REVIEW

Impact of iodination on thyroid pathology in Africa

O E Okosieme

J R Soc Med 2006;**99**:396–401

INTRODUCTION

Thyroid disorders are common worldwide.[1] In Africa, dietary iodine deficiency is the major determinant of thyroid pathology, resulting in a spectrum of iodine deficiency disorders, including goitres, hypothyroidism and mental retardation.[2] Of these, mental retardation poses the most severe threat to socioeconomic wellbeing; thus, its prevention has been the focus of current global efforts towards sustainable iodine sufficiency.[3] At least 350 million Africans are at risk of iodine deficiency.[4] According to World Health Organization (WHO) estimates, goitres are present in 28.3% of the African population,[4] and approximately 25% of the global burden of iodine deficiency as measured by disability-adjusted life years (DALYs) occurs in Africa.[5] The demands of communicable diseases, coupled with the challenges of poverty, civil conflicts and fragile political structures, have in the past frustrated efforts at eliminating iodine deficiency in Africa.[6] However, recent decades have seen remarkable improvements in iodine nutrition through salt iodination in the continent.[7] The effect of these developments on the pattern of thyroid gland disease are beginning to unravel and will be relevant to the strategies for extending the present gains. In this article, I examine the impact of recent progress in iodine nutrition on the epidemiology of thyroid gland pathology in Africa.

METHODS

I searched Medline references using the term 'Africa' in combination with various search phrases related to thyroid disease: thyroid, goitre, hyperthyroidism, hypothyroidism, thyroid autoimmunity, thyroiditis, thyroid cancer and iodine. A further query was performed using the individual names of different countries in Africa. In addition, I consulted websites of the International Council for the Control of Iodine Deficiency Disorder (ICCIDD), WHO, and the United Nations Children's Fund (UNICEF).

HISTORICAL ASPECTS

Thyroid disorders have been recognized in Africa since olden times. Indigenous terms for thyroid swellings exist locally and goitres have featured in sculptures dating back centuries.[8] The historian, Leo Africanus, observed tribes with goitres around Timbuktu in 1550.[9] Centuries later, the Scottish surgeon Mungo Park would comment on the occurrence of goitres in his West African expeditions.[9] By the mid-20th century, goitres were clearly endemic in virtually every part of the continent and it had become apparent that iodine deficiency was a significant public health problem in the region.[9] By this period, the detrimental effects of iodine deficiency on fetal development had been established in other parts of the world. Studies in Papua New Guinea, in the 1960s had clearly shown that iodine supplementation was effective in preventing brain damage.[10] In 1983, Hetzel introduced the term iodine deficiency disorders, thus shifting the emphasis away from the benign neck swelling to encompass the more serious and wide-ranging effects of iodine deficiency on growth and development.[2] The ICCIDD was founded soon afterwards in 1985, as an expert consultative group to oversee the control and monitoring of iodine deficiency disorders at regional and international levels.[11]

DEVELOPMENTS IN IODINE NUTRITION

For most of the period before the 1990s, progress in Africa remained slow; prevention of iodine deficiency was low on the priorities of regional governments, structured programmes were lacking, and iodine supplementation was often approached erratically. As a result, this era saw only modest improvements in iodine intake. The introduction of formal iodine deficiency prevention programmes in the 1990s marked a turning point in the drive towards sustainable iodine sufficiency in Africa. In 1990, the World Summit for Children endorsed a resolution aimed at the virtual elimination of iodine deficiency worldwide.[12] Through joint efforts by ICCIDD, WHO, UNICEF, and individual regional authorities, a strategy of universal salt iodination was promoted within the region. Iodized salt has since been made available to 62% of households[7] and iodine sufficiency has thus been attained in at least 20 African countries, representing more than half the entire continent's population (Figure 1, Table 1). [4] Despite these gains, however, at least 350 million of the population remain at risk of iodine deficiency disorders.[4] Within iodine sufficient African countries, pockets of severe deficiency

Clinical Research Fellow, Centre for Endocrine and Diabetes Science, School of Medicine, Cardiff University, Cardiff, UK

