THYROID DISEASE IN KENYA

including

a general review of thyroid disease in East Africa, a report of endemic goitre in Mwezi, Tanzania and an account of simple goitre, thyroid carcinoma and thyrotoxicosis in Kenya.

by

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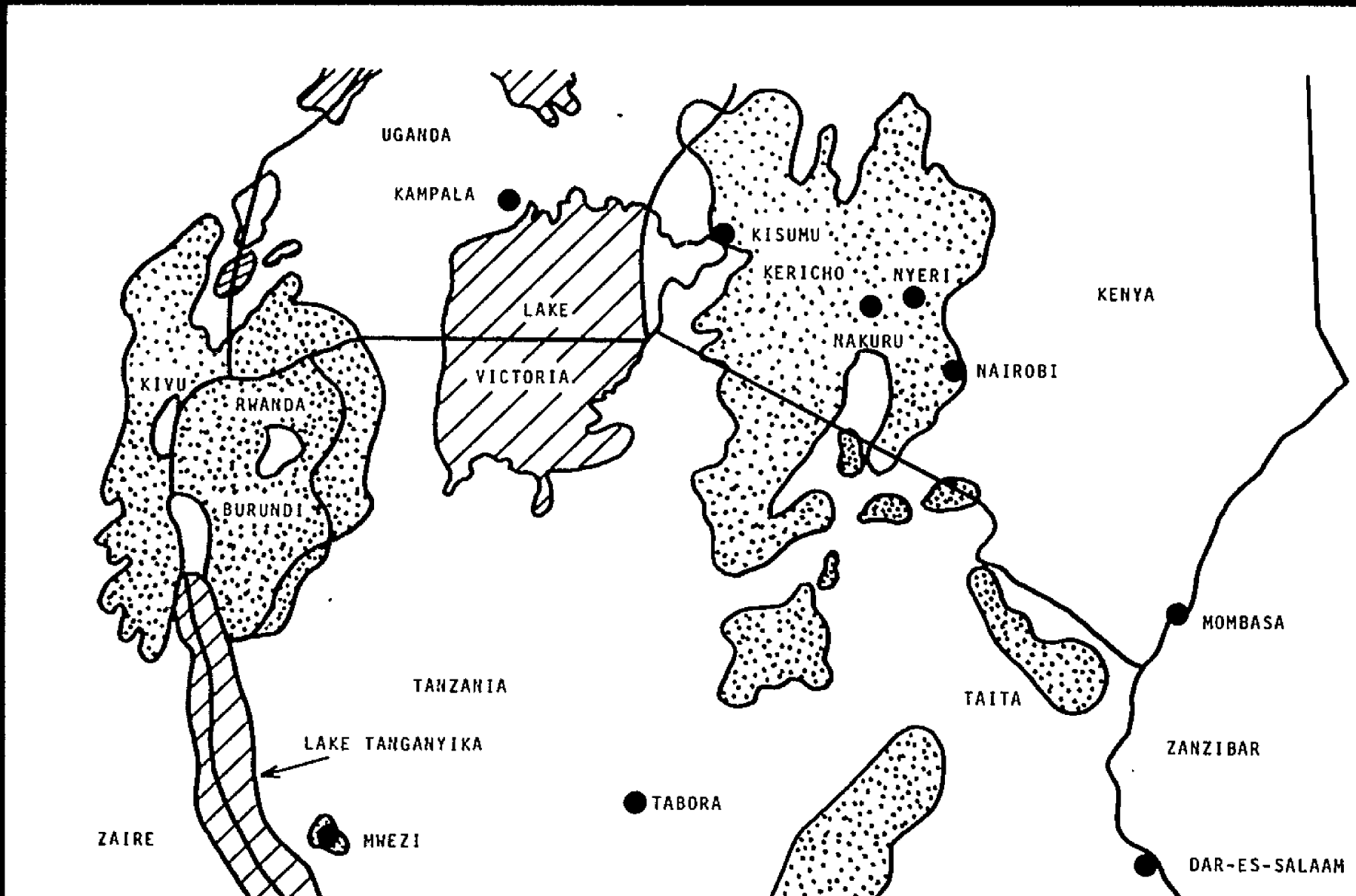
CONTENTS.

INTRODUCTION

One of the earliest examples of the use of geographical pathology was the study of the distribution of endemic goitre in the populations of Europe. In this thesis consideration is given to the distribution and types of thyroid disease in East Africa in general and Kenya in particular and to their diagnosis and management.

Fig. 1 - Map of East Africa showing main centres and highland areas



KENYA

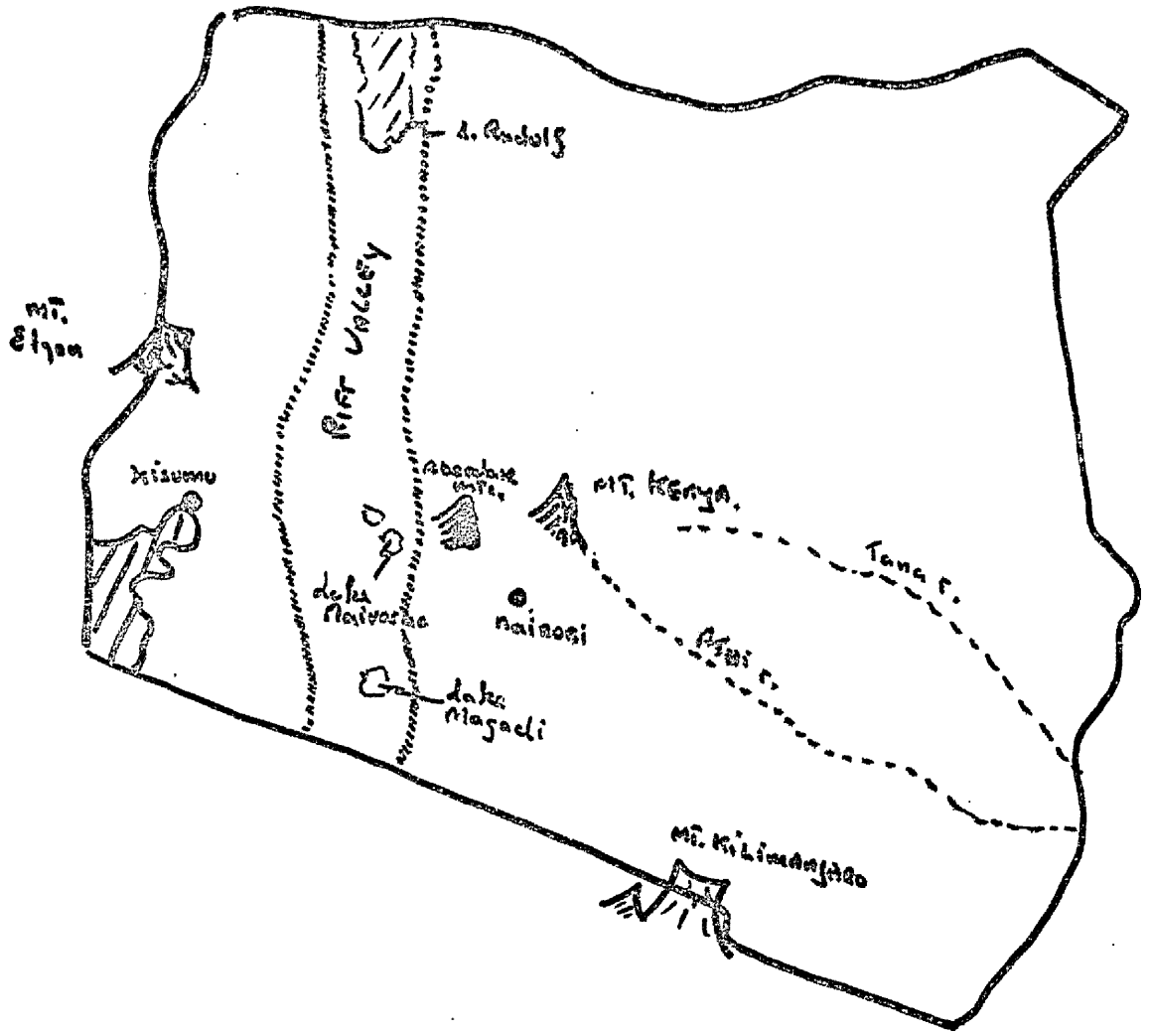
The Country.

The general topography and main centres of East Africa are shown in figure 1a. Central and South West Kenya consist largely of a highland plateau. Probably about 60 per cent of the population of Kenya live on or in close proximity to the plateau at altitudes of between 4,000 and 8,000 feet above sea level. The plateau is split into an Eastern and a Western portion by the Great Rift Valley and the three giant mountains, extinct volcanoes, Elgon, Kilimanjaro and Kenya stand sentinal on the fringes of the plateau (figure 1b). To the East the descent to the coast is gradual through sparsely populated scrub and plains. To the North towards Ethiopia and Somalia are vast tracts of desert land. By contrast the land in the South West corner of Kenya around Lake Victoria is densely populated. For administrative purposes Kenya has been divided into seven provinces: Coast, Eastern, North Eastern, Central, Rift Valley, Western and Nyanza (figure 6), page 27).

The Peoples.

The indigenous population of Kenya (approximately 10 millions) is more mixed in character than any other country in Africa. There are four main ethnic groups: in order of numbers there are the Bantu, Nilo-Hamitic, Nilotic and Hamitic. There are two main groups of Bantu, Eastern and Western. The Western, or Nyanza Bantu comprise the Abaluyia (about one million) the collective name for the tribes who inhabit the highland areas above the Kavirondo Gulf of Lake Victoria around Kakamega and the Kisii tribes further to the south (half a million). The Eastern Bantu live to the East of the Rift Valley and include the largest tribe in Kenya, the Kikuyu, (one and a half millions) who

Tohography of Kenya (Fig. 1b)



occupy most of the Central Province: the Meru and Embu tribes who live on the Northern and Eastern Slopes of Mount Kenya: the Kamba (one million) who inhabit the hills around Machakos and Kitui in the Eastern Province. On the coast live the detribalised coastal Bantu who have absorbed a significant amount of Arab blood. The Luo (one million) who live in the South West of Kenya around Kisumu on the shores of Lake Victoria are the only Nilotic tribe in Kenya. The Nilo-Hamitic comprise chiefly the Kalengin (one million), the collective name for a group of tribes who inhabit the highlands west of the Rift Valley. They include the Kipsigis tribe around Kericho and the Nandi around Eldoret in the Nandi Hills. The Masai (150,000) are a pastoral semi-nomadic tribe who inhabit the lowlands of the Rift Valley and South West Kenya, and the adjacent plains of Tanzania. The Turkana and Samburu ($\frac{1}{4}$ million) occupy the whole of the arid North West of Kenya and the last racial group, the Hamites (Rendille, Somali and Boran tribes) live in the vast desert regions of the North East Province.

Table 1.

Thyroid disorders in 550 Kenyan African Patients seen over 18 months at the Kenyatta National Hospital, Nairobi.

Nontoxic Goitre.

Diffuse	Multinodular	Single Nodule	Thyrotoxicosis	Cancer	Miscellaneous
180	255	58	31	18	8

The large majority of goitres seen in patients in Kenya are non-toxic. (Table 1). As there are several possible aetiological factors which may occur either alone or in combination, non-toxic goitre should be considered as a clinical syndrome rather than a specific disease entity. All of these factors in one way or another produce a fall in circulating thyroid hormone, causing increased secretion of thyrotrophin (thyroid-stimulating hormone: TSH) by the pituitary, which in turn may stimulate hyperplasia and hypertrophy of thyroid tissue.

Simple Non-Toxic Goitre.

The commonest variety of non-toxic goitre is the simple non-toxic goitre which may be diffuse or nodular, and which is defined as a benign enlargement of the thyroid gland not due to thyroiditis, dyshormonogenesis, goitrogenic drugs or neoplasm.

There are striking geographical variations in the incidence of simple goitre on both a national and regional basis. Where many individuals in a given population exhibit clinical thyroid enlargement, the condition is termed endemic goitre. Goitre occurring in individuals or families, in a community where the thyroid gland size is otherwise normal, may be termed sporadic goitre.

ENDEMIC GOITRE.

Aetiology and Pathogenesis: Environmental iodine deficiency is the main cause of endemic goitre and formal proof has been supplied by the considerable drop in the prevalence of goitre following the introduction of additional iodine into the diet in affected regions. The references are too numerous to list, and a full account is given in the World Health Organisation Monograph on Endemic Goitre (1960) by Matovinović and Ramalingaswami.

Although naturally occurring goitrogens may play an additional role in the aetiology of endemic goitre they have never convincingly been proved to be the sole cause.

Iodine Metabolism. Because of its importance a brief simplified account is given here. Iodine, an essential component of the thyroid hormone, thyroxine, exists in the plasma in two forms.

1). Free plasma inorganic iodide (P.I.I.) derived largely from dietary iodine and also from the recirculation of iodide.

2). Organic iodine (thyroid hormone) bound to proteins (P.B.I.)

Circulating inorganic iodide is trapped by the thyroid and eventually incorporated into thyroxine through a series of enzymatically assisted steps. Any factor interfering with the utilisation of iodine (iodine deficiency, goitrogens, inherited enzyme deficiencies) may produce a fall in level of the circulating thyroxine (the P.B.I.). Subsequent anterior pituitary stimulation with release of thyrotrophin (T.S.H.) increases the capacity of the thyroid to trap and handle iodine. Thus in iodine deficiency, the low P.I.I. is compensated for by a relative increase in iodine uptake, by the thyroid, restoring the absolute iodine uptake and consequently

the P.B.I. to a normal or near normal value. This process may be accompanied by an increase in volume of the gland. However, it is well known that in apparently uniformly iodine deficient communities, there are some individuals who do not develop goitre. Iodine metabolism studies show that these individuals may have a more efficient mechanism for trapping and handling iodine, and family studies seem to indicate that this may be genetically determined. (Malamos et al. 1965: Lewitus and Lubin 1965). Increased demands for thyroid hormone during puberty and pregnancy are probably responsible for the development of the "physiological" goitre. Such a goitre usually regresses spontaneously, but repeated pregnancies, exposure to moderate iodine deficiency or a genetic predisposition, may be responsible for failure to regress, and for the eventual development of a multi-nodular gland.

In severe iodine deficiency, or in moderate deficiency with a sudden increase in demand (e.g. pregnancy), this mechanism may be unable to compensate and the gland becomes "decompensated". The iodine uptake is maximal, but the P.B.I. drops below the normal value. Chronic exposure to iodine deficiency results in a series of morphological and structural changes in the thyroid gland. In a proportion of individuals the diffuse, potentially reversible, hyperplastic gland eventually becomes a firm, and irregular, adenomatous or multi-nodular goitre, which may reach enormous proportions and is characterised by cyst formation, fibrous bands and often calcification.

The importance of endemic goitre in a community lies in the disturbance of normal hormone synthesis, rather than in the presence of swollen necks of which only a very small percentage will cause mechanical obstruction or gross disfigurement. Endemic goitre is not

Fig. 2. - Brothers aged 4 and 2 years with severe hypothyroidism. Not established whether due to specific inherited enzyme defect or iodine deficiency. Good response to thyroxine.

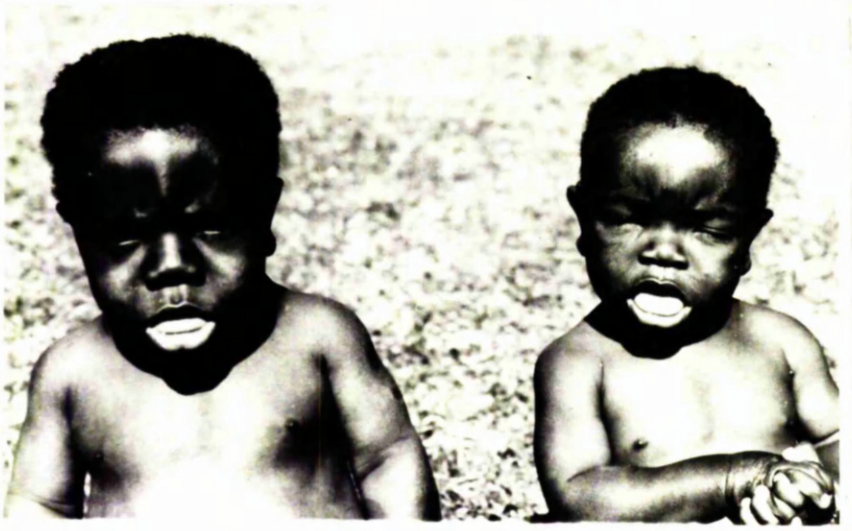
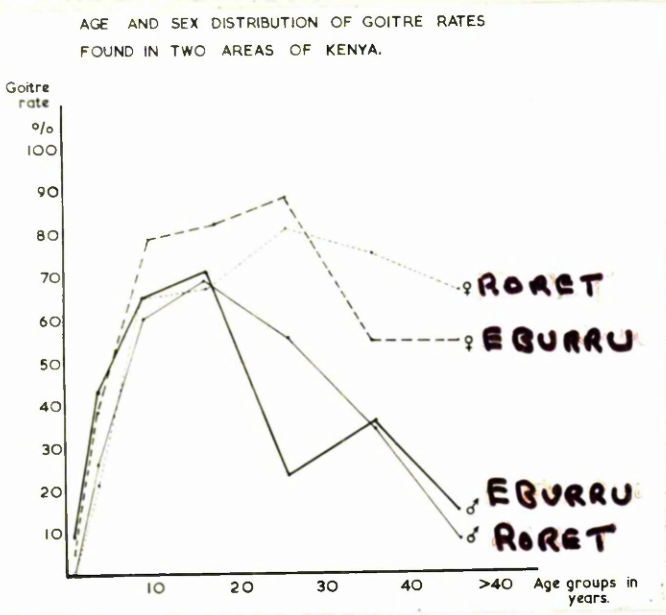


Fig. 3.



a "killer" disease, but even in its milder forms it probably has adverse effects on the mental, physical, social and economic well-being of the population affected, although formal proof is difficult to obtain. The sequelae of endemic goitre vary from a poor performance in school or a decreased physical activity in a community to the occurrence of endemic cretinism.

Endemic cretinism (in contrast to sporadic cretinism which is unrelated to endemic goitre) is the collective term for a number of developmental abnormalities which geographically coincide with severe endemic goitre and are caused by abnormalities occurring before, or shortly after birth. More precisely, it may be defined as an excess of abnormalities in a goitrous population as compared with a similar population without goitre and which in due time may be abolished by adequate goitre prophylaxis. (Querido 1969).

There are two distinct clinical types of endemic cretinism: euthyroid "nervous cretinism" characterised by idiocy, deaf-mutism and spastic paraplegia, and "myxoedematous cretinism" characterised by severe hypothyroidism, dwarfism and mental retardation without any other signs of neurological damage. Both types may occur in any given endemic, but one type usually predominates: e.g. in Central Africa the "myxoedematous" type is common (figure 2) and in New Guinea the "nervous" type is more prevalent.

Why this should be so is not clear. Recent work from New Guinea has shown that iodised oil will prevent "nervous" endemic cretinism only if given before conception, suggesting that elemental or inorganic iodine is concerned somehow with the very early development of the central nervous system. (Pharaoh et al. 1971). From Idjwi Island (Republic of Zaire), where myxoedematous cretinism is particularly

prevalent recent studies have shown that hypothyroidism develops before or around the time of birth, and thyroid failure may be the result of combined iodine deficiency and a food goitrogen, possibly a thiocynate derived from cassava. (Delange et al. 1972).

Epidemiology.

Endemic goitre is usually, but not always, found in mountainous regions, remote from the sea, where by flooding or intense glaciation the soil iodine has been grossly depleted. Goitre can occur at any age in a person living in an endemic area. When the goitre prevalence is high, and iodine deficiency severe, neonatal goitre may occasionally be seen. In moderately endemic areas, goitres usually develop slowly during childhood. The highest incidence usually occurs in adolescence, when the needs of growth and puberty create demands for thyroxine which cannot be satisfied by the limited amounts of iodine available. The decreasing incidence after this peak is usually marked in males but is only slight in females, reflecting the demands for extra thyroxine in women of child-bearing age.

