia, E., Pinchera, A., and Baschieri, L. (1981): Il gozzo endemico in provincia di Pisa. Aspetti epidemiologici e metodologia della ricerca. Rivista Italiana d'Igiene, 41:104-111.
- 8. Dunn, J.T., and Medeiros-Neto, G.A. (1974): Endemic goiter and cretinism: Continuing threats to world health. Pan American Health Organization, Scientific Publication No. 292, pp. 1-304. World Health Organization, Washington, D.C.
- 9. Eberhard, H., Eigenmann, F., Schärer, K., und Bürgi, H. (1983): Auswirkungen der verbesserten Kropfprophylaxe mit jodiertem Kochsalz auf den Jodstoffwechsel in der Schweiz. Schw. med. Wschr., 113:24-27.
- 10. Escobar, De, Rey, F., Gomez-Pan, A., Obregon, M.J., Mallol, J., Arnao, M.D.R., Arnada, A., and Morreale de Escobar, G. (1981): A survey of schoolchildren from a severe endemic goitre area in Spain Quart J. Med., 50:233-246. 11. Frey, H., Rosenlund, B., and Storli, U. (1974): Utskillelse av jod i urinen i enkelte norske
- befolkningsgrupper 1971-1972. Tidsskrift for Den norske laegeforening, 94:982-987.
- 12. Gutekunst, R., Groth, K., Scriba, P.C., und Windler, B. (1983): Zur Kritik der Strumaepidemiologie (III). Dtsch. med. Wschr., 108:1985-1986.
- 13. Habermann, J., Heinze, H.G., Horn, K., Kantlehner, R., Marschner, I., Neumann, J., und Scriba, P.C. (1975): Alimentärer Jodmangel in der Bundesrepublik Deutschland. Dtsch. med. Wschr., 100:1937-1945.
- 14. Habermann, J., Jungermann, A., und Scriba, P.C. (1978): Qualität und Stabilität von jodierten Speisesalzen. Ernährungsumschau, 25:45-48.
- 15. Horster, F.A., Klusmann, G., und Wildmeister, W. (1975): Der Kropf: Eine endemische Krankheit in der Bundesrepublik? Dtsch. med. Wschr., 100:8-9.
- 16. Koutras, D.A. (1980): Survey Europe and The Middle East. In: Endemic goiter and endemic cretinism, edited by J.B. Stanbury and B.S. Hetzel, pp. 79-100. J. Wiley and Sons Inc., New York.
- 17. Koutras, D.A. Katsouyanni, E.K., Livadas, D.P., Piperingos, G.D., Tzonou, A., and Trichopoulos, D. (1982): An epidemiologic survey of thyroid enlargement among school children in a non-endemic area. Endokrinologie, 79:349-354.
- 18. Lamberg, B.A., Haikonen, M., Mäkelä, M., und Jukkara, A.(1982): Wirksamkeit der Jodprophylaxe in Ostfinnland. In: Schilddrüse 1981, edited by P.C. Scriba, K.H. Rudorff, and B. Weinheimer, pp. 248-257. Thieme, Stuttgart - New York.
- 19. Lamberg, B.A., Haikonen, M., Mäkelä, M., Jukkara, A., Axelson, E., and Welin, M.G. (1981): Further decrease in thyroidal uptake and disappearance of endemic goitre in children after 30 years of iodine prophylaxis in the east of Finland Acta endocr., 98:205-209.
- 20. Langer, P. (1980): Eastern and southeastern Europe. In: Endemic goiter and endemic cretinism, edited by J.B. Stanbury and B.S. Hetzel, pp. 141-153. J. Wiley and Sons Inc., New York.
- 21. Lopes de Oliveira, A., Sobrinho, L.G., Botelho, L.S., Oliveira, P.A., Conçalves, M.J., and Antunes, M.T. (1983): Bócio endémico no sul de Portugal. Medicina Cirurgia, 3: 269-330.
- 22. Meng, W., Ventz, M., Weber, S., und Bednar, J. (1981): Struma und alimentärer Jodmangel in der DDR. Das deutsche Gesundheitswesen, 36:1275-1279.
- 23. Munker, T. (1969): Urinary excretion of 127 iodine in the Danish population. Scand. J. Clin. and lab. Invest., 24:Suppl. 110, 134.
- 24. Pflüger, H. (1937): Die geographische Verbreitung des Kropfes in Europa, Dtsch. Arch. klin. Med., 180:212-132.
- 25. Podoba, H., und R. Reisenaurer (1982): Die Wirksamkeit der Jodprophylaxe in der CSSR. In: Schilddrüse 1981, edited by P.C. Scriba, K.H. Rudorff and B. Weinheimer, pp. 239-247. Thieme, Stuttgart-New York.
- 26. Review: Goiter and iodine deficiency in Europe. Report of the Subcommittee for the Study of Endemic Goiter and Iodine Deficiency of the European Thyroid Association. In preparation, 1985.
- 27. Squatrito, S., Delange, F., Trimarchi, F., Lisi, E., and Vigneri, R. (1981): Endemic cretinism in Sicily. J. Endocr. Invest., 4: 295-302.

- 28. Stanbury, J.B., and Hetzel, B.S., editors (1980): Endemic goitre and endemic cretinism. J. Wiley and Sons Inc., New York.
- Urgancioglu, I., Hatemi, H., Kögoglu, E., Güven, Y., Sür, N., and Yilmaz, O. (1982): Iodine determination in drinking water samples of Turkey: In: *Relation to the endemic goiter problem.* University of Instambul, Cerrahpasa Medical Faculty. Publication No. 3, Istanbul, pp. 1-16.
- pp. 1-16.
 30. Vigneri, R., Squatrito, S., Polley, R., Polosa, P., Ermans, A.M., and Ingbar, S.H. (1982): Iodine prophylaxis in an endemic area in Sicily: A new method for iodine supplementation. In: *Diminished thyroid hormone formation*, edited by D. Reinwein and E. Klein, pp. 187:193. F.K. Schattauer, Stuttgart - New York.