E-mail: okosiemeoe@cf.ac.uk

Figure 1 **Iodine nutrition in Africa** [data source: *WHO Global Database on Iodine Deficiency*, Ref. 4]. Median urinary iodine (mcg/L) □ Moderate deficiency: 20–49; ▒ mild deficiency 50–99; ▒ optimal: 100–199; ■ more than adequate: 200–299; ■ excess: >299; □ status uncertain

persist and vulnerable population sub-groups like neonates, toddlers and pregnant women continue to be in danger of iodine deficiency disorders.[13,14] Nonetheless, the progress in recent years clearly indicates that iodine sufficiency is truly within reach in Africa.

EVOLVING DISEASE PATTERNS

There is compelling evidence that the pattern of thyroid disorders in a population is dependent on environmental iodine intake.[15] Iodine deficiency disorders abound in areas with inadequate iodine intake while autoimmune thyroid disorders are rare in iodine deficiency but become prevalent with transition to iodine sufficiency.[16] Monitoring disease patterns in Africa has proved challenging in the absence of

Table 1 **Number of African countries in different categories of iodine nutrition, based on urinary iodine excretion** [data source: *WHO Global Database on Iodine Deficiency*, Ref. 4]

Degree of iodine nutrition	*Median urinary iodine (mcg/L)*	*No. of African countries*
Severe iodine deficiency	<20	0
Moderate iodine deficiency	20–49	6
Mild iodine deficiency	50–99	8
Optimal iodine nutrition	100–199	11
More than adequate iodine nutrition	200–299	7
Excess iodine intake	300	2
No data		12

Table 2 **Total goitre prevalence in African countries before and after salt iodination programmes**

	Pre iodization					*Post iodization*				
Country	***Goitre***	***Year***	***Sample size***	***Population age (years)***	***Type of survey***	***Goitre***	***Year***	***Sample size***	***Population age (years)***	***Type of survey***
Chad	63	1993	1171	10–20	National (Ref. 23)	24	2002	1024	7–12	National Ref. 24)
Lesotho	17.5	1993	323	6–16	National (Ref. 25)	4.9	1999	500	10–14	Sub-national (Ref. 26)
South Africa	25.6	1995	565	12.6 (mean)	Sub-national (Ref. 27)	28	1996	536	12.5 (mean)	Sub-national (Ref. 27)
Nigeria	29	1995	590	6–14	Sub-national (Ref. 28)	2.9–33.3	1998	2372	8–12	Sub-national (Ref. 29)
Côte d'Ivoire	45	1997	419	5–14	Sub-national (Ref. 30)	29	2001	526	5–14	Sub-national (Ref. 30)

comprehensive biomedical information. Goitre surveys in children are frequently conducted in schools within accessible locations. The occurrence of other thyroid disorders is extrapolated from hospital case records and histopathology reviews. While providing useful information, these methods exclude large rural populations who lack access to health and educational facilities. These limitations notwithstanding, several trends in disease pattern have become apparent in recent decades.

Endemic goitre

Goitre due to dietary iodine deficiency is by far the most commonly observed thyroid disorder in Africa.[17–19] The majority of affected people live within subsistence agricultural systems, commonly in mountainous regions which have been deprived of iodine by leaching of the soil. Goitrogens in local foods like cassava and millet accentuate the effects of iodine deficiency[20] and other micronutrient deficiencies such as selenium also play a role in the development of goitres.[21] The prevalence of goitres varies widely but may be as high as 85% in children in some areas.[22] Recent improvements in iodine intake have led to reductions in goitre prevalence (Table 2) but goitres prevail in communities who continue to rely exclusively on home grown crops for nutrition. Children, females and pregnant women remain disproportionately affected. Recent studies have shown total goitre rates of close to a 100% in pregnant women, even in areas within countries with iodine sufficiency status.[13,14]