Figures compiled from two population surveys in Kenya (figure 3) where overall goitre rates of 52 per cent and 50 per cent respectively were found, show this trend. Highest goitre rates were found in males aged 13-20 years and in females aged 20-30 years.

Although dietary iodine deficiency is the main cause of endemic goitre there is evidence that other factors (environmental or genetic) may be involved. Since Chesney et al. (1928) produced goitre in rabbits by feeding them cabbage, a member of the Brassica group, much attention has focused on the role of goitrogens in the food as possible primary causes of endemic goitre. Goitrogenic substances are present in many foodstuffs (Greer and Astwood 1948, Astwood et al. 1949), and Clements (1960) has classified food substances

containing goitrogens into two groups:

a) Those which prevent the uptake of iodine by the thyroid gland (e.g. thiocyanates)

b) Antithyroid compounds which block the organic binding of iodine (e.g. thio-oxazolidine, present in cabbage, cauliflower, Brussel sprouts, etc.).

Vigilance seemed to be rewarded when Clements (1955) first suggested that a thyroid blocking agent might play a part in the prevalent goitre in Tasmania. The putative goitrogen was present in the milk of cows fed on kale (brassica oleracea). Clements (1955) claimed that it might be responsible for goitre in Tasmanian school-children who at that time were thought to be receiving adequate supplies of iodine. However, iodine balance studies were never performed and conclusive proof of the hypothesis was never obtained. (Clements, 1956, Bachelard and Trikojus, 1960). It is now clear that environmental iodine deficiency was the chief cause of the simple goitre in Tasmania. The initial prophylaxis scheme consisted of the distribution of potassium iodate tablets at weekly intervals to schoolchildren and others and was clearly an inadequate method of delivering iodine supplements. Goitre has now been abolished in Tasmania following the introduction of potassium iodate into bread. (Clements et al. 1970, Connolly 1971). "The Tasmanian goitrogen should be forgotten or perhaps remembered as a remote and unproved possibility" (Baikie and Connolly 1973).
A goitrogenic factor present in Cassava (manioc) has been implicated in the aetiology of endemic goitre in Eastern Nigeria. (Nwokolo et al. 1966). Thiocyanate is goitrogenic, (Clements 1960) and is the main detoxification product of cyanide which is derived from the hydrolysis of linamarin, present in very high concentration in the outer integument and leaves of cassava. Its antithyroid activity resembles that of perchlorate and the effect should be to block the thyroidal uptake of iodine. Cassava, when fed to rats however,

produces a defect in the intrathyroidal transfer of radio-iodine, resembling more the action of carbimazole or the brassica vegetables, (Ekpechi 1967). Despite this conflicting data, there is strong circumstantial evidence supporting a role for a constituent of cassava (? thiocyanate) in the aetiology of severe endemic goitre on Idjwi Island, Lake Kivu, Republic of Zaire. Despite uniform iodine deficiency the inhabitants of the North of the island have a 55 per cent goitre rate compared with a 5 per cent rate in the South, (Delange et al. 1968): cretinism is common in the north and absent in the south: the rat population of the north have a much higher goitre rate than that of the south, (Orts et al. 1971). The rats live largely on human food waste. Cassava is a staple in the diet of the native population of the north but not the south of the island. While these observations are obviously fascinating, the most important observation from the point of view of the inhabitants is that a single intramuscular injection of a slowly resorbed iodised oil has been followed by a dramatic fall in the incidence of goitre. This observation stresses again the importance of iodine deficiency in the aetiology of endemic goitre. (Delange et al. 1968).

There are innumerable descriptions of goitre attributed to the poor quality of drinking water, dating from 770 B.C. (Langer 1960) to the present day. (Gaitan et al. 1969). Experimental goitre has been produced in man and animals by the administration of "goitrogenic water" by McCarrison (1928) who was probably the first to suggest that iodine deficiency was not the sole or even the most important cause of endemic goitre. He observed that goitre increased from the top to the bottom of a series of villages in the Gilgit Valley, India, and suggested that the drinking of polluted water was responsible. However, a recent investigation in this area has demonstrated once more

the presence of severe iodine deficiency. Moreover there was no correlation of bacterial counts in the water with the prevalence of goitre. (Chapman et al. 1972). Bacterial contamination of drinking water may be responsible for the modest endemic goitre which has been described in the presence of apparently adequate iodine nutrition in Kentucky (London et al. 1965) and in Northern Virginia (Vought et al. 1967). A goitrogenic factor (an aliphatic disulphide) has been suggested responsible for the residual endemic goitre in the Cauca Valley, Colombia (Gaitan et al. 1969). Despite 14 years of apparently adequate iodine supplementation the goitre rate in some areas of the Cauca Valley remains at 30 per cent, a situation reminiscent of Tasmania. (Gaitan et al. 1968). However, in Colombia iodised salt is used as the prophylactic agent but whether this is used in adequate amounts by all the population is not known. Other possible goitrogenic factors which may be found in water include calcium and fluoride. In rats calcium increases substantially goitre produced by iodine deficiency. (Taylor 1954). In a recent report from Nepal (Day and Powell-Jackson 1973) goitre rate correlated with water hardness and fluoride content. Water iodine content, however, was uniformly low. Fluoride has been suggested as a cause of, or an aggravating factor in, endemic goitre (Wilson 1941) and this is of some interest in Kenya where a high frequency of dental fluorisis has been recorded in nearly all tribal groups. (Bohdal et al. 1968).

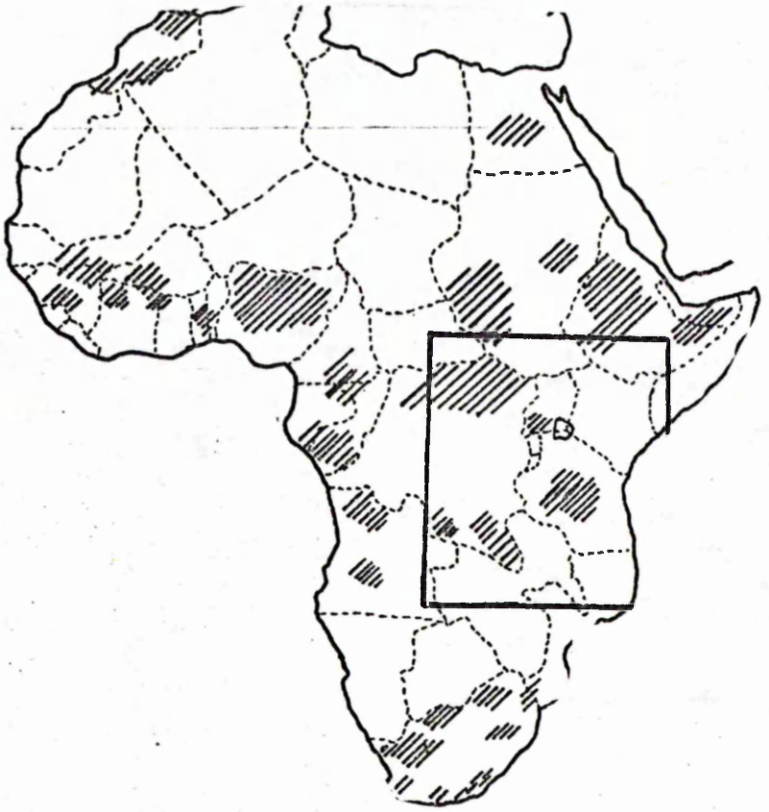
Last among the environmental factors which may produce goitre on an endemic scale is iodide in excess. A remarkable example exists in the Japanese island of Hokkaido where large quantities of iodide are ingested in a diet rich in seaweed. (Suzuki et al. 1965).

As mentioned already, not all subjects in a uniformly iodine deficient community develop thyroidal enlargement (Roche 1959, Choufoer et al. 1963, Malamos et al. 1966$^{\alpha}_{\beta}$). The reasons are not clear but are

probably related to individual "sensitivity" to iodine deficiency, which may be genetically determined. The adaptation to severe iodine deficiency in humans can certainly occur without the development of significant enlargement of the thyroid gland. J. B. Stanbury (1958) who has contributed so much to the understanding of physiological response of the human thyroid gland to iodine deficiency states that "there is little profit in arguing whether iodine deficiency or goitrogenic agents in the diet are responsible for endemic goitre. It is a demonstrated fact that both factors may be operative and indeed be operative at the same time. It is more to the point to suggest that a given endemic be investigated by the proper and appropriate modern epidemiological and laboratory tools in order that each endemic may be properly defined as to its own nature."

Fig. 4. - Geographical Distribution of endemic goitre in Africa according to Kelly and Snedden, (1960).

☐ Area presently under review.



PREVALENCE AND GEOGRAPHICAL DISTRIBUTION OF ENDEMIC GOITRE IN EASTERN AFRICA.

Endemic goitre is still widespread and present on all continents. In World Health Organisation monograph No. 44 (1960) entitled "Endemic goitre", Kelly and Snedden provide a comprehensive summary of the known world prevalence and geographical distribution of endemic goitre. Figure 4 shows the goitre map of Africa compiled by them. The existence of endemic goitre in West, Central and North Africa is well documented in contrast to the dearth of reports from the three East African countries, Kenya in particular.

Investigations carried out since 1960 in the three countries and their immediate neighbours make it possible to add some more epidemiological data to the goitre map of Africa, and there follows a review of the current literature on the occurrence of endemic goitre in East Africa. The map in figure 5 indicates only the areas where goitre has been found. Blank areas do not specifically indicate the absence of goitre, but rather lack of data. No attempt is made to include in the map the severity of the endemic.

Sudan.

Kelly and Snedden (1960) report at least five centres of endemic goitre in the Sudan, mainly quoting from Woodman's description of endemic goitre in Central Africa (1956). The Zande endemic area in South West Sudan apparently is a continuation of the vast endemic area in the Northern Congo (Uele: now Republic of Zaire). Kambal et al. (1969) found a goitre rate of 57.5 per cent in Darfur Province of West Sudan, a focus hitherto considered to be of comparatively minor importance (Kelly and Snedden, 1960).

Republic of Zaire (formerly Congo).

The Uele endemic goitre area in Northern Zaire is probably one of the largest and most severely affected in the world. Extensive studies of this endemic area have been carried out by investigators from Louvain and Brussels Universities (Ermans et al. 1961. De Visscher et al. 1961. Bastenie et al. 1962). Further south in the Sampwe region of Katanga, Calonne (1939) has reported a moderate incidence of goitre. This endemic area probably continues into Zambia, where Beet (1951) carried out a nutritional survey among Lala children at 17 schools in Serenje and Mkushi district and found a goitre rate of 38 per cent. As already mentioned, Delange et al. (1968 and 1971) have reported a fascinating situation on Idjwi Island in Lake Kivu where the prevalence of endemic goitre and cretinism is very high in the North East and low in the South West part, while the degree of iodine deficiency in the two areas is not significantly different.

Uganda.

Van Campenhout (1934) in a paper on goitre in the Belgian Congo mentions its occurrence in the Ruwenzori Mountains and the basin of the Semliki river. This focus of endemic goitre is believed to extend across the border into Western Uganda. Dean (1954) reported that he had found an enlarged thyroid gland in nearly every Baganda child at one primary school in Kampala. Connor and Follis (1966) found thyroid hyperplasia in 40 out of 45 unselected autopsy cases of different tribal origin at Mulago Hospital. Although none of the patients had a clinically recognized goitre this was considered to reflect a low intake of dietary iodine. Follis and Connor (1966)

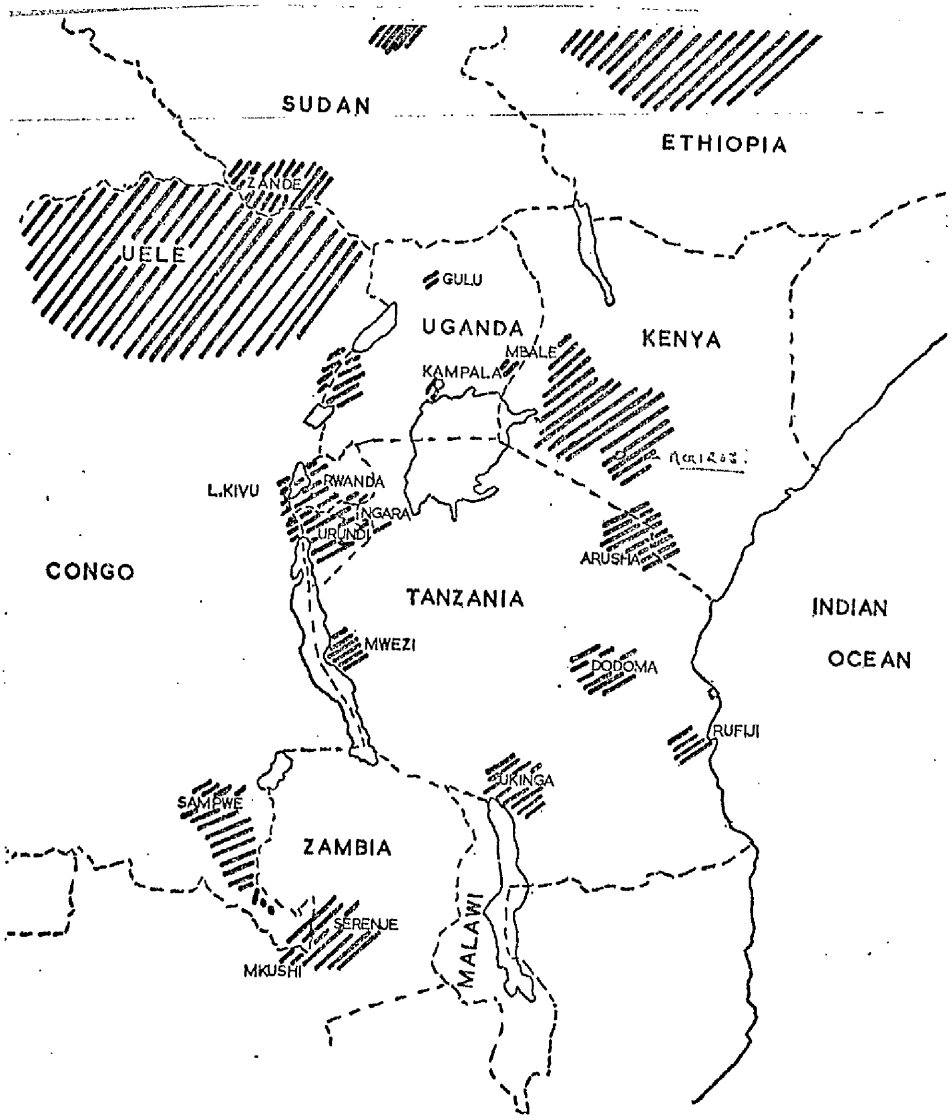


Fig 5.

Distribution of reported goitre areas in EASTERN AFRICA

confirmed this suspicion by assessing the pattern of iodine excretion in six sites in Uganda. They found a practically normal excretion pattern in Karamoja, slightly lower values in two schools in Kampala, definitely low values among schoolchildren in Gulu and Gayaza, and extremely low values in Mbale Prison.

As the finding of a low urinary iodine excretion probably indicates a low dietary iodine intake, one would expect to find endemic goitre to be prevalent in the last three areas. Apart from a single report of an "epidemic" in Mbale Prison in 1964, (Follis and Connor 1966) no goitre figures of these areas are yet available. Recently high radio-iodine uptakes have been reported in patients with nontoxic goitre studied at Mulago Hospital, Kampala, (Kajubi, 1971).

Tanzania.

Trolli (1933) mentions the occurrence of goitre in the "mountainous region", probably referring to North West Tanzania bordering the former Belgian Congo and Ruanda-Burundi. This report has led Kelly and Snedden (1960) to indicate as goitrous a large part of Central Tanzania on their goitre map of Africa (figure 4), almost certainly an exaggeration. Figure 5 is probably a more accurate representation. Latham (1965) reports a serious goitre endemic (76 per cent goitre rate) in Ukinga division of Njombe district in Southern Tanzania. A case of goitrous cretinism was reported from this area, and this is probably the first report of endemic cretinism in East Africa, in contrast to the common endemic cretinism in Zaire in the Uele region (Ermans et al. 1961, Dumont et al. 1963) and Lake Kivu (Delange et al. 1968). Latham also found low goitre rates in the coastal Rufiji district (13.9 per cent) and in the Dodoma and Kondoa district

(10 per cent) in the Central Region of Tanzania, and mentions that goitre is believed to be fairly common in the Arusha district, especially around the base of Mount Meru. This endemic area probably continues into Kenya where a goitre rate of 28 per cent was found among schoolchildren in the Taita hills by Munoz (Bohdal et al. 1968). A new focus of endemic goitre on the Eastern border of Lake Tanganyika at Mwezi is reported in this thesis.

Kenya.

Although the World Health Organisation monograph (1960) does not mention goitre in Kenya, data collected during the last decade have shown that endemic goitre exists in the highlands of Kenya. A W.H.O. nutrition team under the direction of J. A. Munoz, conducted an extensive survey on the prevalence of endemic goitre in the schoolchildren of Kenya in 1962-64. The findings were published in 1968 (Bohdal et al. 1968) with the recommendation that the distribution of iodised salt should be undertaken as a preventative measure. Acting on this advice the Ministry of Health commenced distribution of iodised salt in 1970, and legislation to ensure the compulsory iodisation of all salt for human consumption is to be implemented. Briefly the W.H.O. findings were as follows (Table 2): over 28,000 children in 108 schools spread over the districts were examined. Goitre rates varying from 15 per cent to 72 per cent were found, the highest rates being recorded in the highland areas of the Rift Valley, Western and Central Provinces of Kenya. Additional surveys, all involving schoolchildren, were undertaken in presumed endemic areas of the Rift Valley and Western Provinces in 1969, (Hanegraaf et al. 1969, Hanegraaf and Taylor 1969, Hanegraaf and McGill, 1969). The results are summarised in Table 2.

Table 2: Prevalence of Goitre in School Children according to the Districts of Kenya in 1962-64.
(Bohdal et al. 1968)
and others (1) McGill 1968 (unpublished)
(2) Hanegraaf et al. 1969
(3) Hanegraaf and Taylor (1969)
(4) Hanegraaf and McGill (1969)

District	Number Examined	GOITRE GRADES I	II	III	% of children with goitre
Kericho	932	397	264	64	72.4%
Nandi Hills	3,426	1,221	813	199	65.17%
Kiambu	342	136	15	1	44.4%
Nyeri	2,935	754	284	25	36.1%
Kakamega	780	215	36	0	32.2%
Nakuru	3,121	731	198	23	30.5%
Taita Hills	1,033	282	10	0	28.2%
Central Nyanza	2,700	615	110	5	27.0%
Embu	414	56	31	3	21.7%
Machakos	182	39	0	0	21.4%
Mombasa	5,335	755	197	2	17.9%
Nairobi	6,039	887	110	1	16.5%
Nanyuki	67	8	2	0	14.9%
Narok	1,196	161	15	3	14.9%
Kericho (1)	128	57	26	2	66.0%
Kericho (2)	370	160	78	2	65.0%
Nandi Hills (Kimeloi) (3)	151	60	53	2	76.0%
Nandi Hills (Kaptumo) (3)	773	289	161	0	62.0%
Nandi Hills (Kabiyet) (3)	913	175	46	0	24.0%
Nakuru (Eburru) (4)	98	34	46	1	83.0%

Hanegraaf and Taylor (1969) found considerable variation in goitre frequency in three locations in the Nandi Hills (24-75 per cent) but the overall results were similar to those of the W.H.O. team and confirmed the desirability of iodine prophylaxis. Additional surveys, involving schoolchildren were also undertaken in areas on the Northern and Eastern slopes of Mount Kenya not visited by the W.H.O. team, by Dr. Hanegraaf and myself and the results are reported in this thesis.

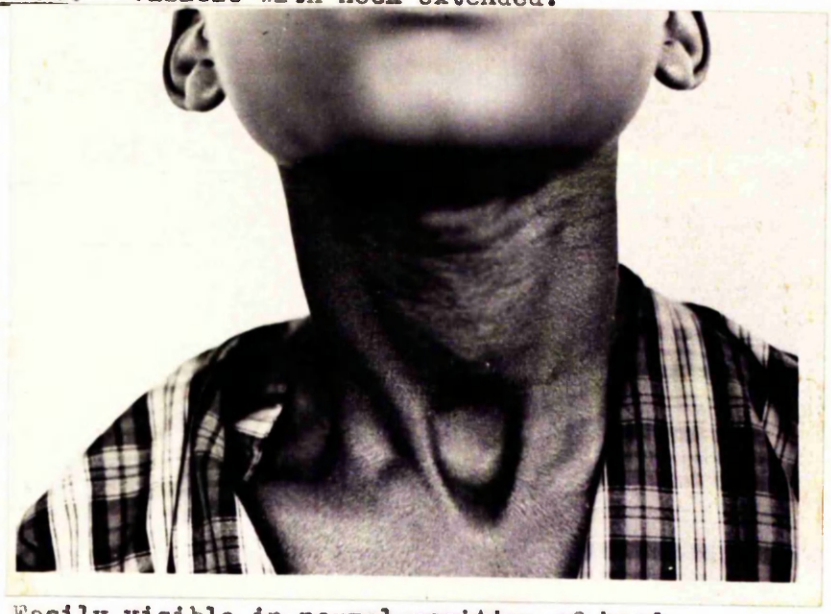
Although surveys of schoolchildren are a useful method of assessing the prevalence and geographical distribution of endemic goitre there are certain disadvantages in this method of sampling. Firstly, although the goitre rate in young prepubertal children is a more sensitive index to the total goitre rate of the population than older pubertal children, these rates do not necessarily reflect the goitre rate of the total population in the area. Secondly, and more important, in the absence of compulsory education in Kenya, cases of mental and physical abnormality related to endemic cretinism are unlikely to be found in children attending school. Intensive studies require therefore the involvement of population groups or cluster samples of these, preferably in a house to house survey. Moreover, if possible, some measure of environmental iodine content or iodine nutrition of the population should be available. Community surveys had not been performed in Kenya and no measurement of environmental iodine, iodine nutrition or thyroid function was available. The Ministry of Health of Kenya decided to postpone the introduction of iodised salt from 1969 until 1970 to allow the additional information to be collected. Studies of iodine metabolism in selected communities in Kenya and in patients with simple goitre attending a hospital clinic in Nairobi confirm iodine deficiency as the

main cause of simple goitre in Kenya. These data are reported and discussed in this thesis, and they will be used in the future evaluation of the iodised salt scheme.

PERSONAL INVESTIGATIONS.

Grade 1 goitre. Visible with neck extended.

Fig. 6a



Grade 2. Easily visible in normal position of head.

Fig. 6b.

Grade 3. Large goitre.

Fig. 6c

ENDEMIC GOITRE IN KENYA

School Surveys: Mount Kenya Area.

Goitre prevalence was assessed in 1103 children aged 5-15 years attending five schools located near Embu, Meru and Nanyuki. (See figure 11, page for precise locations).

Methods: Goitre prevalence was investigated according to the recommendations of Perez et al. (1960). If the lateral lobes of the thyroid gland have a volume greater than the terminal phalanx of the thumb of the person being examined, the gland is considered to be enlarged. Goitre size was graded in groups 0, 1, 2 and 3, using the criteria established by Perez et al. (1960). (Table 3, figures 6a, b, c.) Each child was examined by two observers and in the case of disagreement the lower goitre size was recorded.

TABLE 3.

The W.H.O. (Perez) Goitre Classification.

Group 0: No goitre, but palpable enlargements up to 4-5 times are included in this group.

Group 1: Palpable goitres were then 4-5 times enlarged. Mostly visible with the head fully extended.

Group 2: Readily visible with the head in normal position.

Group 3: Very large goitres readily visible at a considerable distance.

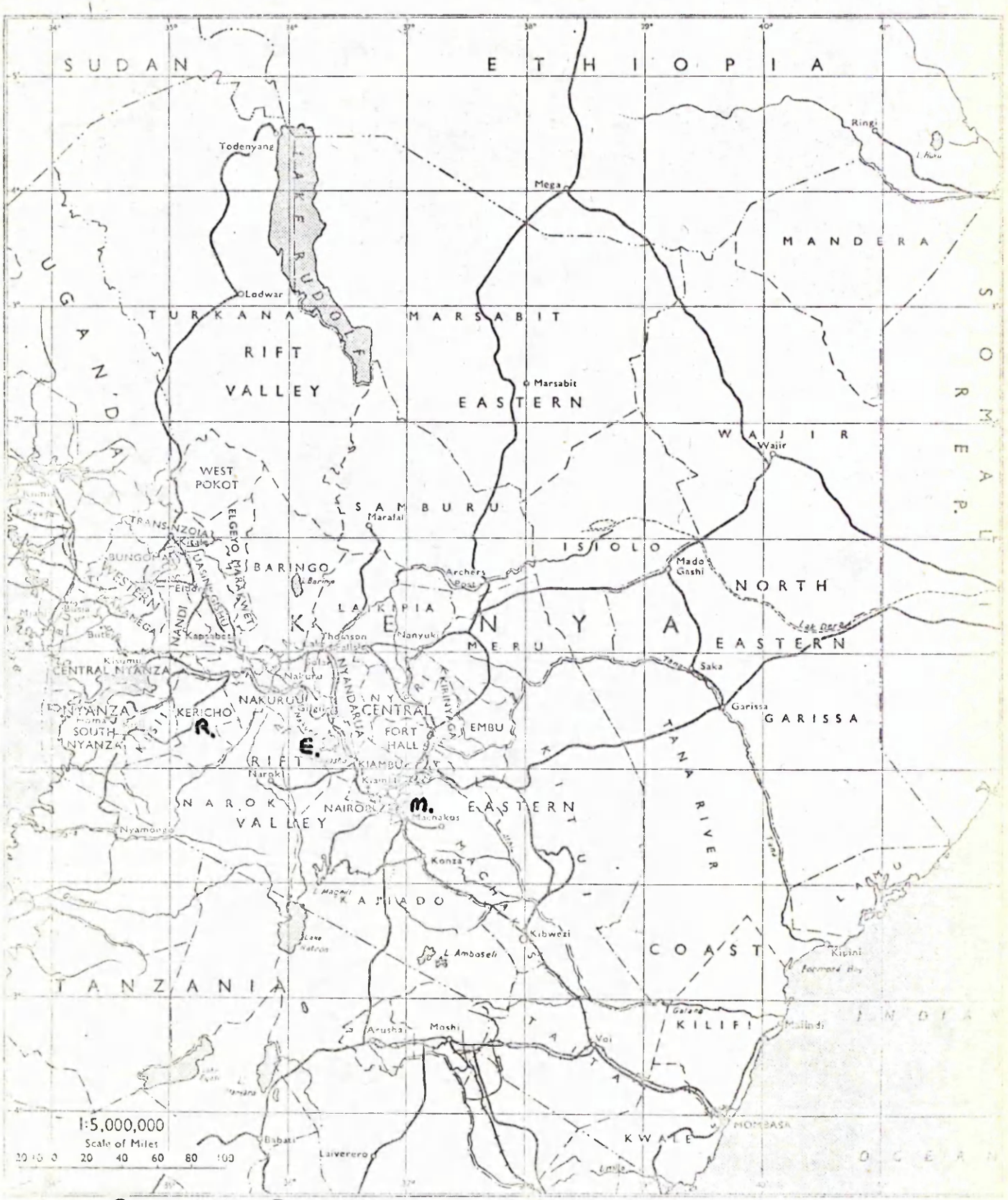


Fig. 7. R = Ronet. E = Eburru. M = Mufutuni.

Map of Kenya with exact locations of three villages where intensive surveys were performed in 1969

COMMUNITY SURVEYS.

Two highland and one lowland village were selected for intensive study. Reasons for selection included a high goitre frequency in the schoolchildren, cooperation of the inhabitants and local authorities and accommodation for the mobile team.

Eburru.

A preliminary school survey revealed a very high goitre rate of 83 per cent in 98 schoolchildren. Eburru (figure 7 and map on appendix page 179)is situated in the Rift Valley Province, 75 miles North West of Nairobi between Lake Naivasha and Lake Elementeita at the edge of the Eburru Forest, high in the Eburru Hills at almost 9,000 feet altitude. There were approximately 150 families (approximately 900 people) mainly of the Kikuyu tribe living in this area. All homes were visited and 699 people examined.

Roret/Tulwet.

A preliminary survey in schoolchildren revealed a goitre rate of 67 per cent (Hanegraaf et al. 1969). These adjacent villages are situated near Kericho (figure 7 and appendix p. 178) at an altitude of 7,000 feet. One hundred and forty homes were visited in this densely populated area and 732 people were examined.

Mutituni.

A low goitre rate (21 per cent) was found in schoolchildren by the W.H.O. team at Machakas in the Eastern Province (Bohdal et al. 1968). Mutituni is a village situated 10 miles north of Machakos, 40 miles east of Nairobi at an altitude of 2,000 feet (figure 7). One hundred and ten homes in this area were visited and 494 people examined.

Fig. 8 - Apparatus used to measure uptake of radio-iodine by the thyroid gland.

METHODS.

Clinical.

The homes were visited by a team which consisted of a physician, health assistant and 'local man' acting as guide and interpretor. Goitre size was assessed by palpation and inspection using the international classification (Perez et al. 1960). All available inhabitants were examined. A note was made on a specially designed family card (see appendix page166) of the following: age, sex, goitre size, duration of residence, physical or mental abnormalities: family absentees were also recorded.

Laboratory Studies.

After informed consent had been obtained additional laboratory studies were undertaken on subjects of both sexes as follows.

Roret: Fifteen men with and 9 without goitre.
Twenty seven women with and four without goitre.

Eburru. Twenty three men with and ten without goitre.
Twenty one women with and six without goitre.

Mutituni. Four men with and five without goitre.
Seven women with goitre.

Investigations.

(1) Thyroidal uptake of radio-iodine: An oral dose of 40 μc ^{131}I was administered and the thyroidal uptake was measured after 4 and 24 hours using a portable collimated Geiger-Muller tube connected to an appropriate scaler (20th Century Electronics G. 10, Pb.). The working distance was 30 cms. from the sternal notch and counts from the patient's neck were compared with those of the standard from a phantom neck. Thyroidal uptake was expressed as a percentage of the administered dose.

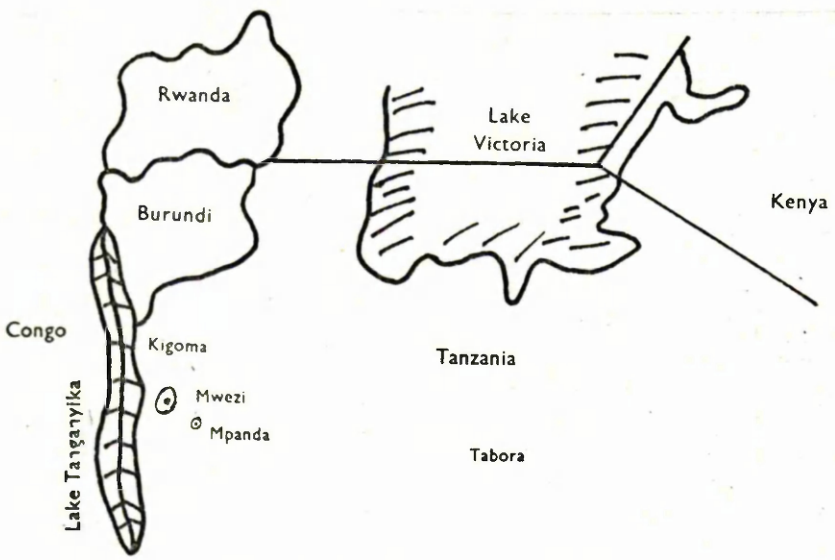
(2) Urinary Iodine. Urine was collected into sterile iodine free containers acidified, stored at 4°C in a portable refrigerator, transported to Nairobi and then sent by air to the Department of Pathological Chemistry, University of Leiden, Holland. Urinary iodine was estimated by a modified chloric acid procedure (Benotti and Benotti 1963) and urinary creatinine by a standard method using an autoanalyser. The 24 hour urinary excretion of iodine was calculated from the iodine/creatinine ratio using the equation (Jolin and del Rey 1965)

$$\text{Urine I (ug/24 hr.)} = \frac{\text{I (casual sample) ug/L.}}{\text{creatinine (casual sample) g/L.}} \times \text{K (creatinine g/24 hr.}$$

Urinary creatinine (g/24 hr) = K { 1.0 for women
1.7 for men
0.018 x body wei ht (Kg) girls
0.020 x body weight (Kg) boys.

Blood was withdrawn into sterile iodine free containers and centrifuged. The serum was separated and stored frozen until transported by air to the above laboratory for estimation of the serum protein bound iodine (P.B.I.) by antoanalyser.

Mwezi
Mountain



Map showing the Location of Mwezi.

ENDEMIC GOITRE IN MWEZI, TANZANIA.

Mwezi (figure 9) is situated in a remote highland area of Western Tanzania, near Lake Tanganyika, 500 miles from the sea, at an altitude of 6,000 feet. During 1964/65 some 3,000 Ruandan refugees of the Watutsi tribe settled in Mwezi. Although originally from Ruanda, all had spent about two years in the Congo before moving to Tanzania. In addition there were approximately 1,000 people of local tribes in the settlement area. The goitre frequency was assessed in the Mwezi schoolchildren and the urinary and plasma iodine were measured.

Methods.

Approximately 530 children aged 5-17 years lived in the area. Thyroid gland size was recorded in 373 who were attending school (285 Ruandan immigrant children; 88 'local' children), using the international classification previously described (Perez et al. 1960). A house to house survey was not possible mainly because of lack of time. The survey was completed during routine trips by the East African Flying Doctor Service to Mwezi.

After examination of the thyroid gland, urine samples were obtained from 100 children, and in 50 of these a simultaneous blood sample was taken. As in adults the iodine/creatinine ratios of casual urine samples may be used to obtain a representative index of the urinary iodine excretion of schoolchildren under field conditions (Follis 1964). The daily iodine excretion was calculated from the formula on page 31. Daily urinary iodine output, although used as an index of iodine intake is not equivalent to iodine intake and may not be a wholly accurate index of iodine nutrition. The plasma inorganic iodine (P.I.I.) is considered by some investigators to be the most useful non-isotopic epidemiological technique for assessing

iodine deficiency (Boyle et al. 1965). The P.I.I. is calculated from the formula (Vought et al. 1963)

$$\text{P.I.I. (ug/100 ml)} = 4 \times \frac{\text{Urinary I ug/100 ml x serum creatinine (ug/100 ml)}}{\text{Urinary creatinine (ug/100 ml.)}}$$

Values for P.I.I. using this method correlate closely with those obtained using conventional isotopic methods (Harden et al. 1965). Serum and acidified urine samples were refrigerated and sent by air to the Department of Medicine, Western Infirmary, Glasgow. Iodine was estimated chemically in the urine by the chloric acid digestion method (Wayne et al. 1964). Serum and urine creatinine were estimated by a standard autoanalyser technique (Technicon Instruments Limited).

QUANTITTIVE STUDIES OF IODINE METABOLISM.

In a preliminary study, thyroidal uptake of radio-iodine was measured in 18 goitrous patients and six control subjects. The individual values are shown in table 4. The results show an "iodine deficiency" pattern in many of the patients and in three of the control subjects.

A more detailed study of thyroid function was considered appropriate.

Materials and Methods.

All subjects were Kenyans of African origin attending a special thyroid clinic at the Kenyatta National Hospital, Nairobi. The majority lived in the Central Province of Kenya and were members of the Kikuyu tribe. There were 10 males and 53 female patients with goitre. Their ages ranged from 15-60 years. The diagnosis of simple non-toxic goitre was established by excluding thyrotoxicosis

TABLE 4.

4 and 48 hour Thyroidal Radio-iodine Uptake Values (% dose) of 18 Goitrous Patients and 6 Control Subjects.

Patients

Sex	Age	Goitre*	4 hr.	48 hr.	$PB^{131}I$(48 hr)
MF	19	D	26	40	
F	17	N	30	40	
F	30	D	65	68	
-	-	-	54	64	
F	40	N	21	47	
F	55	N	33	38	
F	35	D	27	51	0.18
F	15	D	56	78	0.16
-	-	-	64	68	0.17
M	21	D	62	57	0.06
F	30	D	53	70	0.16
F	50	D	66	85	
F	20	D	40	62	
F	14	D	50	61	
F	18	N	38	51	0.25
-	-	-	39	51	0.31
-	-	-	61	70	0.08
F	25	D	64	86	
		Mean	46	60	0.17

Control Subjects.

Sex	Age	4 hr.	48 hr.
F	17	25	39
F	35	65	71
M	25	54	68
M	40	22	35
F	30	18	38
F	40	36	48

* D = Diffuse } — on Palpation.
N = Nodular }

(normal P.B.I. value) and Hashimoto's thyroiditis (negative thyroid antibodies). No patient with proved or suspected malignant disease of the thyroid gland was included in the study. Three males and fifteen females without goitre were also studied. They had been referred to the clinic with suspected thyroid disease but were subsequently found to be euthyroid. The results from these patients will be used as control values. All sera were tested for antibody to thyroglobulin by a tanned red blood cell haemaglutination method, using Burroughs Wellcome reagents and a microtiter apparatus (Goldin et al. 1967).

Methods. The patients received an oral dose of 40 μc ^{131}I. (25 μc ^{131}I given to those below 21 years). Thyroidal uptake of ^{131}I was measured using a Geiger-Muller counter connected to an appropriate scaler. This apparatus was used in the community surveys (figure 9). The working distance was 30 cms. and the counts from the patient's neck were compared with those of the standard from a phantom neck. The radioactivity of plasma and urine samples was measured in a $1\frac{1}{2}$" well-type scintillation counter (Echo Electronics Ltd.). Serum P.B.I. and urine inorganic iodine were estimated in the Department of Medicine, Western Infirmary, Glasgow by standard methods. The theoretical and practical aspects of the metabolic studies performed are fully discussed by Alexander et al. (1962) and Wayne et al. (1964).

The following measurements were made:

(1) Thyroidal radio-iodine uptake at $2\frac{1}{2}$ hrs. (% dose).
(2) Thyroidal clearance of radio-iodine (Th. Cl.) in ml./min.
(3) Plasma Inorganic Iodine (P.I.I.) in μg./100 ml.
(4) Absolute Iodine Uptake (A.I.U.) by the thyroid in μg./hr.
(5) Renal clearance of iodide (in ml./min.)

Due to an error renal clearance was measured in 15 goitrous patients only.

Briefly, the Th. Cl. was calculated by dividing the increment in the thyroidal ^{131}I uptake between 1 and $2\frac{1}{2}$ hr. by the plasma

radioactivity at the midpoint. The P.I.I. was measured by an isotope dilution technique following a tracer dose of ^{131}I as

$$P.I.I. = \frac{^{131}I \text{ plasma} \times I \text{ urine}}{^{131}I \text{ urine}},$$

where

^{131}I = the radioiodine concentration in the plasma or urine and

I urine = the chemical (stable) iodine concentration in the urine.

The A.I.U. was calculated as the product of the P.I.I. with the Th. Cl.

STATISTICS.

Standard deviation and standard error of the mean were calculated on a desk computer (Olivetti Instruments). Students 't' test (Bradford-Hill, 1967) was used to test significance of difference between values.

RADIOTHYROXINE STUDIES.

The peripheral metabolism of thyroid hormones in endemic goitre has failed to attract much attention in contrast to the general aspects of iodine metabolism. In almost every severe goitre endemic there are euthyroid individuals who have subnormal P.B.I. values. The possibility that alterations in the peripheral metabolism of thyroxine might be responsible for maintaining the euthyroid state in these subjects seemed possible. There follows an account of radiothyroxine studies in five euthyroid goitrous subjects with subnormal P.B.I. values.