Endemic cretinism

The extreme form of iodine deficiency, endemic cretinism has been well characterized in Central Africa, where up to 2–6% of the overall population may be affected.[31] The myxoedematous form of cretinism is highly prevalent in this population and hypothyroidism is seen in as much as a quarter of children in endemic areas.[32] This pattern contrasts with other parts of the world where the neurological variety, characterized by mental deficiency, deaf mutism and spastic diplegia prevails.[33] However, gross neurological defects are also seen in African populations and were described in 10% of patients with cretinism in the Kivu area of Democratic Republic of Congo.[33] Less obvious disorders of cognition and intellect in infancy and childhood are likely to be even more widespread and to potentially constitute a greater burden on the economic output of affected communities. An analysis in Sierra Leone estimates that the future five-year productivity losses in the country, resulting from intellectual impairment associated with iodine deficiency would be in excess of US$42.5 million.[34]

Iodine-induced thyrotoxicosis

Thyrotoxicosis may occur in chronically iodine deficient individuals who are exposed to sharp increases in iodine intake.[35] It is more likely in older patients with longstanding thyroid nodules. Toxic change in such nodules may be accompanied by biochemical or clinically overt thyrotoxicosis. Death from cardiac failure and arrhythmias may occur.[35] Between 1991 and 1995, a sudden rise in the incidence of thyrotoxicosis was noted by physicians in Harare, Zimbabwe. The majority of these patients had toxic nodular goitres and 14 deaths were recorded.[36] Likewise, biochemical thyrotoxicosis was diagnosed in 14 of 191 patients with goitres in Kivu, a previously iodine deficient area of Northern Zaire.[37] These incidents followed the introduction of iodized salt to both countries. A multicentre study subsequently conducted by a team of seasoned

Table 3 **Histological types of thyroid cancer in African countries.** Figures are percentages of the total number of cases of thyroid cancer

		Histological type of cancer					
Country	**Period of study**	**Follicular**	**Papillary**	**Medullary**	**Anaplastic**	**Sample size**	**Reference**
Capetown, South Africa	1952–1975	31	27	4	10	254	Selzer *et al*. (Ref. 49)
Ibadan, Nigeria	1957–1970	60	14	0	10	109	Olurin *et al*. (Ref. 18)
Ibadan, Nigeria	1965–1984	45	45	5	4	137	Thomas *et al*. (Ref. 50)
Nairobi, Kenya	1968–1973	55	30	0	15	20	Gitau *et al*. (Ref. 19)
Algiers, Algeria	1966–1981	36	39	4	16	385	Bakiri *et al*. (Ref. 51)
Khartoum, Sudan	1982–1989	42	22	2	21	112	Omran *et al*. (Ref. 52)
Algiers, Algeria	1982–1991	40	46	4	8	615	Bakiri *et al*. (Ref. 51)
Ile-Ife, Nigeria	1983–1993	69	11	6	3	36	Lawal *et al*. (Ref. 53)
Addis Ababa, Ethiopia	1994–1998	16	77	6	2	64	Tsegaye *et al*. (Ref. 17)
Durban, South Africa	1990–1997	68	16	13	3	100	Mulaudzi *et al*. (Ref. 54)

international researchers established that the problem was likely transient and not widespread on the continent.[38] Accordingly, recommended levels of salt iodization in the region have been reduced to 20–40 ppm.[38]

Graves' disease

Graves' disease is the commonest cause of hyperthyroidism in iodine-replete parts of world.[1] The average annual incidence of Graves' disease in Whickham, UK, is approximately 80/100 000 for females.[39] In Johannesburg, the incidence is about 10 times less (8.75/100 000 per year).[40] Graves' disease was believed to be rare in Africa, based on the early experience of physicians in the region.[41] However, it is now more frequently reported across the continent. In South Africa, a 60% rise in its incidence was observed over an 11-year period.[40] This was most apparent in iodine sufficient urban dwellers, a significant proportion of who were recent migrants from iodine deficient areas.[40] The clinical presentation of Graves' disease appears no different from elsewhere; females are more commonly affected,[40] ophthalmopathy is common,[42] and thyroid-stimulating hormone-receptor antibodies are present in over 80% of patients.[43] However, as a result of late presentations, a disproportionate amount of cardiac complications are seen.[44] The approach to management is dictated by existing local facilities. Radioiodine is not widely available so the options vary between medical and surgical treatments. Surgery is sometimes the more practical alternative due to the unaffordable cost and lengthy hospital follow up of medical treatment.