Subjects and Methods.

Three male and two female patients with goitre from the Eburru settlement were studied. All were clinically euthyroid despite subnormal P.B.I. values. Serum protein values were normal. All had high thyroidal radio-iodine uptake values and low urinary iodine values. The purpose of the study was explained to them and they cooperated willingly. The studies were performed at the Kenyatta National Hospital, Nairobi. Each patient received 50 μc ^{125}I labelled thyroxine (T_4) by intravenous injection. Plasma samples were taken at 10 minutes after injection of T_4 and then daily for 10-12 days. Total radioactivity of the plasma of all samples was measured at the completion of the study in a well-type scintillation counter (Echo Electronics Ltd.). Potassium perchlorate (400 mg. q.d.s.) was given for 24 hours before and throughout the study to prevent the re-utilization by the active iodine deficient gland of iodine released from peripheral hormone degradation. The serum P.B.I. and total T_4 (TT_4) were measured in samples of serum taken on day six of the study, the midpoint. Total T_4

was measured using the "Tetrasorb 125" Kit (Abbot Laboratories, Chicago, Ill.) (Medical Faculty, Rotterdam, Netherlands). The calculations used were those of Sterling and Chodos (1965). Briefly, the $\frac{1}{2}$-life of T_4 was obtained graphically from the linear component of the disappearance curve extrapolated back to zero-time. The turnover rate (K) was computed from the $\frac{1}{2}$-life. The calculation for subject E. M. is shown in the appendix, pages 171 - 173.

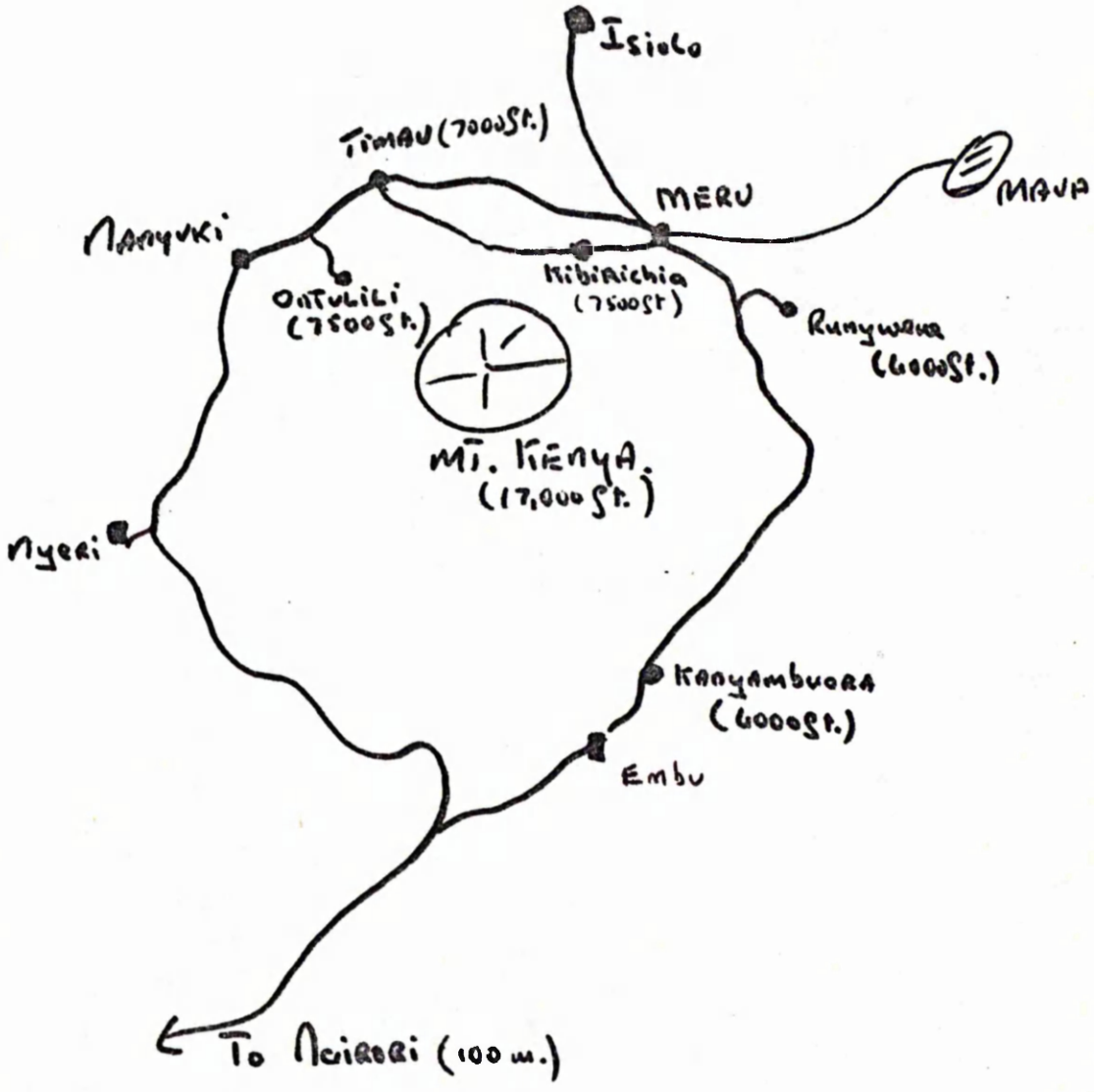

Isiolo
TIMAU (7000 Ft.)
MERU
MAUA
NANYUKI
OLTULILI (7500 Ft.)
KIBIRICHIA (7500 Ft)
RUNYWERA (6000 Ft.)
MT. KENYA (17,000 Ft.)
NYERI
KANYAMBUORA (6000 Ft.)
Embu
To NAIROBI (100 m.)

TABLE 5.

Prevalence of Goitre in 1103 Schoolchildren in Locations around Mount Kenya.

School	Number Examined	Goitre Grades 1	2	3	% of children with goitre
Kanyuamboro	270	20	3	0	8.6
Runywene	75	3	0	0	4.0
Kibirichia	396	126	28	0	39
Timau	256	64	7	0	28
Outulili	106	21	8	0	27

RESULTS.

School Surveys - Mount Kenya Area:

(figure 10. Table 5 and table on appendix page 168).

Embu District:

At a primary school, North East of Embu, at Kanyuambora, (altitude 4,000 feet above sea level) 270 primary schoolchildren aged 5-15 years were examined. The overall goitre rate was 8.6 per cent.

Meru District:

In a primary school ten miles south of Meru at Runyweni (4,000 feet) the overall goitre prevalence among 75 schoolchildren aged 5-12 years was 4 per cent.

At Kibirichia, on the Northern slopes of Mount Kenya, (7,000 feet) 396 children aged 5-15 years were examined. The overall goitre rate was almost 40 per cent in boys and girls.

In the North West corner of Mount Kenya at Timau (6,000 feet) 256 schoolchildren aged 5-15 years were examined; the overall goitre rate was 27 per cent; 23 per cent boys; 35 per cent girls. At Ontulili the goitre rate was similar (28 per cent) in 106 children aged 5-15 years.

AREA	OVERALL GOITRE RATE %	I-EXCRETION 24 HOURS (µg)	PBI (µg/100 ml.)	I^{131} THYROID UPTAKE AFTER 4 HOURS (%)	I^{131} THYROID UPTAKE AFTER 24 HOURS (%)
Eburru (Naivasha Area)	51·5 (n=699)	24·6 (s=18.3) (n=61)	4·0 (s=1.0) (n=44)	65·7 (s=17.7) (n=56)	80·0 (s=12.0) (n=55)
Roret (Kericho distr.)	50 (n=732)	20·6 (s=21.3) (n=56)	4·1 (s=0.9) (n=57)	58·4 (s=127) (n=51)	72·9 (s=14.9) (n=55)
Mutituni (Machakos distr.)	9·9 (n=494)	113·9 (s=56.8) (n=17)	5·5 (s=1.1) (n=17)	20·4 (s=6.7) (n=18)	39·6 (s=9.3) (n=16)

Table 6 - Summary of all results from three communities in Kenya.

Figure 1: Age and sex distribution of goitre rates found in two areas of Kenya

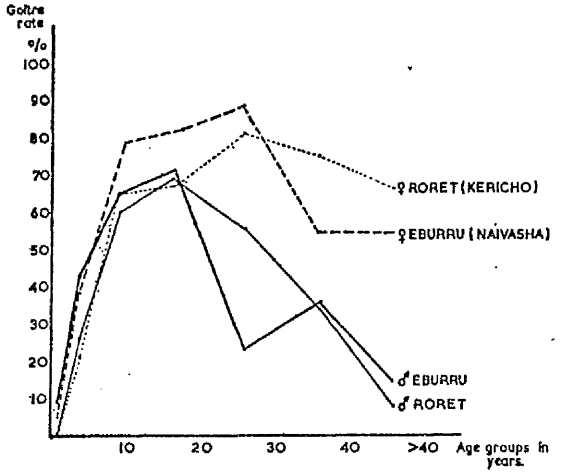


Table 7: Distribution of goitres according to age and sex among the total population of 3 rural areas in Kenya (June/July 1969)

AREA		EBURRU (NAIVASHA)									ROR	ET (KERICHO)									MUTITUNI (MACHAKOS)								
AGE GROUPS:		0-1	2-5	6-12	13-20	21-30	31-40	>40	Sub Total	%	0-1	2-5	6-12	13-20	21-30	31-40	>40	Sub Total	%	0-1	2-5	6-12	13-20	21-30	31-40	>40	Sub Total	%
MALES	0	30	42	30	8	19	20	41	190	58.5	40	56	41	16	7	9	27	2N 196	60	20	57	54	26	10	13	14	194	96
	1	3	23	28	7	IN 4	7	4	IN 76	23.5	—	17	IN 41	17	1	3	1	IN 80	24.5	—	2	2	1	2	1	—	8	4
	2	—	8	28	IN 12	2	4	3	IN 57	17.5	—	2	18	19	8	2	1	50	15	—	—	—	—	—	—	—	—	—
	3	—	—	—	1	—	—	—	1	0.5	—	—	1	1	—	—	—	2	0.5	—	—	—	—	—	—	—	—	—
	Sub Total	33	73	86	IN 28	IN 25	31	48	2N 324	100	40	75	IN 101	53	16	14	2N 29	3N 328	100	20	59	56	27	12	14	14	202	100
FEMALES	0	34	47	18	6	7	16	20	148	39.5	32	59	33	11	12	8	13	168	42	27	56	58	27	37	17	IN 29	IN 251	86
	1	2	21	24	2	20	IN 2	10	IN 81	21.5	—	16	39	14	16	9	13	107	26.5	—	—	2	7	IN 18	5	4	IN 36	12
	2	—	10	40	IN 23	2N 34	3N 17	3N 12	9N 136	36.5	—	—	IN 23	IN 37	4N 36	4N 14	2N 12	12N 122	30	—	—	—	1	1	1	2	5	2
	3	—	—	—	3	4	—	3N 3	3N 10	2.5	—	—	—	IN 4	IN 1	1	IN 1	3N 7	1.5	—	—	—	—	—	—	—	—	—
	Sub Total	36	78	82	IN 34	2N 65	4N 35	7N 45	13N 375	100	32	75	IN 95	2N 66	5N 65	4N 32	3N 39	15N 404	100	27	56	60	35	IN 56	23	IN 35	2N 292	
GRAND TOTAL		69	151	168	2N 62	3N 90	4N 66	7N 93	16N 699		72	150	2N 169	2N 119	5N 81	4N 46	5N 68	18N 732		47	115	116	62	IN 68	37	IN 49	2N 694	
GOITRE RATE %	M	9.1	42.5	55.0	71.5	24.0	35.0	14.6	41.3	51.5	0	25.3	60	70	56.2	35.7	6.9	40.3	50	0	3.4	3.6	3.7	16	7	0	4	9.9
	F	5.8	39.7	78.0	82.2	59.2	54.4	55.6	60.3		0	21.4	65.2	67.8	81.5	75.0	66.8	58.2		0	0	3.3	23	34	26	17	14	
(N= NODULAR GOITRE)		No of people absent: 176 (25%)									No of people absent: 256 (26%)									No of people absent: 250 (33.5%)								

RESULTS.

Community Surveys.

All results are summarised in Table 6.

Goitre

The distribution of goitre according to age and sex among the total population of three rural areas in Kenya is shown in Table 7. Overall, high goitre rates were found in Eburru (55 per cent) and in Roret (50 per cent). A low rate was found in Mutituni (9.9 per cent). In Eburru and Roret the total goitre rate in males was approximately 40 per cent and in females 60 per cent. In general larger goitres with nodules were found in females. No obvious cretins, spastics or deaf mutes were encountered and overall general nutrition was fairly good, although a few cases of overt malnutrition were encountered (Kwashiorkor). Endemic cretinism is therefore not present in these endemic goitre areas.

Age and Sex.

The age and sex distribution of goitre in Roret and Eburru are illustrated in figure 11 (repeat of figure 2). The male/female incidence rises very steeply and simultaneously until about the age of 20 years when the male incidence declines sharply.

Urinary Iodine.

The results are expressed as mean $\pm$ standard deviation (table 6).

In Eburru: The mean daily urinary iodine excretion was 24.6 $\pm$ 18.3 ug.

In Roret: 20.6 $\pm$ 21.3 ug.

In Mutituni: 113.9 $\pm$ 56.8 ug.

SUMMARY OF THE RADIO-IODINE UPTAKE, URINARY IODINE AND SERUM P.B.I. VALUES IN THREE COMMUNITIES IN KENYA.

GROUPS AND LOCATIONS		4 hour uptake (% dose)			24 hour uptake (% dose)			Serum P.B.I. (µg/100 ml.)			Urinary Iodine (µg./24 hrs.)		
		No.	Mean	s.d.	No.	Mean	s.d.	No.	Mean	s.d.	No.	Mean	s.d.
Roret													
men	with goitre	13	64,6	11,1	15	82,0	8,4	15	3,6	0,9	14	15,7	6,2
	without goitre	8	47,0	13,3	7	71,4	9,8	9	4,4	0,9	9	24,6	9,5
women	with goitre	25	50,6	20,3	27	69,6	11,4	27	4,3	1,0	26	16,7	7,6
	without goitre	4	55,8	23,2	4	76,0	19,2	3	4,0	0,3	4	18,1	9,0
Eburru													
men	with goitre	18	66,9	17,4	18	81,1	12,0	19	3,8	1,0	23	31,5	32,6
	without goitre	10	54,0	7,9	10	76,3	4,6	7	4,2	0,5	10	33,1	20,1
women	with goitre	21	72,0	13,7	20	85,0	8,8	15	3,8	1,1	21	15,8	5,8
	without goitre	5	64,6	31,0	5	69,0	16,5	2	4,7	0,8	6	29,7	15,7
Mutituni													
men	with goitre	4	15,0	3,4	4	27,3	5,1	4	5,8	1,4	3	148,4	73,5
	without goitre	5	21,2	5,8	4	39,3	6,9	5	5,1	1,0	5	128,8	70,8
women	with goitre	7	23,4	7,8	7	47,0	5,1	7	5,7	1,1	7	98,4	44,7
	without goitre	-	-	-	-	-	-	-	-	-	-	-	-

Protein Bound Iodine:

In Eburru the mean value was 4.0 ± 1 µg. per 100 ml.

In Roret 4.1 ± 0.9 µg. per 100 ml.

In Mutituni 5.5 ± 1.1 µg. per 100 ml.

Six subjects in Eburru and seven in Roret had values of P.B.I. less than 3.0 µg. per 100 ml. No patient with overt hypothyroidism was observed during the surveys. I personally re-examined all the Eburru subjects and found no clinical evidence of hypothyroidism.

In Eburru 13 pregnant subjects had a mean P.B.I. value of 5.0 ± 2.2 µg. per 100 ml.,

in Roret the mean P.B.I. value in 8 pregnant patients was 5.0 ± 1.5 µg. per 100 ml. These values are subnormal for pregnancy.

In Mutituni the mean value of 5 pregnant patients was 8.8 ± 1.4 µg. per 100 ml., which is within the expected range for pregnancy.

Radio-Iodine Uptake:

In Eburru the mean 4 hour uptake was 65.7 ± 17.7 per cent of the administered dose; at 24 hours 80 ± 12.0 per cent.

In Roret the 4 hour uptake was 58.4 ± 12.7 per cent and the 48 hour uptake 72.9 ± 14.9 per cent.

In Mutituni the 4 hour uptake was 20.4 ± 6.7 per cent and the 24 hour uptake 39.6 ± 9.3 per cent.

The results of the various investigations according to sex and goitre are shown in table 8. Inspection shows no clear difference between goitrous and nongoitrous in values of urinary iodine, serum P.B.I. or radio-iodine uptake.

ENDEMIC GOITRE IN MWEZI.

Results.

Goitre.

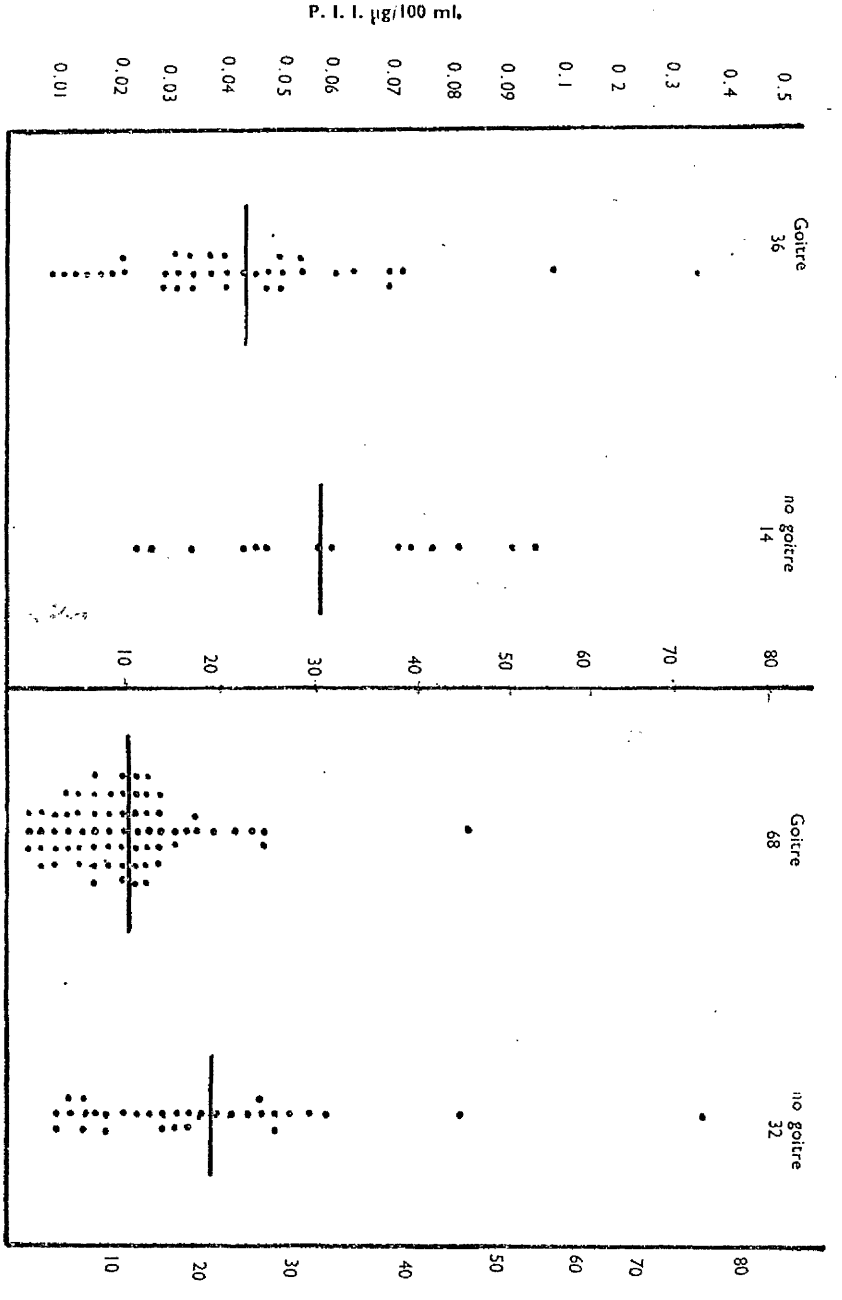
Table 9 shows the goitre rates in the schoolchildren. In the age group 5-11 years, goitre was present in 48 per cent of 200 immigrant children and 67 per cent of 65 native children. Significant thyroid enlargement was found in 66 per cent of 85 older(12-17 years) immigrant children and nearly all of 23 older native children. No difference in male/female goitre rate was recorded, although girls usually had larger (grade 2) goitres. Fifteen glands were nodular on palpation.