Autoimmune hypothyroidism

The spectrum of autoimmune hypothyroidism includes Hashimoto's thyroiditis, primary myxoedema and post-partum thyroiditis. These conditions form the bulk of the thyroid physician's workload in iodine sufficient countries.[1] The reverse is seen in Africa where autoimmune hypothyroidism is rarely encountered, either by clinicians[18,19] or histopathologists.[17] In striking contrast to Graves' disease, the incidence of autoimmune hypothyroidism in African blacks does not appear to have been amplified by improvements in iodine intake. One possible explanation for this discrepancy may lie with recognition. Unlike Graves' disease, autoimmune hypothyroidism is particularly difficult to diagnose on clinical grounds alone and, in the absence of sensitive laboratory facilities, it is not improbable that cases will be missed. However, it is likely that genetic factors also contribute to the relative rarity of thyroid autoimmunity in Africans. Black Africans have lower levels of thyroid antibodies than Africans of European or Asian descent.[40] Interestingly, induction of thyroid antibodies following iodine supplementation has been reported in Europe[45] and Asia,[46] but this has not been the case in Africa.[47] Prospective population-based studies are needed to determine the true occurrence of autoimmune hypothyroidism in Africans.

Thyroid malignancy

The histology of thyroid cancers in a population is dependent on the ambient iodine intake. A high proportion of aggressive follicular and anaplastic tumours are seen in iodine deficiency while the more benign papillary type is common in iodine-rich populations.[48] Follicular carcinoma is the predominant histological variety in Africa (Table 3). This pattern has prevailed over the decades, suggesting persisting iodine deficiency. However, the incidence of anaplastic carcinoma appears to be falling and other reports suggest a relative rise in papillary tumours, implying

improved iodination on the other hand (Table 3). This mixed picture may thus reflect a transitory period in iodine nutrition coupled with regional variations in iodine status. Nonetheless, it is doubtful if reversals in cancer histology will necessarily translate to improvements in prognosis in Africa. Advanced disease at presentation and poor follow up are common in Africans with limited access to health services.[52,55] A study in Algeria showed that survival rates in patients with differentiated thyroid carcinoma were related to the level of health service provision rather than the effects of iodine status on cancer histology.[51]

FUTURE CHALLENGES

If the present momentum is anything to go by, then iodine sufficiency could be attained in most parts of the continent within the next decade. However, maintenance of these gains will prove challenging in an African climate marred by wars, famine and political instability. Experience from iodine sufficient countries has shown that interruption of iodine replacement is rapidly followed by relapse of iodine deficiency.[56] Sustained political will and robust legislative structures will be required to ensure the continued availability of iodized salt. With improvements in iodine nutrition, the pattern of thyroid disorders is expected to continue evolving. It remains to be established if autoimmune hypothyroidism will emerge in the stead of endemic goitres as has happened in parts of Europe. However, the primary goal of salt iodination remains the prevention of brain damage due to iodine deficiency; therefore the risks associated with iodine replacement in the African population are clearly outweighed by its benefits and should not deter continued iodine prophylaxis. Nonetheless, the possibility of side effects calls for increased vigilance in monitoring the effects of iodination.

CONCLUSION

Despite incomplete biomedical information, it is apparent that the pattern of thyroid disorders in Africa is evolving with increasing iodine sufficiency. Total goitre prevalence has fallen in populations with salt iodination programmes. However, pockets of goitres persist, and more subtle effects of iodine deficiency on cognition and intellect in childhood are likely to be still widespread. The incidence of Graves' disease is rising, particularly in African populations exposed to sharp increases in iodine consumption. In addition, transient iodide-induced thyrotoxicosis was potentially fatal in two African countries. While consolidating the present gains, salt iodination programmes must now target poor rural populations, and vulnerable sub-groups including pregnant women and children who remain at significant risk of iodine deficiency. On the other hand, researchers and clinicians in the region will need to be adequately resourced to identify and manage emerging thyroid disorders.