TABLE 9.

Goitre rates in Mwezi schoolchildren

TRIBE	Age (years)	Numbers Examined	Goitre Rate
Ruandan	5-11	200	48%
Ruandan	12-17	85	65%
Native	5-11	65	67%
Native	12-17	23	90%

Total goitre rate = 208/373 = 56%.



The plasma inorganic iodine and daily urinary iodine excretion values in Mwezi schoolchildren.

The individual daily iodine excretion in the urine and the plasma inorganic iodine values (P.I.I.) are shown in figure 12.

Urine Iodine.

The mean daily urinary iodine excretion was 14 ± 9 (S.D.) µg. The goitrous children had a mean value of 11.4 ± 7 µg. and the non-goitrous 19.5 ± 10 µg. - these values are significantly different ($p < 0.01$) but nearly all values are very low.

Plasma Inorganic Iodine.

The mean P.I.I. value was 0.047 ± 0.03 (S.D.) µg. per 100 ml. The mean P.I.I. value in the children with goitre was 0.042 ± 0.02 µg. per 100 ml. and in the nongoitrous children 0.057 µg. per 100 ml. These values are significantly different, ($P < 0.05$).

TABLE 10. Iodine Metabolism in Simple Goitre.

	Controls (18 cases)	Normal Th. Cl. (26 cases)	High Th. Cl. (37 cases)	High Th. Cl. Normal P.B.I. (30 cases)	High Th. Cl. Low P.B.I. (7 cases)	Total (63 cases)
Th. Upt. at $2\frac{1}{2}$ hrs. (%)	20.0 ± 1.6 (6.5 - 37.0)	23 ± 1.5 (12 - 36)	37 ± 2.0 (19 - 65)	35 ± 1.4 (19 - 48)	52 ± 2.0 (36 - 65)	32 ± 3 (12 - 65)
Th. Cl. (ml./min.)	26 ± 4.7 (5.7 - 73)	24 ± 1.7 (8.5 - 37)	114 ± 13 (40 - 400)	87 ± 6.1 (40 - 147)	227 ± 12 (92 - 400)	76 ± 18 (8.5 - 400)
P.I.I. (ug./100 ml.)	0.18 ± 0.03 (0.02 - 0.52)	0.14 ± 0.01 (0.04 - 0.29)	0.07 ± 0.015 (0.01 - 0.15)	0.07 ± 0.01 (0.01 - 0.15)	0.07 ± 0.01 (0.01 - 0.15)	0.1 ± 0.02 (0.01 - 0.2)
A.I.U. (ug./hr.)	1.6 ± 0.2 (0.5 - 5.2)	1.97 ± 0.19 (0.7 - 4.4)	4.6 ± 0.6 (0.7 - 17.3)	3.5 ± 0.3 (0.7 - 6.9)	6.8 ± 2 (1.3 - 17.3)	3.2 ± 0.3 (0.7 - 17.3)
P.B.I. (ug./100 ml.)	5.5 ± 0.2 (3.5 - 8.5)	5.2 ± 0.18 (4.1 - 6.8)	3.6 ± 0.3 (1.2 - 7.4)	5.0 ± 0.19 (3.7 - 7.4)	2.5 ± 0.1 (1.2 - 2.9)	4.5 ± 0.3 (1.2 - 7.4)
P.B.I./A.I.U.	4.9 ± 0.6	3.4 ± 0.4	1.65 ± 0.2	2.2 ± 0.4	0.6 ± 0.18	2.2 ± 0.2

QUANTITATIVE STUDIES OF IODINE METABOLISM

Results.

The results of the six parameters studied in the control and goitrous patients are shown in table 10 and the individual values on page 174 in appendix. The results are expressed as the mean and the standard error (S.E.) of the mean with the numbers and the observed range in brackets. The standard error is not ideal, as individual biological values may not always follow a normal distribution (Wootton et al. 1951). However, other workers have expressed their data in this way and I have chosen this method for comparison with their data. (Alexander et al. 1962).

Controls.

Thyroid Radio-Iodine Uptake.

The mean values and range of the $2\frac{1}{2}$ hr. uptake (20 ± 1.6 per cent) are similar to those reported by others (Alexander et al. 1962 - 21.6 ± 1.4 per cent).

Thyroid Clearance of Radio-Iodine. (26 ± 4.7 ml. per min.)

The mean values are similar to those found by other workers. Alexander et al. (1962) established the normal range by inspection as 8 - 40.0 ml. per min. This contained the large majority of normal cases and gave good separation of normal persons from those with hypo- or hyperthyroidism. My control group consisted of patients without goitre from the Central Province of Kenya and values ranged from 6 - 73 ml. per min. Eight of these patients were iodine deficient at the time of study on the basis of a low P.I.I. value (< 0.08 µg. per 100 ml.) and three had a high thyroidal clearance value. This would be expected in a sample population which is likely to contain some iodine deficient subjects with no goitre. Thus, the range of values of thyroid clearance is broader than the observed range quoted by Alexander et al. (1962).

Plasma Inorganic Iodine (P.I.I.) 0.18 ± 0.03 µg. per 100 ml.)

The mean values in the control patients are similar to those reported by Perry and Hughes (1952) (0.17 ± 0.009) and Alexander et al. (1962) (0.19 ± 0.02).

Absolute Iodine Uptake. (1.6 ± 0.2 µg. per Hr.)

The mean value is similar to the value of 2.3 ± 0.2 found by Alexander et al. (1962), 2.3 ± 0.3 Zingg and Perry (1952) and 2.8 ± 0.6 (Reilly and Scott et al.).

Protein Bound Iodine. (5.5 ± 0.2 per 100 ml.)

The mean value is also well within the normal range of others (Alexander et al. 1962).

PATIENTS

Total (63)

Thyroid uptake at 2½ hrs: The mean value of the 63 patients was 32 ± 3 per cent. This value is significantly higher than the value of the control group ($P < 0.01$).

Thyroid clearance: The mean value was 76 ± 18 ml. per min. This value is significantly higher than the value of the control group. ($P < 0.001$).

Plasma Inorganic Iodine: The mean value was 0.1 ± 0.02 µg. per 100 ml. This value is significantly lower than the value of the control group. ($P < 0.01$).

Absolute Iodine Uptake: The mean value was 3.2 ± 0.3 µg. per hr. This value is significantly higher than the value of the control group. ($P < 0.01$).

Protein Bound Iodine: The mean value was 4.5 ± 0.3 µg. per 100 ml. This value is significantly lower than the value of the control group. ($P < 0.02$).

Renal Clearance of Iodine: The mean value in 15 patients was 31.2 ± 3.0 ml. per min. which is within the range found by Alexander et al. (1962).

Normal Clearance Group. (26)

Twenty six patients had uptake and clearance values within the normal range quoted by Alexander et al. (1962). (< 40 ml. per min. clearance). The mean P.I.I. value was 0.14 ± 0.01 µg. per 100 ml. This value is not significantly lower than the value of the control group. The A.I.U. and P.B.I. values were well within the normal range, and were not significantly different from the values of the control group.

High Clearance Group.(37)

Thirty seven patients had high uptake and clearance values. The mean P.I.I. value in this group was 0.07 ± 0.01 µg. per 100 ml. This value is significantly lower than the value of the control group. ($P < 0.001$). The mean A.I.U. value was 4.6 ± 0.6 µg. per hour. This value is significantly higher than the value of the control group. ($P < 0.01$). The mean P.B.I. value was 3.6 ± 0.3 µg. per 100 ml. This value is significantly lower than the value of the control group. ($P < 0.01$).

The high clearance group was subdivided into

a) Thirty patients with a normal P.B.I. value

b) Seven patients with a low P.B.I. value.

In subgroup (a) the mean P.I.I. value was 0.07 ± 0.01 µg. per 100 ml. The mean A.I.U. value was 3.5 ± 0.3 µg. per hr. This value is significantly

TABLE 11.

Goitrous patients with low P.B.I. and high clearance values.

Clinic No.	Sex	Age	Th. Upt. $2\frac{1}{2}$ hrs. (% dose)	Th. Cl. (ml/min.)	P.I.I. (ug/100 ml)	A.I.U. (ug/hr)	P.B.I. (ug/100 ml)	P.B.I./A.I.U.
543	F	16	36	92	0.14	8.8	2.4	0.3
432	M	23	49	144	0.1	8.3	2.0	0.2
457	F	30	65	148	0.01	1.3	2.4	1.8
538	M	18	39	400	0.04	7.4	1.2	.16
366	F	18	55	260	0.05	7.02	2.8	0.4
363	F	30	60	258	0.04	5.9	2.9	0.5
522	F	15	60	289	0.1	17.3	2.7	0.15

higher than the value of the control group ($P < 0.01$). The mean P.B.I. value was 5.0 ± 0.19 ug. per 100 ml.

In subgroup (b) the thyroidal uptake and clearance values are very high (table 11). The mean P.I.I. value was 0.07 ± 0.01 ug. per 100 ml. The mean A.I.U. value was 6.8 ± 2 ug. per hour. This value is at the upper limit of the normal range. The mean P.B.I. value was 2.5 ± 0.1 ug. per 100 ml.

Of the seven patients four were young (14-18 years of age) with diffuse goitres, two of which had a bruit. Patient No. 538, table 11, developed tracheal compression and thyroidectomy was performed. The gland was diffusely enlarged and histologically uniform parenchymatous hyperplasia was found. (figure 16 page 69).

Radio-Thyroxine Studies.

The individual results are presented in Table 12.

Protein Bound Iodine:

Values ranged from 1.5 - 3.0 ug. per 100 ml. with a mean value of 2.1 ug. per 100 ml.

Total Thyroxine (TT_4):

Values ranged from 2.0 - 5.0 ug. per 100 ml. The normal range of TT_4 in the laboratory in Amsterdam where the estimations were performed is 6.8 - 14.4 ug. per 100 ml.

Kinetic Studies:

There are no "normal" data for Africans. In an extensive review of the available literature, Rall et al. (1964) concluded that in normal Caucasians the average $T\frac{1}{2}$ was 6.9 days, extrathyroidal pool 516 ug. iodine, amount of T4 degraded daily 51.6 ug. iodine.

Half Life of T_4 ($T\frac{1}{2}$):

The values ranged from 2.9 - 8.1 days. Two subjects had normal values, and three values were within the range found in hyperthyroidism. (Subjects N.W., E.N., and M.W.).

TABLE 12.

Radiothyroxine turnover data. (Figures in parenthesis from Rall et al. 1964)
(Values adjusted to 70 kg. body weight)

Patient	Sex and age (yrs)	$PB^{127}I$ µg/100 ml.	TT_4 (µg/100 ml)	$T_{\frac{1}{2}}$ (days)	K (%/day)	Extrathyroidal Thyroxine (ETT)		Degradation rate (D)	
						(µgI)	(μgT_4)	(µgI/day)	(μgT_4/day)
M.W.	M, 19	1.5	2.9	2.9	23	180	270	43	65
E.N.	M, 20	2.6	4.3	4.3	16	328	547	52	87
N.W.	F, 25	1.4	2.0	4.7	15	150	205	22	31
G.N.	M, 50	3.0	5.0	7.8	9.0	430	590	38	50
W.M.	F, 60	2.0	4.0	8.1	8.6	300	410	25	35
Mean		2.1	3.6	5.7	14.2	278	404	36	54
Rall et al. (1964)		5.5		6.9	10.0	516		51.6	

Turnover rate (K): Values ranged from 8.6 per cent to 23 per cent. Three subjects (M.W., E.N., and M.W. had high values (> 10 per cent).

Extrathyroidal thyroxine pool (as µg. Iodine).

Values ranged from 150 - 430 µg. for iodine and 205 - 590 µg. for thyroxine. In two subjects, G.N. and W.M., values were at the lower limit of the normal range. The remainder were subnormal.

Degradation Rate: Values ranged from 22 - 52 µg. daily for iodine and 31 - 87 µg. daily for thyroxine. One subject, E.N., had a degradation rate which was normal; the value for M.W. is at the lower limit of the normal range, while the remainder are all clearly subnormal.

CLINICAL STUDIES.

Between August 1968 and April 1970, 560 patients were examined at the thyroid clinic, Kenyatta National Hospital, Nairobi. There were 550 Kenyans of African origin and 10 of Asian origin. They represent the majority of patients who attended or were admitted to the Kenyatta National Hospital for treatment and for investigation of overt or suspected thyroid disease, during this period. The clinic was established with a view to rationalising the treatment of the very large numbers of patients with non-toxic goitre who presented for treatment. Increasing numbers of patients were being subjected to surgery of the thyroid gland and it was felt by physicians and surgeons alike that more rigorous selection of patients for surgery was desirable. In time, all varieties of disease of the thyroid gland presented at the clinic and an estimate of the relative frequency of these various disorders could be made. These aspects are discussed further in the sections on thyrotoxicosis and carcinoma of the thyroid.

The Distribution of the various disorders of the thyroid are shown in table I (repeated below).

Thyroid disorders in 550 Kenyan African Patients seen over 18 months at the Kenyatta National Hospital, Nairobi.

Diffuse	Multinodular	Single Nodule	Thyrotoxicosis	Cancer	Miscellaneous
180	255	58	31	18	8

This section is confined to non-toxic goitre.

There were 493 African patients in whom the diagnosis of simple nontoxic goitre was made. Two hundred and fifty had obvious multinodular glands some of which were huge (figure 13 a and b).

Fig. 13a and b. - Huge goitre

Fig. 13b. - Thyroid specimen weighing 1.5 kg. from patient (a) above.

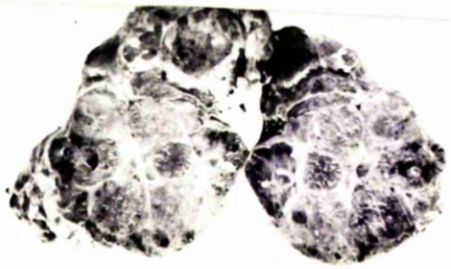


Fig. 14 a. - The single thyroid nodule Clinical.

Fig. 14b. - Radiological.

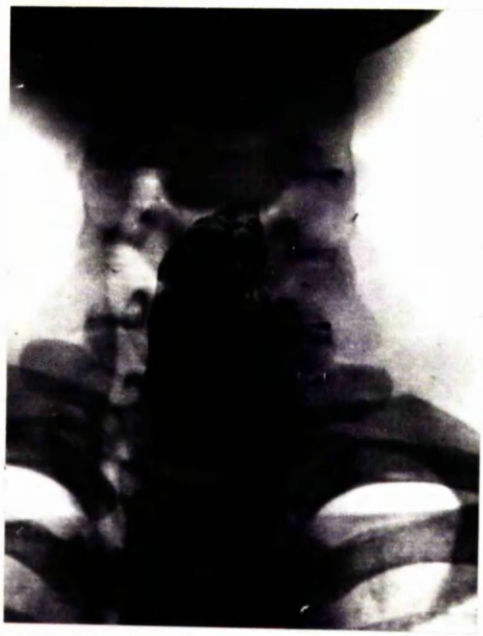
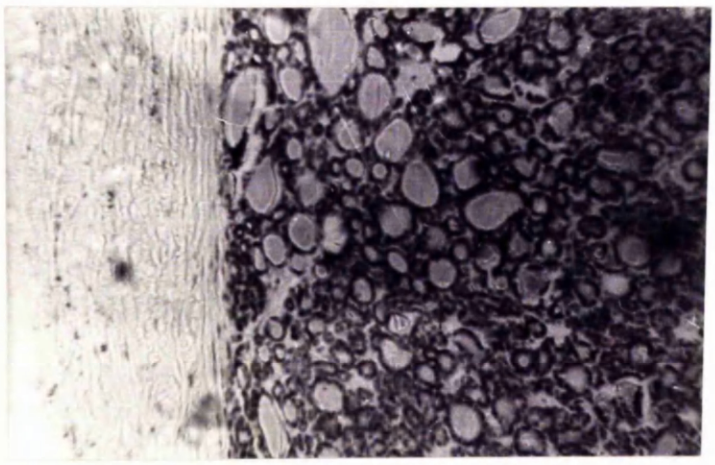


Fig. 14c. - Histological.



Fifty eight had a single nodule on palpation (figure 14a,b,c. The remainder (180) appeared on palpation to be diffuse.

Thirty one patients had hyperthyroidism and in 18 patients the diagnosis of thyroid carcinoma was established. The miscellaneous group included patients with thyroglossal cysts (2), subacute thyroiditis (2), dyshormonogenesis (3), post-operative hypothyroidism (1). No case of spontaneous myxoedema nor Hashimoto's thyroiditis were encountered in any indigenous African patient; occult thyroiditis was excluded in over 300 African patients who had negative tests for thyroid antibodies. Only ten Asian patients were reviewed during this period yet Hashimoto's thyroiditis was diagnosed in one patient. The remainder included thyrotoxicosis (2), papillary carcinoma (1), simple goitre (6).

Age and Sex Distribution of the African patients is shown in figure 15. The large majority were females aged 25-45 years, and members of the Kikuyu tribe from the Central Province of Kenya.

Geographical distribution is shown in table 13. Twenty five per cent of the patients lived in Nairobi City at the time of review. For many this was a recent move (within 3-5 years), from the rural areas of the Central Province. Of the remainder the majority were resident in the Central Province at the time of review. A small minority travelled very long distances from the highland endemic goitre areas of the Rift Valley and Western Provinces (up to 200 miles). No patient travelled the equivalent distance from the Coast Province and only two patients lived in the Eastern Province where endemic goitre has not been found.

Figure 15

Age and Sex Distribution.

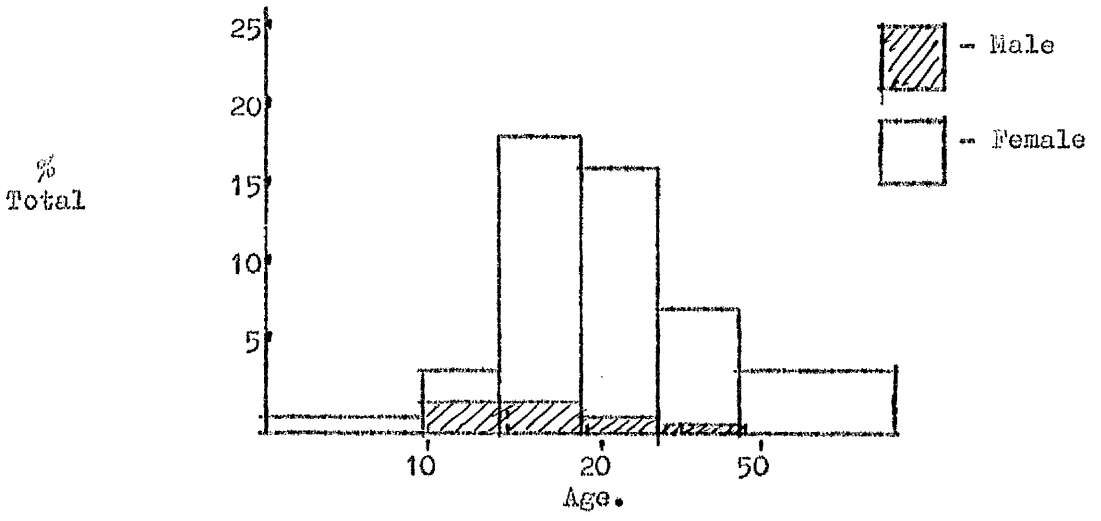


Table 13

Geographical Distribution.

Location	Nos.	%
Nairobi City	176	34%
Central Province	260	51.6%
Western and Rift Valley Province	70	14.3%
Eastern Province	2	.1%
Coast Province	0	0%
TOTAL	508	100%.

TREATMENT.

Medical.

1. In almost 50 per cent of cases no specific treatment was given. Patients with long-standing multinodular glands in whom there was no evidence of pressure symptoms or suspicion of malignancy were simply reassured. Operation was not performed solely for cosmetic reasons.

2. Thyroxine. One hundred and twenty patients with diffuse glands on palpation and forty with multinodular glands were given thyroxine sodium 0.3 mg. daily. The majority tolerated this dose well, but in a few the dose was reduced to 0.2 mg. per day because of the development of mild hyperthyroidism. The size of the thyroid gland was assessed by palpation, before and at intervals during treatment and recorded as

a) unchanged

b) smaller

c) normal.

To be classified as "smaller" an estimated reduction of 50 per cent in the size of the gland was required.

After at least six months treatment with thyroxine the following results were recorded.

Commenced treatment: 120 patients with diffuse goitre

Lost to follow-up: 20 patients

Smaller: 55 patients

Normal: 25 patients. Unchanged: 20 patients.

After two to three months of treatment with thyroxine, the tense, diffuse gland had in many cases shrunk to a smaller, slack gland in which small nodules were palpable.

These glands which were multinodular at the outset of treatment, showed a less convincing response to treatment with thyroxine. Forty patients with multinodular goitre were given thyroxine sodium. Of the original group of 40 patients ten were lost to follow-up. Out of the 30 who remained, 10 reduced in size, but none returned to normal proportions. These observations indicate that the more widespread use of thyroxine should be encouraged, particularly in those younger patients with diffuse goitre.

The mean thyroid clearance value of 18 patients with clinically diffuse goitre was 120 ml. per min. (table 14) and in 16 patients with clinically multinodular, usually long established glands, 35 ml. per min.

The response to treatment with thyroxine was judged to be good in 14 patients who had high thyroidal clearance. (Mean value 131 ml. per min.). In 10 patients in whom no change in goitre size was recorded the mean thyroidal clearance was lower - mean 38 ml. per min.

The histological appearances of the thyroid gland in seven patients showed multinodular colloid groitre with fibrosis. The mean thyroidal clearance was 21 ml. per min. In two patients with diffuse parenchymatous hyperplasia, the clearance values were 89 and 400 ml. per min.

Surgery.

Seventy nine patients were submitted to surgery (15 per cent of total).

Forty had multinodular glands producing pressure symptoms, usually tracheal compression. One of these patients developed acute stridor during labour and had the unusual combined surgery of a partial thyroidectomy followed immediately by a caesarean section. She and her infant made an uneventful recovery.

TABLE 14

Goitre	No.	Mean Th. Cl. (ml. per min.)
Diffuse goitre	(18)	120
Nodular goitre	(16)	35
Good response to T_4	(14)	131
No Response to T_4	(10)	38
Histological appearances: Colloid fibrosis	(7)	21
Histological appearances: Parenchymatous hyperplasia	(2)	89 and 400 ml./min.

TABLE 15

Histology of 79 thyroid glands.

Colloid goitre	53
Benign adenoma	20
Parenchymatous hyperplasia	2
Probable dyshormonogenesis	1
Carcinoma	3
TOTAL	79

Two patients, both males, with large diffuse glands causing pressure collapse of the trachea, required surgery.

Thirty seven patients with single thyroid nodules on clinical examination were submitted to surgery.

Pathology.

The pathological diagnosis of the 79 glands removed surgically is shown in table 15. One patient presenting with a multinodular goitre had an unsuspected follicular carcinoma. Two single nodules were malignant on histological scrutiny.

Single thyroid nodule.

This diagnosis was made only when the remainder of the thyroid gland could neither be seen nor felt, and the swelling was mobile with no evidence of pressure or displacement of neck structures.

I examined 58 patients in whom this diagnosis was made on clinical grounds. All were treated initially with 0.3 mg. of thyroxine sodium for three months. If the nodule had not diminished during this period and certainly if it had enlarged, surgery was performed.

Sex: There were 54 female and 4 male patients.

Duration: This varied from 1-3 years in the majority of patients.

Examination: In 23 cases the nodule seemed to be located in the right lobe, 14 in the left lobe and 21 in the isthmus of the thyroid gland.

Ten patients were lost to follow-up and 10 showed a significant reduction in the size of the nodule following treatment with thyroxine 0.3 mg. daily for three months. Surgery was performed in 37 cases of "clinically single" nodules. At surgery 19 were multinodular and 18 single, a diagnostic accuracy of only 50 per cent (table 16).

On histological examination of the clinically single nodules, 35 were benign and two were malignant, an incidence of carcinoma of 5.7 per cent (table 17). Assuming that the 10 nodules which shrunk on T_4 therapy were benign, the total incidence of malignancy in the group of 45 patients with a single nodule on clinical examination was therefore 4.4 per cent (2/47). One was a localised follicular carcinoma and the other a papillary carcinoma and each was a single nodule.

TABLE 16

Thyroid nodules, single by clinical, surgical and histological criteria.

	No.	%
Clinically	37	100
Surgically	18	49
Histologically	16	44

TABLE 17

Pathology of 37 clinically single nodules

Classification	Nodularity		Total
	Single	Multiple	
Benign	16	19	35
Malignant	2	0	2
Total	18	19	37

Overall Incidence of Carcinoma 5.5 per cent.

PATHOLOGY

The Medical Research Laboratory, Nairobi, provides the only histological services in Kenya and thus receives specimens from all Government and Mission Hospitals in Kenya. All specimens of thyroid tissue received at the laboratory from hospitals throughout Kenya in the periof 1964-69 inclusive were reviewed. Six hundred and forty five specimens were received. Adequate tissue was available for microscopic re-examination together with clinical details in 598 cases.

Distribution of Disease. TABLE 18

Diffuse Hyperplasia	Colloid Goitre	Adenoma	Carcinoma	Thyrotoxic	Miscellaneous
10	351	125	66	35	6

Eighty three per cent of thyroidectomies were for non-toxic goitre or benign adenoma; 11 per cent for carcinoma and 6 per cent for hyperthyroidism. The "miscellaneous" group included one Hashimoto's thyroiditis, two subacute thyroiditis (De Quervain's), two probable dyshormonogenetic goitres, one Riedel's thyroiditis.

All sections were inspected for the pr sence of round cell infiltration (lymphocytes and plasma cells) with almost completely negative results in the colloid goitre and adenomatous group. Some foci were detected in sections of papillary carcinoma and toxic goitre. This aspect will be discussed in more detail in the secti n on toxic goitre. The femmle/male ratio was 6/1.

Geographical Distribution.

The majority (60 per cent) of patients lived in the Central Province of Kenya: 20 per cent in the Rift Valley Province and 12 per cent in Nyanza and Western Provinces: four per cent in the Eastern and Coastal Provinces.

Histology.

Ten specimens consisted almost entirely of diffuse parenchymatous hyperplasia in all sections studied with a minimum of colloid material (figure 16). Macrofollicular colloid goitre

Fig. 16. - Diffuse parenchymatous hyperplasia. (H & E x 250)

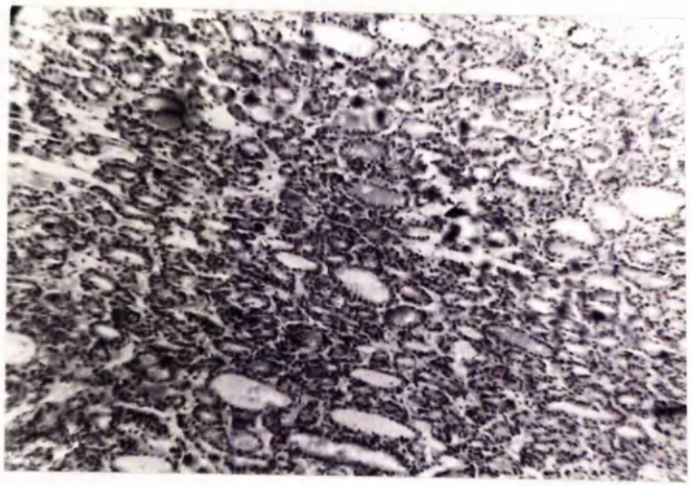


Fig. 17.- Macrofollicular or colloid goitre. (H & E x 250)

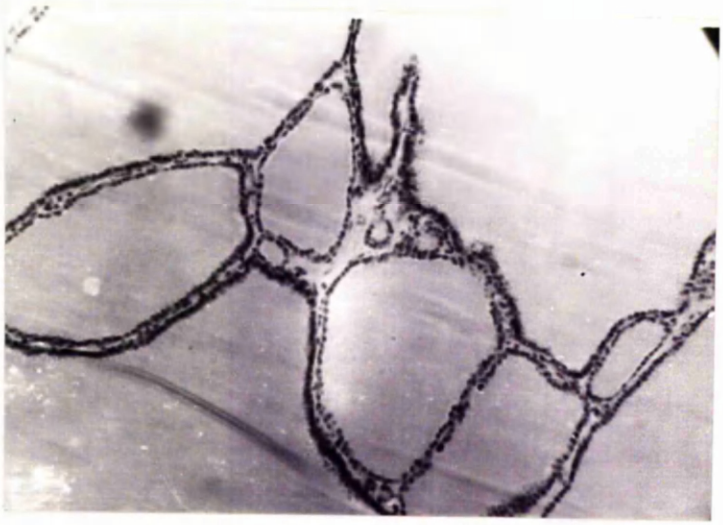
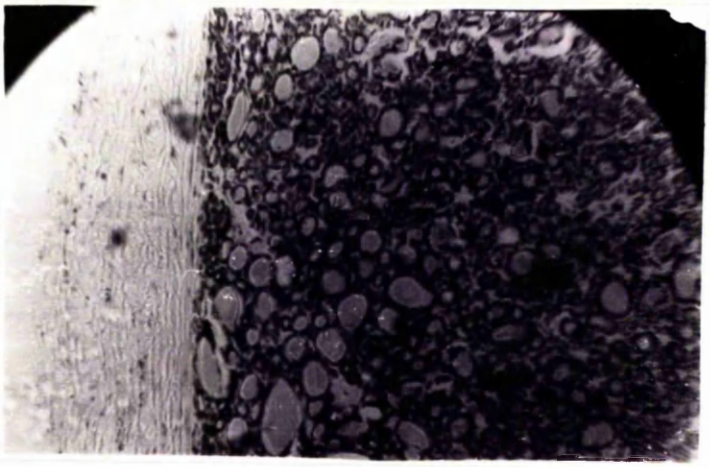


Fig. 18. - Microfollicular adenoma. (H & E x 250).



(figure 17) was a feature of most glands examined whether diffuse or nodular. Scarring, fibrosis, cyst formation were constant features of the older longstanding case. However, in approximately 30 per cent of cases areas of parenchymatous hyperplasia were found side by side with macrofollicular colloid areas. The parenchymatous areas when encapsulated were considered to be examples of nodular parenchymatous hyperplasia and not true adenomata, although on occasion I found the distinction impossible.

Neoplastic adenomata (benign)figure 18, were distinctly demarcated, encapsulated lesions usually microfollicular or "foetal" in type. Hurthle cell areas were observedbbut only three adenomata seemed to be entirely of this variety.

Recurrent goitre.

Thyroidectomy was performed on two or more occasions in 12 patients. Carcinoma was found at the second operation in four patients:- two papillary and one follicular carcinoma appearing within two years of the initial operation and one anaplastic carcinoma after 20 years interval. Six patients underwent repeated surgery (3-4) operations for recurrent simple goitre.

Single Nodule.

There were 105 surgical thyroid specimens in which the accompanying clinical diagnosis indicated the possibility of a single lesion of the thyroid gland. The 105 included the 37 cases of my own, already described. Thus there were 68 thyroid specimens "possible single nodules", from a variety of sources other than the

thyroid clinic. An analysis of these is shown in table 19. At surgery only 21 proved to be truly single (31 per cent accuracy), and of these four were malignant and 17 benign nodules on subsequent histological examination. (Table 20). In the multinodular group 1 was malignant and 46 benign. Thus, of the original 68 nodules presumed solitary five were malignant, an incidence of 7.8 per cent. In my personal series of 37 cases going to surgery as a clinically single nodule there were two cases of carcinoma, an incidence of 5.5 per cent. Therefore in the surgical series as a whole (105 cases) there were seven cases of thyroidal malignancy presenting as a single nodule, an incidence of 6.6 per cent (7/105).

TABLE 19

Thyroid Nodules, single by Clinical, Surgical and Histological criteria

	No.	%
Clinically	68	100
Surgically	21	31
Histologically	17	25

TABLE 20

Pathology of 68 clinically single nodules.

Classification	Nodularity		Total
	Single	Multiple	
Benign	17	46	63
Malignant	4	1	5
Total	21	47	68

Overall incidence of carcinoma 7.8 per cent.

DISCUSSION.

DISCUSSION.

It has long been recognised that endemic goitre and environmental iodine deficiency are found especially (but not exclusively) in areas at high altitude distant from the sea. From a geographical standpoint the highland plateau of Kenya, 300 - 500 miles from the sea at 3,000 - 9,000 feet above sea level, is a region where the presence of endemic goitre might be anticipated. Environmental iodine deficiency exists in terrains subjected to erosion by flood and past glaciation or volcanic activity. (Goldschmidt, 1954. Chilean Iodine Educational Bureau, 1956). These geological conditions are found on the highland plateau of Kenya, which is composed largely of a broad belt of alkaline volcanic rocks extending from Lake Magadi in the south to Lake Rudolf in the north, following the course of the Rift Valley. Extensive lava flows occurred to the east and west of the Rift Valley. On the fringes of the main volcanic belts lie the three isolated mountains of East Africa, Elgon, Kenya and Kilimanjaro, all major central volcanoes generated during the development of the Rift Valley (figure 1 b). The general elevation of the plateau is 5,000 - 8,000 feet above sea level with extremes of 3,000 - 9,000 feet in the inhabited areas. The terrain is generally hilly, with erosion prominent on many hill tops. It has been estimated that about 70 per cent of the land lies on slopes of 35^{0} or more, especially in the Central Province (Bohdal et al. 1968). The rural peoples normally live in scattered homesteads, on the tops or slopes of hills, surrounded by their farms. (figure 19).

As already mentioned in the introduction, the recognition of endemic goitre as a significant public health problem in Kenya is

Fig. 19. - Kikuyu farms.

a recent event. Greenwald (1949) in his comprehensive account of goitre in Africa makes no mention of endemic goitre in Kenya, and Kenya is not mentioned in the W.H.O. monograph (1960) on endemic goitre. Nevertheless in 1926, Allen recognised that "goitre occurs in the Kikuyu tribe" and much later, Miller (1964), describing the general pattern of surgical diseases in Nairobi declared "the largest goitres come from the high country around Kericho and Kapsabet, but Kiambu may also be an endemic area". In many countries endemic goitre is known to exist simply because the prevalence of visible goitre is obvious to even the casual observer. Sometimes when other regions of these countries have been considered goitre free, careful surveys have revealed previously unsuspected high goitre frequency. This has proved to be true in all Latin American countries where nationwide surveys have been undertaken (Perez et al. 1960). It seems likely, therefore, that certain circumscribed areas in Kenya were tacitly recognised as "goitre areas" but the full extent of the problem was not appreciated until formal surveys had been undertaken and the results published.

In Latin America, Euruguy in particular, the goitre rate increases from the sea-board to the Andean Corderilla (Kevany 1969) and in the Huon peninsula of Papua and New Guinea, a direct correlation between visible goitre rate and altitude has been demonstrated (Buttfield and Hetzel 1970). In Kenya a similar relationship between goitre and altitude is apparent, both on a regional and local basis. The cumulative evidence of the goitre surveys, the geographical distribution of patients attending the thyroid clinic, the sources of pathological thyroid tissue and the thyroidectomy rates in the various hospitals of Kenya (Table 21) indicate that in Kenya endemic goitre is to be found in locations at

TABLE 21.

Kenya Hospital Thyroid Operation Records (1967)
Data from Neville and Kungu (1969)

	Total	% of Total Operations
NAIROBI (7086)	77	1.1%
NAKURU (3500)	60	1.7%
KISUMU (3780)	12	0.3%
MACHAKOS (1661)	11	0.7%
NYERI (3000)	36	1.2%
MOMBASA (2926)	11	0.4%
MERU (CHOGORIA) (2250)	3	0.1%
TOTAL	210	

altitudes in excess of 5,000 feet in the highlands of the Central Rift Valley and Western Provinces. (Neville and Kungu 1969). No evidence has been obtained of the presence of endemic goitre in the Coast, Western or Nyanza Provinces, where the altitude is below 5,000 feet. There are striking variations in goitre incidence. In Eburru at 9,000 feet the goitre rate in schoolchildren was 83 per cent: in nearby Nakuru, at 5,500 feet, the goitre rate was 30 per cent according to the W.H.O. survey (Bohdal et al. 1968). Children living around 4,000 feet near Meru (Runywene) had a 4 per cent goitre incidence, and 10 miles "up the road" at Kibirichia (7,000 feet) the goitre rate was 40 per cent. Sufficient community surveys have not been performed to give the complete picture of the extent and severity of endemic goitre in Kenya. It would not be safe to assume that all communities living at 7,000-8,000 feet have a goitre incidence comparable to Roret or Eburru (50 per cent). In the Central Province, goitre rates in schoolchildren living at this altitude were around 30-40 per cent, much lower than the 60-80 per cent incidence in the children of the Rift Valley and Central Provinces, living at a similar altitude. The average community goitre rate in the Central Province is probably around 20 per cent. Nevertheless, a considerable proportion of the population of Kenya (possibly 50 per cent) live between 5,000 and 9,000 feet above sea level. The available evidence indicates that the overall incidence of simple goitre and the degree of iodine deficiency are sufficient to fully justify the prophylactic iodised salt programme already introduced to Kenya.

In Eburru the goitre rate in children at school was 83 per cent and the community rate was 51 per cent. While this incidence is undoubtedly high (probably the highest in Kenya) there are regions elsewhere in tropical Africa where much higher goitre

rates have been recorded and where endemic cretinism occurs. Two well known examples in neighbouring Central Africa are the Uele endemic and the Idjwi Island endemic in Zaire. (Bastenie et al. 1962, Delange et al. 1968). Endemic cretinism seems to occur only in very poor undernourished socially backward communities, almost always universally afflicted by goitre. I am fairly certain that the combination of malnutrition and a very high goitre rate does not exist in Kenya, and hence endemic cretinism is not to be found. Nevertheless despite the absence of endemic cretinism the degree of handicap imposed by simple goitre alone although hard to define cannot be negligable. Endemic cretinism probably represents the "tip of the iceberg", but data is scanty concerning the more subtle health consequences of endemic goitre. Goitrous children have a poorer school performance than non-goitrous children (Matovinovic, 1958). Iodine supplementation appears to have had a beneficial effect on the intellectual capacity of young Andean schoolchildren (Hodge 1968). In a recent study from the Himalayan endemic goitre area, (Kochupillai et al. 1973), raised serum T.S.H. levels were found in almost all patients studied. None of the patients had clinical evidence of hypothyroidism. Some, however, had T.S.H. levels in the range found in patients with clinical hypothyroidism due to auto-immune thyroiditis. The authors concluded that raised T.S.H. levels in endemic goitre indicate a state of "subclinical hypothyroidism".