Competing interests None declared.

REFERENCES

1 Vanderpump MPJ, Tunbridge WMG. The epidemiology of thyroid diseases. In: Braverman LE, Utiger RD, eds *The Thyroid.* 7th ed. Philadelphia: Lippincott Raven, 1996:474–82

2 Hetzel BS. Iodine deficiency disorders (IDD) and their eradication. *Lancet* 1983;**2**:1126–9

3 Maria Andersson, Bahi Takkouche, Ines Egli, Henrietta E. Allen, & Bruno de Benoist. Current global iodine status and progress over the last decade towards the elimination of iodine deficiency. *Bull World Health Organ* 2005;**83**:518–25

4 World Health Organization. *Iodine Status Worldwide: WHO Global Database on Iodine Deficiency*. Geneva: WHO, 2004:1–58. (www.whqlibdoc.who.int/publications/2004/9241592001.pdf)

5 World Health Organization. Annex 3: Burden of disease in DALYs by cause, sex and mortality stratum in WHO regions, estimates for 2001. In: *The World Health Report*. Geneva: WHO, 2002:192–7. (www.who.int/whr/2002/whr2002_annex3.pdf)

6 Ekpechi OL. Iodine deficiency disorders in Africa. In: Hetzel BS, Dunn JT, Stanbury JB, eds *The Prevention and Control of Iodine Deficiency Disorders.* Amsterdam: Elsevier Science Publishers (Biomedical division), 1987:219–36

7 ICCIDD. *IDD Newsletter* 2003;**19**(1):1–6

8 Wells C. Goitre in two African sculptures. *Med Hist* 1968;**12**: 89–91

9 Kelly FC, Snedden WW. Prevalence and geographical distribution of endemic goitre. *Bull World Health Organ* 1958;**18**:5–173

10 Pharoah PO, Buttfield IH, Hetzel BS. Neurological damage to the fetus resulting from severe iodine deficiency during pregnancy. *Lancet* 1971; **1**:308–10

11 Hetzel BS, Eliminating iodine deficiency disorders—the role of the International Council in the global partnership. *Bull World Health Organ* 2002;**80**:410–13

12 www.unicef.org/wsc/goals.htm (accessed April 2005)

13 Adesunkanmi AR, Makinde ON. Goitre prevalence in pregnant women attending antenatal clinic in a teaching hospital. *J Obstet Gynaecol* 2003;**23**:156–9

14 Torheim LE, Granli GI, Sidibe CS, Traore AK, Oshaug A. Women's iodine status and its determinants in an iodine-deficient area in the Kayes region, Mali. *Public Health Nutr* 2005;**8**:387–94

15 Laurberg P, Pedersen KM, Hreidarsson A, Sigfusson N, Iversen E, Knudsen PR. Iodine intake and the pattern of thyroid disorders: a comparative epidemiological study of thyroid abnormalities in the elderly in Iceland and in Jutland, Denmark. *J Clin Endocrinol Metab* 1998;**83**:765–9

16 Doufas AG, Mastorakos G, Chatziioannou S, Tseleni-Balafouta S, Piperingos G, Boukis MA, Mantzos E *et al*. The predominant form of non-toxic goiter in Greece is now hyroiditis. *Eur J Endocrinol* 1999;**140**:505–11

17 Tsegaye B, Ergete W. Histopathologic pattern of thyroid disease. *East Afr Med J* 2003;**80**:525–8

18 Olurin EO, Itayemi SO, Oluwasanmi JO, Ajayi OO. The pattern of thyroid gland disease in Ibadan. *Nig Med J* 1973;**3**:58–65

19 Gitau W. An analysis of thyroid diseases seen at Kenyatta National Hospital. *East Afr Med J* 1975;**52**:564–70

20 Ermans AM, Delange F, Van der Velden M, Kinthaert J. Goitrogenic action of cyanogenic glucosides present in cassava: a possible etiologic

factor of endemic goiter in the Idjwi island. *Acta Endocrinol Suppl (Copenh)* 1973;**179**:31