In Mutituni subjects, the goitre rate was 9 per cent and the mean daily iodine excretion was 114 ug. This value of urinary iodine indicates an adequate dietary iodine intake and would be considered normal almost anywhere in the world. In Europe, in non-endemic areas, variable values have been found:

Finland, 47 ug. per day (Lamberg et al. 1962)

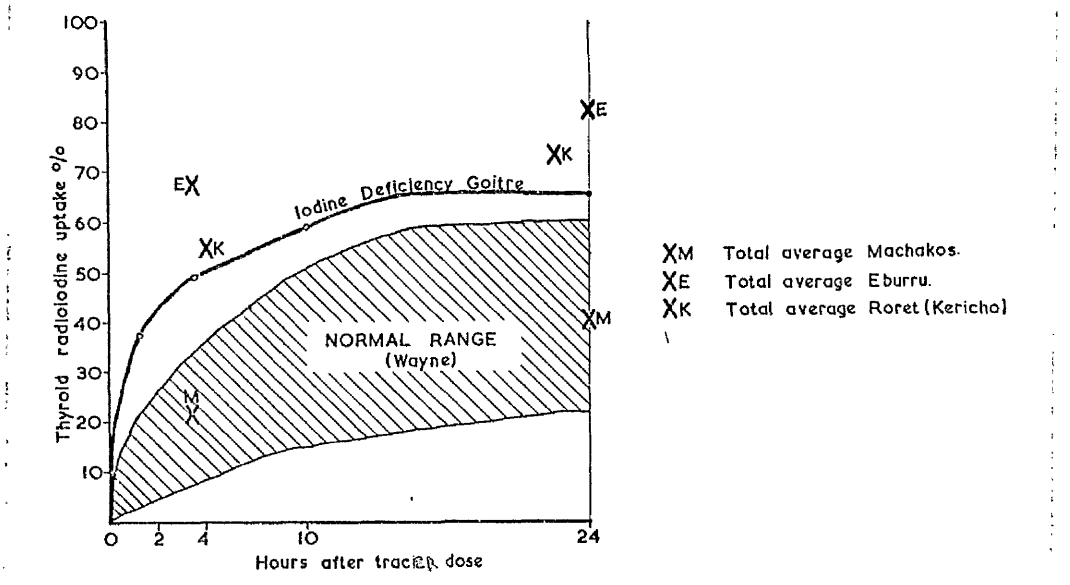
Holland 182 ug. per day (Terpstra and Querido (1959)

Glasgow, Scotland, 44 - 171 µg. per day (Wayne et al. 1964). In the U.S.A. where the use of iodised salt is widespread, generally higher values are found: 72 - 343 µg. per day (Curtis et al. 1937). Riggs (1952) has calculated the mean overall urinary iodine excretion in non-endemic areas to be approximately 150 µg. per day. Stanbury et al. (1954) considered 40 µg. per day to be the lower limit of the normal range, values lower than this being associated with a rise in thyroidal uptake of radio-iodine.

In a pioneer study in Switzerland, Von Fellenberg (1926) found daily urinary iodine excretion values of 17 µg. and 19 µg. in two endemic areas but in an area free of goitre the mean daily excretion was 112 µg. These values are very similar to those found in the community studies in Kenya, viz., Eburru 24 µg. per day, Roret 20 µg. per day, Mutituni 114 µg. per day. In severe goitre areas urinary iodine values are usually below 25 µg. per day and values below 10 µg. per day are commonplace. For example, in the hyperendemic area in the Uele the mean value for urinary iodine was 18 µg. per day (de Visscher et al. 1961) and in New Guinea 12 µg. per day (Buttfield et al. 1966).

In Mutituni subjects, radio-iodine uptake values were within the generally accepted normal range. Much higher values were found in Eburru and Roret subjects. Thyroidal avidity for iodine in iodine deficiency states is reflected in the higher than normal uptake values of radio-iodine usually found in subjects living in endemic iodine deficient areas. Notable studies include those in Argentina, Stanbury et al. (1954): Finland, Lamberg et al. (1962): Venezuela, Roche et al. (1957): Uele, De Visscher et al. (1961): Idjwi Island, Delange et al. (1968): New Guinea, Choufoer et al. (1963): Greece, Malamos et al. (1966): Himalayas, Ramalingaswami et al. (1961).

Fig. 20. Mean Radio-iodine uptake values for Eburru, Roret and Mutituni.



As predicted, the serum thyroid stimulating hormone (T.S.H.) level is raised in endemic goitre in man. (Buttfield et al. 1966: Adams et al. 1968: Delange et al. 1971: Kochupillai et al. 1973). Correction of the iodine deficiency in endemic goitre subjects restores T.S.H. levels to normal and the raised radio-iodine uptake and goitre prevalence fall.. (Buttfield et al. 1966). Similar observations have been made in experimental goitre in animals (Studer and Greer 1968). Thus, the classical hypothesis that the adaptation to iodine deficiency is accomplished by an increased secretion of T.S.H. has now been amply confirmed. The hyper-stimulation is responsible for increased thyroidal avidity for iodine, as a result of which the gland accumulates a normal amount of stable iodide despite dietary iodine deficiency (Wayne et al. 1964: Degrossi et al. 1969: Malamos et al. 1966). This phenomenon is reflected in the increased accummulation of radio-iodine so characteristic of endemic goitre, referred to above and observed in Kenya. (figure 19).

In Mutituni subjects the mean serum P.B.I. values were normal. Lower P.B.I. values were recorded in subjects in the endemic areas. Similar observations have been recorded in most severe goitre endemics, particularly Uele (de Visscher et al. 1961), West New Guinea (Choufoer et al. 1963), East New Guinea (Buttfield et al. 1966). In all of these regions, including Eburru and Roret in Kenya, there were goitrous individuals with subnormal serum P.B.I. levels who by all conventional clinical criteria were euthyroid. An attempt was made to gain additional insight into this intriguing problem by studying the peripheral metabolism of thyroxine (T_4) in five Eburru subjects who were clinically euthyroid despite a subnormal serum P.B.I. value. All subjects had low or very low extrathyroidal pools of thyroxine (T_4). In two elderly subjects the turnover rates of T_4 were normal

and thus the daily degradation rates were very low. In the three younger subjects the extrathyroidal pools were also low, but increased turnover rates of T_4 were recorded and the daily degradation of T_4 was raised to values approaching normal. The increased turnover rate of T_4 appeared to compensate for the reduced extrathyroidal pool of T4 and may account for the fact that these subjects appear to catabolise an amount of thyroxine greater than would be expected from the level of serum P.B.I. and T_4. When low serum P.B.I. values are accompanied by overt hypothyroidism the half life of T_4 is invariably prolonged (9.7 days), the turnover rate reduced (7.3 per cent per day), hence the total amount of T_4 catabolised daily is also uniformly reduced (266 µg.) (Sterling and Chodos, 1956). The reverse is true in hyperthyroidism.

There is no evidence to suggest that a high environmental temperature increases the peripheral metabolism of thyroid hormones. (Freinkel and Lewis 1957: Kassenaar et al. 1959). Reduced thyroid activity and thyroxine turnover rates have been reported in normal Jamaicans (Harland et al. 1971: Cobb et al. 1970) and in most mammalian species exposed to hot conditions for prolonged periods. (Collins and Weiner 1968). Beckers et al. (1963) in Uele and Barcelatto et al. (1967) in Pedregrosa, Chile, also found an increased turnover of T_4 in endemic goitre subjects. Initially Beckers et al. (1963) could offer no explanation for their findings. Later, however, Beckers (1969) attributes the increased turnover rates to a reduction of the thyroxine binding pre-albumen (T.B.P.A.) which has been reported in the inhabitants of the Uele endemic. (Van den Schrieck et al. 1965). In theory a fall in serum T.B.P.A. should be accompanied by a rise in serum free thyroxine (Surks and

Oppenheimer, 1964). Simultaneous measurement of T.B.P.A. and thyroxine-binding globulin (T.B.G.), serum free and total thyroxine might help to resolve this issue.

In contrast to my findings, Koutras et al. (1970) found reduced T_4 turnover in endemic goitre subjects in Greece. However, in this study, thyroid activity was not blocked by perchlorate, the subjects studied did not have subnormal P.B.I. values and probably had a less severe degree of iodine deficiency than the Kenya subjects. Both Beckers et al. (1963) and Koutras et al. (1970) however, have found an accelerated turnover of tri-iodothyronine (T_3) in their subjects with endemic goitre, implying an increased secretion of T_3 by the thyroid. Increased serum T_3 levels have been found in endemic goitre subjects recently in the Himalayan goitre belt, (Kochupillai et al. 1973), and after iodine deprivation in the rat (Greer et al. 1968). Moreover euthyroid subjects with low serum T_4 levels following radio-iodine treatment have normal or raised serum T_3 levels (Sterling et al. 1969). It may be, therefore, that an increased secretion of T_3 is the most important component of thyroid secretion in endemic goitre, and would appear to represent an important and possibly essential step in the biological adaptation to iodine deficiency. It is however possible that the increased serum level of T_3 is the result of increased peripheral conversion of T_4 to T_3 and not solely the result of an increased secretion by the thyroid. In either case an acceleration in the turnover of T_4 should ensure a more efficient utilisation of available iodine and be, in part, responsible for the absence of clinical hypothyroidism in many subjects with endemic goitre who have low serum T_4 levels.

The prevalence of endemic goitre in the highland provinces of Kenya undoubtedly accounts for the large numbers of patients who present to the Kenyatta National Hospital, Nairobi, for treatment of

established non-toxic goitre. Community studies had not been performed in the Central Province and thus the opportunity was taken to study thyroid function in patients from the Central Province who attended the thyroid clinic. The studies were restricted to those with moderate thyroid enlargement, as thyroidal uptake measurements may not be wholly accurate when a goitre is very large, and to patients who had travelled from home to hospital on the day of study in order to eliminate any acute changes in the plasma inorganic iodine (P.I.I.) concentration due to local variations in dietary iodine content.

In a pilot study the majority of patients and some of the control subjects had high thyroidal radio-iodine uptake values suggesting iodine deficiency as the cause of goitre. The detailed quantitative studies confirmed iodine deficiency in the goitrous group as a whole. The mean P.I.I. value in the goitrous group was 0.1 µg. per 100 ml. compared to a mean value of 0.18 µg. per 100 ml. in the control subjects. Normal values for P.I.I. vary from country to country, and region to region. Values are generally higher in North America where iodised salt is in wide use (around 0.5 µg. per 100 ml.) (Reilly et al. 1958: Wagner et al. 1961) than in Europe where values from 0.14 to 0.3 µg. per 100 ml. have been recorded. (Malamos et al. 1966b; Wayne et al. 1964: Greig et al. 1967: Beckers 1962). It has been suggested that a value of below 0.08 µg. per 100 ml. should be considered as evidence of iodine deficiency (Wayne et al. 1964). In some endemic areas very low P.I.I. levels have been reported; 0.04 µg. per 100 ml. Uele, (De Visscher et al. 1961) and in Darfur Province in the Sudan (Kambal et al. 1968). In the West of Scotland patients attending hospital with simple goitre had P.I.I. values ranging from 0.01 - 0.35 µg. per 100 ml. (mean 0.08) (Wayne et al. 1964). In the present study, the

group with high thyroidal clearance values were more clearly iodine deficient (mean P.I.I. 0.07 µg. per 100 ml.) than the group with normal thyroidal clearance values (mean P.I.I. 0.14 µg. per 100 ml.). Some individuals with normal thyroidal clearance values were iodine deficient on the basis of a low P.I.I. level, but many were not iodine deficient at the time of study. It is possible that past iodine deficiency may have been responsible for enlargement of the thyroid gland, which had persisted even after the iodine deficiency no longer existed. There was no evidence in this study, in a limited number of observations, of an increased urinary loss of iodine, which has been suggested as a cause of iodine deficiency. (Cassano et al. 1961).

The range of P.I.I. values in the control group was wide. Seven of the 18 subjects had P.I.I. values below 0.08 ug. per 100 ml. and in three the thyroid clearance was high. Clearly in some individuals an iodine deficiency state does not always produce enlargement of the thyroid gland or even a compensatory increase in activity. Roche (1959), Choufoer et al. (1963) and Delange et al. (1968) have described very high thyroid uptake in the absence of endemic goitre among populations affected by severe iodine deficiency, indicating that the human thyroid is capable of adapting itself adequately to a severe iodine deficiency without significantly increasing in size. In many endemic goitre areas a recurring question has been why only a proportion of individuals develop goitre. Those with goitre may be slightly more iodine deficient (Malamos et al. 1966b) or they may not (Choufoer et al. 1963) but most workers conclude that in areas where iodine deficiency is endemic, factors other than iodine deficiency may be involved in goitrogenesis. (Stanbury et al. 1954, Wayne et al. 1964, Malamos et al. 1967, Koutras 1972). In subjects living in the endemic

iodine deficient areas in Kenya there was no clear difference in the urinary iodine excretion, thyroidal uptake of radio-iodine or serum P.B.I. values between those with and those without goitre. It seems likely that the development of goitre in an individual may be the result of failure to adapt to iodine deficiency rather than quantitative differences in iodine intake.

It is, therefore, of interest that in the study of patients attending the thyroid clinic, in addition to moderate iodine deficiency, an apparent defect in the thyroidal utilisation of iodine was observed in those patients with goitre. Although the goitrous had lower P.I.I. values than the controls, because of the greatly increased thyroidal clearance they had a significantly higher absolute iodine uptake (A.I.U.). Moreover, despite the higher A.I.U. serum P.B.I. values were lower in the goitrous. The combination of a high or high normal A.I.U. and low or low normal P.B.I. value denotes a defect in the utilisation of iodine by the thyroid gland, without of course, indicating at what stage in hormone synthesis the defect occurred or how it was caused. An "iodine utilisation" index has been devised by Koutras et al. (1960) to express numerically the dissociation between the quantity of iodine taken up by the thyroid gland and the amount of hormone produced. The index is the ratio of P.B.I./A.I.U. and in their normal cases lay between 1 - 8.0. In the present study (table 9) values for the index were roughly similar (range 1.2 - 10, mean 4.9) in the control group. The mean index in the goitrous group was lower (2.2), even in those with normal clearance values (3.4). In the group with high clearance values the utilisation index was low at 2.2 and very low values (mean 0.6) were found in the group with high clearance and low P.B.I. values. There are a number of possible causes of the defective utilisation of iodine observed in

this study.

(1) Dyshormonogenesis. Values of the utilisation index in the subgroup with high clearance and low P.B.I. values were within the range of values found in specific defects of thyroid hormone synthesis (dyshormonogenesis) - (Koutras et al. 1960). Some patients may have had a specific hereditary defect but such individuals are often hypothyroid and in the Caucasian race at least, account for a very small proportion of the non-toxic goitre population. (McGirr 1960).

(2) Auto-immune thyroiditis. Metabolic defects leading to faulty utilisation of iodine have been described in auto-immune thyroiditis (Buchanan et al. 1961). In this study, occult thyroiditis was excluded as only one serum sample from 63 patients gave a low positive titre of antibody to thyroglobulin.

(3) Beckers (1969) has proposed that the defect in the utilisation of iodine in non-toxic goitre may simply be a manifestation of degenerative changes of a chronically enlarged colloid goitre. This explanation is unlikely in this study in which the most clear cut abnormalities were observed in young patients with a diffusely enlarged gland. Moreover, the histological appearance of two glands examined showed a diffuse hyperplasia with almost no colloid (figure 16, page 69) similar to that found in endemic goitre subjects in the Himalayas (Roy et al. 1964) and in New Guinea (Buttfield and Hetzel 1969).

(4) Minor defects in Thyroid Hormone Synthesis. This problem has been studied in depth in the endemic goitre areas of Greece. Although no single specific abnormality was detected, Koutras (1972) considers that the goitrous iodine deficient gland may have an inferior capacity for trapping and handling iodine and mentions evidence to support this view, including mild defects in hormone

synthesis, (Malamos et al. 1967) and the escape of non-hormonal iodide (Ermans et al. 1963).

In the present study the defect in thyroid hormone synthesis was more clear cut and severe than in the Greek study. This may simply be due to selection of cases, the thyroid clinic attracting patients with larger goitres and hence possibly more severe abnormalities. However, in a study similar to the present study, Alexander et al. (1963) found no evidence of defect utilisation of iodine in patients with simple goitre due to iodine deficiency in Glasgow.

5. Goitrogens. Quantitative studies of iodine metabolism have not been undertaken in endemic goitre areas where dietary goitrogens have been implicated, thus comparative data is lacking. Goitrogens usually effectively reduce the uptake of radio-iodine by the thyroid gland. Alexander et al. (1963) however, have described a patient with goitre due to resorcinol in whom the A.I.U. was high normal and the serum P.B.I. low, an acquired dyshormonogenesis, and similar to the findings in the present study. An unidentified goitrogen, therefore, might be responsible for the defective utilisation of iodine observed in Kenya subjects with non-toxic goitre.

Dietary surveys have shown that in Kenya in general and in the Kikuyu tribe in particular there is a very high consumption of foodstuffs (cabbage, spinach, kale) which may contain active goitrogens (Greer and Ashwood, 1948). Cooking, the common practice in Kenya, prevents the formation of goitrin from progoitrin, a substance present in the turnip family. Milk-borne goitrogens are unlikely candidates in Kenya where milk consumption is low. (Peltola 1969). Cassava, the likely source of a goitrogen in Nigeria (Ekpechi 1967) and Idjwi Island (Delange et al. 1969) is consumed only sporadically

by the Kikuyu in Kenya (Bohdal et al. 1968). Green Vegetables (cabbage, kale) are staples in the Kikuyu diet, however, and may be a source of goitrogen, sufficient in quantity to induce or aggravate goitre in the presence of iodine deficiency. Another possibility is fluoride which has implicated as a goitrogen in association with iodine deficiency (Wilson 1941: Day and Powell-Jackson 1972). Dental fluorosis is endemic in Kenya and its distribution parallels, approximately, the distribution of endemic goitre (Bohdal et al. 1968). Theoretically fluoride should have a perchlorate-like action and cause a reduced thyroidal uptake of iodine. However, Stöckx and Podoba (1960) have found that fluoride in rats, inhibits the coupling of iodo-tyrosines to T_3 and T_4 producing in effect an acquired dyshormonogenesis.

Nevertheless, iodine is the indispensible mineral nutrient and although the argument that fluoride may act as a possible goitrogen in association with iodine deficiency is attractive and interesting, it does not affect the practical solution that the most effective method of preventing endemic goitre is to provide an adequate daily supply of iodine to all members of the community. Abolition of iodine deficiency nearly always reverses the effects of other factors which, working in concert with iodine deficiency, may provoke the emergence of endemic goitre (Delange et al. 1969: Clements et al. 1970).

The most popular, practicable and effective method of providing supplementary iodine is the iodisation of domestic salt, a measure which was introduced to Kenya in 1970. Reinforced by law and introduced on a nationwide basis, the method should prove successful, provided that the fortified salt reaches the populations at risk and that sufficient amounts are consumed regularly.

Preliminary follow-up studies in Kenya in 1973 have shown a reduction in the incidence of visible goitre. (Hanegraaf 1973). Should goitre prophylaxis with iodine appear to be unsuccessful, before attributing the residual goitre to the effects of other environmental agents, such as dietary goitrogens or fluoride, efforts should be directed at ensuring the delivery of adequate supplies of iodine to the affected populations, if necessary by the injection of iodised oil, used so successfully in New Guinea (Buttfield and Hetzel 1969) and in Idjwi Island (Delange et al. 1969).

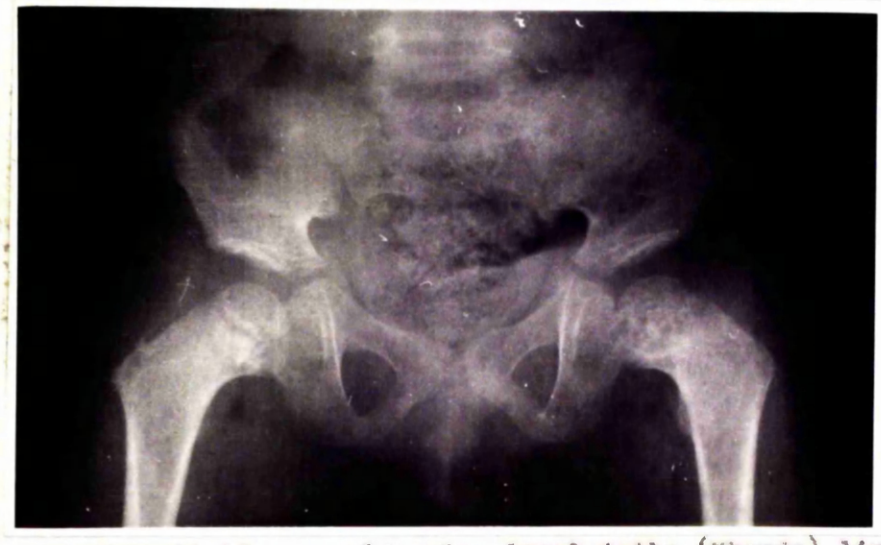
ENDEMIC GOITRE IN MWEZI, TANZANIA.