21 Thilly CH, Swennen B, Bourdoux P, Ntambue K, Moreno-Reyes R, Gillies J, *et al*. The epidemiology of iodine-deficiency disorders in relation to goitrogenic factors and thyroid-stimulating-hormone regulation. *Am J Clin Nutr* 1993;**57**(2 Suppl):267S–70S

22 Eltom M, Hofvander Y, Torelm I, Fellstrom B. Endemic goitre in the Darfur region (Sudan). Epidemiology and aetiology. *Acta Med Scand* 1984;**215**:467–75

23 Wyss K, Guiral C, Ndikuyeze A, Malonga G, Tanner M. Prevalence of iodine deficiency disorders and goitre in Chad. *Trop Med Int Health* 1996;**1**:723–9

24 Beasley M, Brooker S, Ndinaromtan M, Madjiouroum EM, Baboguel M, Djenguinabe E *et al*. First nationwide survey of the health of schoolchildren in Chad. *Trop Med Int Health* 2002;**7**:625–30

25 Jooste PL, Langenhoven ML, Kriek JA, Kunneke E, Nyaphisi M, Sharp B. Nutritional status of rural children in the Lesotho Highlands. *East Afr Med J* 1997;**74**:680–9

26 Sebotsa ML, Dannhauser A, Jooste PL, Joubert G. Prevalence of goitre and urinary iodine status of primary-school children in Lesotho. *Bull World Health Organ* 2003;**81**:28–34

27 Jooste PL, Weight MJ, Lombard CJ. Short-term effectiveness of mandatory iodination of table salt, at an elevated iodine concentration, on the iodine and goiter status of schoolchildren with endemic goiter. *Am J Clin Nutr* 2000;**71**:75–80

28 WHO, UNICEF, ICCIDD. *Review of Findings from 7-country Study in Africa on Levels of Salt Iodination in Relation to Iodine Deficiency Disorders, Including Iodine Induced Hyperthyroidism*. Geneva: World Health Organization

29 Egbuta J, Onyezili F, Vanormelingen K. Impact evaluation of efforts to eliminate iodine deficiency disorders in Nigeria. *Public Health Nutr* 2003;**6**:169–73

30 Zimmermann MB, Hess SY, Adou P, Toresanni T, Wegmuller R, Hurrell RF. Thyroid size and goiter prevalence after introduction of iodized salt: a 5-y prospective study in schoolchildren in Côte d'Ivoire. *Am J Clin Nutr* 2003;**77**:663–7

31 Lagasse R, Luvivila K, Yunga Y, Gerard M, Hanson A, Bourdoux P *et al*. Endemic goitre and cretinism in Ubangi. In: Ermans AM, Mbulamoko NM, Delange F and Ahluwalia R, eds *Role of Cassava in the Aetiology of Endemic Goitre and Cretinism*. Ottawa, Canada: International Development Research Centre, IDRC 136e; 1980:45–60

32 Moreno-Reyes R, Boelaert M, el Badawi S, Eltom M, Vanderpas JB. Endemic juvenile hypothyroidism in a severe endemic goitre area of Sudan. *Clin Endocrinol (Oxf)* 1993;**38**:19–24

33 Delange F, Ermans AM, Vis HL, Stanbury JB. Endemic cretinism in Idjwi Island (Kivu Lake, Republic of Congo). *J Clin Endocrinol Metab* 1972;**34**:1059–66

34 Aguayo VM, Scott S, Ross J. Sierra Leone—investing in nutrition to reduce poverty: a call for action. *Public Health Nutr* 2003;**6**:653–7

35 Stanbury JB, Ermans AE, Bourdoux P, Todd C, Oken E, Tonglet R, *et al*. Iodine-induced hyperthyroidism: occurrence and epidemiology. *Thyroid* 1998;**8**:83–100

36 Todd CH, Allain T, Gomo ZA, Hasler JA, Ndiweni M, Oken E. Increase in thyrotoxicosis associated with iodine supplements in Zimbabwe. *Lancet* 1995;**346**:1563–4

37 Bourdoux PP, Ermans AM, Mukalay WA Mukalay A, Filetti S, Vigneri R. Iodine-induced thyrotoxicosis in Kivu, Zaire. *Lancet* 1996;**347**:552–3

38 Delange F, de Benoist B, Alnwick D. Risks of iodine-induced hyperthyroidism after correction of iodine deficiency by iodized salt. *Thyroid* 1999;**9**:545–56

39 Vanderpump MP, Tunbridge WM, French JM, Appleton D, Bates D, Clark F, Grimley Evans J, Hasan DM, Rodgers H, Tunbridge F, *et al*. The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. *Clin Endocrinol (Oxf)* 1995;**43**:55–68

40 Kalk WJ, Kalk J. Incidence and causes of hyperthyroidism in blacks. *S Afr Med J* 1989;**75**:114–17

41 Gelfand M. Thyrotoxicosis in the African: report of a case. *Cent Afr J Med* 1962;**8**:123–4

42 Joffe B, Gunji K, Panz V, Zouvanis M, Swanson J, Ackrell BA et al. Thyroid-associated ophthalmopathy in black South African patients with Graves' disease: relationship to antiflavoprotein antibodies. *Thyroid* 1998;**8**:1023–7

43 Zouvanis M, Panz VR, Kalk WJ, Joffe BI. Thyrotropin receptor antibodies in black South African patients with Graves' disease and their response to medical therapy. *J Endocrinol Invest* 1998;**21**:771–4

44 Kalk WJ. Atypical features of hyperthyroidism in blacks. *S Afr Med J* 1980;**57**:707–10

45 Boukis MA, Koutras DA, Souvatzoglou A, Evangelopoulou A, Vrontakis M, Moulopoulos SD. Thyroid hormone and immunological studies in endemic goiter. *J Clin Endocrinol Metab* 1983;**57**:859–62

46 Premawardhana LD, Parkes AB, Smyth PP, Wijeyaratne CN, Jayasinghe A, de Silva DG *et al*. Increased prevalence of thyroglobulin antibodies in Sri Lankan schoolgirls—is iodine the cause? *Eur J Endocrinol* 2000;**143**:185–8

47 Zimmermann MB, Moretti D, Chaouki N, Torresani T. Introduction of iodized salt to severely iodine-deficient children does not provoke thyroid autoimmunity: a one-year prospective trial in northern Morocco. *Thyroid* 2003;**13**:199–203

48 Feldt-Rasmussen U. Iodine and cancer. *Thyroid* 2001;**11**:483–6

49 Selzer G, Kahn LB, Albertyn L. Primary malignant tumors of the thyroid gland: a clinicopathologic study of 254 cases. *Cancer* 1977;**40**:1501–10

50 Thomas JO, Ogunbiyi JO.Thyroid cancers in Ibadan, Nigeria. *East Afr Med J* 1995;**72**:231–3

51 Bakiri F, Djemli FK, Mokrane LA, Djidel FK. The relative roles of endemic goiter and socioeconomic development status in the prognosis of thyroid carcinoma. *Cancer* 1998;**82**:1146–53

52 Omran M, Ahmed ME. Carcinoma of the thyroid in Khartoum. *East Afr Med J* 1993;**70**:159–62

53 Lawal O, Agbakwuru A, Olayinka OS, Adelusola K. Thyroid malignancy in endemic nodular goitres: prevalence, pattern and treatment. *Eur J Surg Oncol* 2001;**27**:157–61

54 Mulaudzi TV, Ramdial PK, Madiba TE, Callaghan RA. Thyroid carcinoma at King Edward VIII Hospital, Durban, South Africa. *East Afr Med J* 2001;**78**(5):242–5

55 Ketiku KK. Thyroid carcinoma in Nigeria: review of management. *Eur J Surg Oncol* 1990;**16**:443–7

56 Zimmermann MB, Wegmuller R, Zeder C, Torresani T, Chaouki N. Rapid relapse of thyroid dysfunction and goiter in school-age children after discontinuation of salt iodination. *Am J Clin Nutr* 2004;**79**:642–5