Trolli (1933) mentioned the existence of endemic goitre in the "mountainous regions" of Tanganyika" when writing on the occurrence of endemic goitre around Lake Kivu and in Ruanda and Burundi. It is likely that he was referring to the mountains of North West Tanzania immediately adjoining and topographically similar to Burundi. The Mwezi mountain range lies about 100 miles to the south of the Burundi/Tanzanian border, the intervening territory being flat and low lying. At present Mwezi is sparcely populated althou h the influx of refugees from Ruanda in the 1960s and more recent (1969) population movements of indigenous Tanzanians (2,000 Chaga people from Arusha) have considerably boosted the total population.

The goitre rate in the schoolchildren was high - 56 per cent. The highest incidence (67 per cent) was recorded in the children of local tribes (Mbende) - most of whom were prepubertal. All children were exposed to the same environmental conditions and consumed a similar diet. The Mbende children were not more iodine deficient than the Ruandan children and the difference in the goitre rate is probably a manifestation of duration of exposure to the iodine deficiency which was confirmed by the low excretion of stable iodine in the urine and the low P.I.I. values. The mean value of 14 µg. per 24 hours for urinary iodine is low compared to 50 µg. per 24 hours in New York schoolchildren (Follis 1964) and 40 µg. per 24 hours in healthy Madrid children (Jolin and Escobar del Rey 1965). Iodine excretion values of less than 10 µg. per 24 hours were recorded in 50 per cent of the goitrous children and 25 per cent of the nongoitrous children indicating severe iodine deficiency. Normal values for P.I.I. have not been recorded in children. Presumably they are similar to adult

Fig. 20. - Mwezi women.

Fig. 21.



A hypothyroid 16 year old male, local tribe (Mbondo) living in the Mwezi settlement. He was the same height (3 ft. 7 ins.) as his 6 year old sister. He did not attend school. Serum P.B.I. value 1.4 µg. per 100 ml., cholesterol 350 µg. per 100 ml., skull x-ray - normal pituitary fossa; hips - epiphyseal dysplasia.

values and hence the mean value of 0.05 ug. per 100 ml. indicates iodine deficiency. Although the goitrous were apparently more iodine deficient than the nongoitrous the difference is not great and many of those without goitre were iodine deficient. As already described, the development of goitre in an individual may be the result of failure to adapt to iodine deficiency rather than or in addition to quantitative differences in iodine intake.

Despite the fact that the immigrants from Ruanda spontaneously became aware of goitre about two years after their arrival in Mwezi, it is possible that they entered Mwezi with a significant goitre frequency. Endemic goitre has been reported from Ruanda and adjoining areas of the Congo where many of the immigrants lived before moving into Tanzania. (Demayer and Vanderborght 1953, Delannoy and Claeys 1957).

Unfortunately due to lack of time a community survey was not conducted. As an alternative 58 adults (30 males, 28 females) were examined at sight testing clinic at the local hospital. Twenty five had a goitre (25/58 = 43 per cent). At an antenatal clinic 14/16 women had a grade 2 goitre and many easily visible (grade 2 and 3) goitres were observed in adults viewed casually in the villages. (figure 20). Figure 21a shows a dwarfed hypothyroid boy, a probable victim of environmental iodine deficiency.

In view of the isolation of Mwezi, the relatively small population at present and the need for iodine supplementation, the injection of iodised oil would seem to be the most appropriate method of providing iodine. Unfortunately so far this scheme has not proceeded beyond the proposal stage.

Management and Treatment of Established Goitre.

Iodine. Iodine plays a relatively small part in the treatment of the established goitre. In its early stages the diffuse hyperplastic gland, avid for iodine, will revert to normal size during the administration of 150 -500 µg. of potassium iodide, or iodate, daily. (Scrimshaw et al. 1953, Wayne et al. 1964). Lugol's iodine, containing 300 µg. or more of iodine per drop should not be used as there is a risk of precipitating hyperthyroidism (Jod-Basedow disease), causing the goitre to enlarge or in sensitive individuals inducing drug reactions (iodism) (Laroche and Hirsch 1960). The established colloid and nodular goitre will not respond to iodine.

Thyroid hormone. The administration of thyroid hormone (as thyroxine, thyroid extract, or tri-iodo thyronine) is a more effective treatment of simple non-toxic goitre. This treatment was used in Europe during the latter half of the last century (Reinhold 1894), but seems to have been neglected until Greer and Astwood (1953) revived interest in a report of the treatment of 50 patients. They observed complete regression in 40 per cent, partial regression in 35 per cent and in 24 per cent of cases there was no change. In the present series of 120 patients with diffuse goitre, encouraging but less dramatic results were achieved, with 0.3 or 0.2 µg. of thyroxine daily; 25 per cent of goitres disappeared, 40 per cent showed partial regression and no change was observed in 35 per cent of cases. A better clinical response to T_4 was observed in cases where thyroidal clearance was high. The thyroidal clearance values of those who did not respond to T4 were lower and the histological structure in those with normal clearance values was generally of a relatively inert colloid goitre. Wayne et al. (1964) and Gordan et al. (1961) have confirmed the place of thyroxine or tri-iodothyronine in the treatment of diffuse non-toxic

goitre. I am sure the successful use of thyroxine contributed in part to the overall low thyroidectomy rate in the group of non-toxic patients. Its use should be encouraged in developing countries where facilities for thyroid surgery may be limited, and also in those with recurrent goitre, when malignancy has been excluded. When the goitre is long standing and nodular, rigid fibrous tissue, cyst formation and calcification usually prevents goitre regression. Nevertheless, significant reduction in gland size may be achieved in a small proportion, particularly in the younger patient in whom the 'nodules' are composed of parenchymatous hyperplastic tissue. The dosage employed should be that which completely suppresses thyrotrophin (T.S.H.) secretion by the pituitary and is usually in the range of 0.3 - 0.4 mg. thyroxine sodium per day. Some patients may experience thyrotoxic symptoms necessitating a reduction in dosage. Response is usually apparent within 3-6 months and therapy should be continued probably for an indefinite period or until iodine prophylaxis is instituted. Compression is uncommon in diffuse simple goitre and surgical intervention is rarely indicated. Reassurance alone is all that is required for many patients.

General comments on the surgical treatment of thyroid disease.

The indications for surgical treatment in thyroid disease are fairly precise. The success of treatment depends upon careful assessment of the pathological lesion present and upon the facilities available for both medical and surgical therapy. The likelihood of a careful follow-up being possible also has a bearing on treatment in the context of a developing country. The indications may be classified under three main headings:-

Fig. 22. - Post operative hypothyroidism and hypoparathyroidism in a 16 year old female. Thyroidectomy performed for simple goitre.

(i) Non-toxic goitre producing or likely to produce pressure symptoms.

(ii) Toxic goitre.

(iii) Non-toxic goitre which may be malignant.

Thyroidectomy should only be performed when it can be done under reasonably good conditions. This means good anaesthesia (either local or general with intubation), good lighting, facilities for blood transfusion and familiarity with the conditions likely to be met. Under these circumstances the results may be good; where these conditions are not met, the results can be appalling (figure 22).

Non-toxic goitre producing or likely to produce pressure symptoms.

In African countries this is the commonest indication. It is doubtful whether thyroidectomy should ever be carried out for cosmetic reasons alone when the patient cannot be carefully followed or where expert medical care cannot be guaranteed during the rest of the patient's life. Hypothyroidism and parathyroid insufficiency may arise months or years following surgery and failure to detect this may lead to chronic ill-health.

Compression or deviation of the trachea may cause respiratory obstruction. When it will occur is unpredictable but the late weeks of pregnancy may be hazardous. Sudden painful increase in size of such a gland is probably due to degeneration in a nodule with bleeding into the necrotic area.

Malignancy.

The relationship between non-toxic goitre and the development of carcinoma has probably been exaggerated in the past. (Sokal 1959). The true incidence of malignant change in non-toxic goitre is low and may well be no greater than the incidence in glands of normal size. (Miller 1955, Crile 1956). In Kenya, where thyroid carcinoma is

comparatively rare and multinodular goitre very common, the policy advocated by some "authorities" in the U.S.A. (Cole et al. 1949, Cope et al. 1949, and Sloan et al. 1950), namely removal of a multinodular goitre as a prophylactic measure against thyroid cancer is certainly not justified. This is a medically impractical and economically unsound approach to the problem of thyroid carcinoma. In a leading article (Lancet July 14 1973 p. 82) the not unreasonable suggestion is made that a "suspicious" nodular goitre should be removed lest it be malignant. What constitutes a "suspicious" nodular goitre, only careful clinical assessment in the individual case will decide. Nodularity alone, particularly in an endemic area, is not a sufficient indication for surgery, unless accompanied by increasing size, local pressure symptoms or lymph node enlargement. Regional lymphadenopathy is common in Hashimoto's thyroiditis, but this condition is exceedingly rare in Kenya. A painful goitre is rarely malignant, but a single nodule may be regarded with suspicion even in Kenya.

The Single Nodule.

In many patients careful palpation reveals only a single thyroid nodule. The nodule is often a large cyst in a gland where other cysts are present but impalpable. Fifty per cent in my personal series and almost 70 per cent in the retrospective analysis of pathological material fell into this category; a low diagnostic accuracy but expected in an endemic area, and similar to the experience of others (Miller 1955, Leichty et al. 1965, Kambal 1969). The nodule may be a single cyst or a benign adenoma but it may also be a carcinoma and for this reason requires careful scrutiny, even in an endemic goitre area. In my personal series of 48 cases, two malignant nodules were encountered, an incidence of 4 per cent.

However, thyroxine eliminated 10 nodules, and the apparent incidence of malignancy rose to 5.5 per cent (2/38). The incidence of malignancy in the retrospective pathological series was a little higher at 7.8 per cent. These figures appear to confirm the sinister reputation of the single nodule, management of which has always been controversial, mainly because of the wide variation in the reported incidence of malignancy, from 1 per cent (Sokal 1959, Kambal 1969) to 12.5 per cent (Taylor 1969), 24 per cent (Knowlson, 1971) and 33 per cent (Perlmutter and Slater, 1956). It is now believed that many differentiated thyroid carcinomas grow slowly and these nodules are malignant from inception.

The question to be asked is this. Should every individual presenting with a single thyroid nodule be advised to have it removed surgically? I would advise any patient from a non-endemic area in Kenya, e.g. Coast, Eastern or Nyanza Province to have surgery. If the patient is from a known endemic area, then three months' treatment with thyroxine should be the initial step: if no diminution in gland size is observed then the nodule , its capsule and a portion surrounding gland should be removed. The distribution of iodised salt should, in time, substantially reduce the prevalence of simple goitre in Kenya. When this happens it may be desirable to alter these recommendations in favour of surgical and histological inspection of all single nodules.

Pathology.

As expected, simple non-toxic goitre was the most common pathological entity. In Europe, toxic goitre dominates surgical series (Kennedy 1970). In the U.S.A. however, more widespread use of radio-iodine has reduced markedly the thyroidectomy rate for toxic goitre. (San Fellipo 1973). In six years, only 35 toxic goitres from

African patients were received at the Central Government Laboratory in Kenya confirming the rarity of this condition in the indigenous African.

The histological appearances of the simple non-toxic goitre was in general unremarkable, apart from the prevalence of parenchymatous hyperplasia which was extensive in many glands and apparently complete in a few. Marine (1928) has outlined the structural changes which occur in the human thyroid gland in the presence of iodine deficiency. He considered that the initial phase of diffuse hyperplasia was usually followed by colloid distension and a reduction in the areas of focal hyperplasia. Fluctuations in dietary intake of iodine and the variable demands for thyroid hormone result in repetition of this cycle of hyperplasia and involution with ultimately the formation of a multinodular cystic colloid goitre. This is a permanent structure and may cause symptoms. The majority of glands in surgical series of non-toxic goitre are usually of this type (De Smet 1960); but where goitre is prevalent, parenchymatous hyperplasia and compact cellular nodules are common. (Welsh and Correa 1960). McCarrison (1927) recognised "parenchymatous endemic goitre" as the classical type to be found in areas of high endemicity, such as the Himalayas and the Alps; the "diffuse colloid type" occurred more commonly in areas of lower endemicity and also in non-endemic areas. Nevertheless, some controversy still surrounds the natural history of the structural changes which occur in the thyroid gland in endemic goitre. De Smet (1960) considers that the hyperplastic changes cannot continue indefinitely and Hazard (1958) states that diffuse endemic goitres are usually of the colloid type. Intense hyperplasia and no colloid have recently been shown to be a constant feature of the enlarged thyroid glands of peoples of all ages

in severe endemic iodine deficient area . (Roy et al. 1964). The prevalence of environmental iodine deficiency in certain regions in Kenya is reflected in the prevalence of hyperplastic changes in the thyroid tissue of the glands removed surgically.

The incidence of focal thyroiditis in all groups was very low and paralleled the very low incidence of serum thyroid antibodies in the clinic patients. Similarly the rarity of Hashimoto's thyroiditis reflects the rarity of this condition in clinical practice in the indigenous African. Similar findings have been recorded in surgical series from elsewhere in Africa. (De Smet, 1954 and 1960, Taylor 1968). In the Caucasian race focal lymphocytic infiltrates are found in between 10 and 40 per cent of colloid goitres and the incidence in benign adenoma may be higher (Kennedy, 1970, Senhauser 1964, Schade et al. 1960). The rarity of Hashimoto's thyroiditis is striking. The incidence in surgical series in Europe and U.S.A. is usually much higher, estimates varying from 0.2 - 7.2 per cent (Clark 1959). Possible reasons for the rarity of auto-immune thyroiditis in the African are discussed later in the section on thyrotoxicosis.

THYROID CARCINOMA.

Carcinoma of the Thyroid Gland.

Introduction.

The steady flow of data from Africa in the past 20 years has refuted the belief that malignant disease is rare in the tropics, although the pattern of malignant disease is different from that seen in Europe and North America. (Hutt and Burkitt 1965). The incidence of malignant thyroid tumours has been recorded in cancer rate surveys from Africa but there are few detailed accounts of the clinical and pathological features of these tumours from Africa in general, and none from Kenya. There follows an account of thyroid carcinoma in 63 Kenyans of African origin.

Patients.

Group I

Sixteen patients attended the thyroid clinic at the Kenyatta National Hospital, Nairobi between August 1968 and April 1970 when the diagnosis of cancer of the thyroid gland was made. (table 1). Two hospitalised patients with advanced malignant disease of the thyroid gland who died shortly after the diagnosis was established complete the series of 18 patients studied personally by me.

Group II

Histological material and the pathological records of 52 patients with cancer of the thyroid gland were obtained from the archives of the pathological department of the Medical Research Laboratory, Nairobi, which receives specimens for histological analysis from all government and mission hospitals in Kenya. Only those tumours which conformed to the accepted criteria of thyroid malignancy have been included. Difficulty was encountered with seven neoplasms which showed atypical cellular proliferation but with no evidence of capsular or nodal involvement in the available

sections. The remaining 45 cases together with the 18 patients mentioned above make the total of 63 definite cases of cancer of the thyroid gland diagnosed between 1964 and 1969 (table 1). A note was made of the sex, tribe and location of residence of each patient but age recording was unreliable and therefore ignored in the retrospective study. When no record of tribe was available from the pathological record this could usually be ascertained with reasonable certainty from the patient's surname; tribal surnames are distinctive. The location of residence was usually noted on the pathological request form in cases from outwith Nairobi. When surgery was performed at the Kenyatta National Hospital the inpatient records were scrutinised.

Methods.

In all patients the diagnosis was established by the histological examination of tissue obtained at thyroidectomy or at 'open biopsy'. In the prospective group (Group I) after thyroidectomy the gross specimen was carefully inspected and the presence or absence of encapsulation noted. Multiple samples (8 - 10) of the tumours were taken for histological analysis to determine the dominant type of architecture present.

In the retrospective group (Group II) no gross specimens were available for inspection, but sufficient histological sections and paraffin blocks of tissue were available.

Classification.

Papillary Carcinoma.

A slowly growing histologically differentiated tumour, which occurs usually in a younger age group than the follicular carcinoma. Gross encapsulation is not a special feature of this

Fig. 22a. - Papillary carcinoma (H & E x 270)

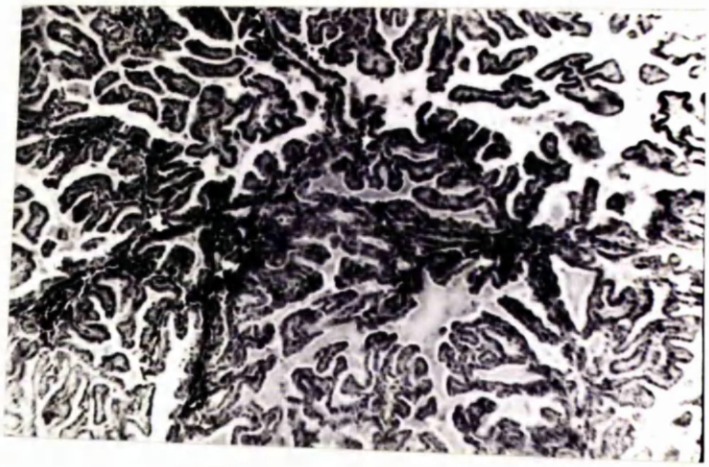


Fig. 22b. - Papillary carcinoma (H & E x 670)

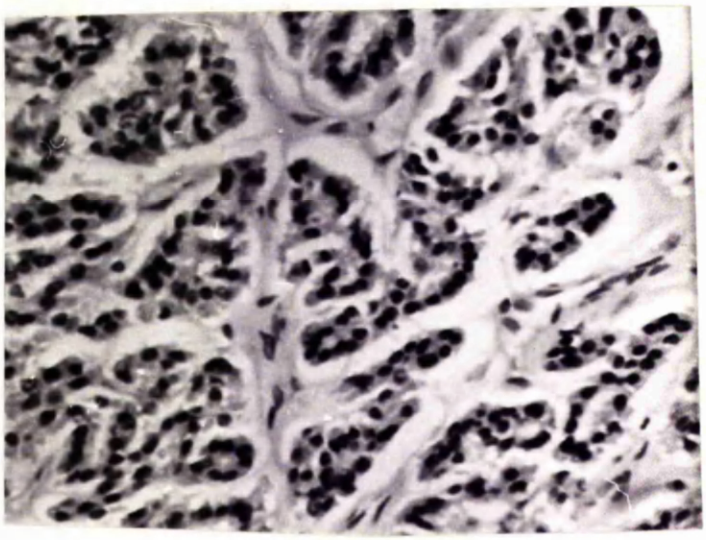


Fig. 22c. - Mixed follicular papillary carcinoma (H & E x 150)

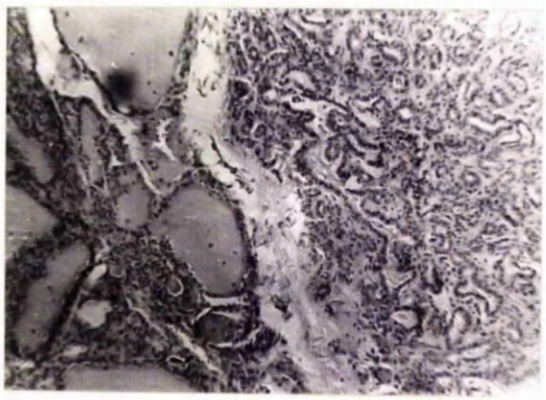


Fig. 23a. - Papillary carcinoma (No. 14, fig. 22) deposit in cervical lymph node. (H & E x)

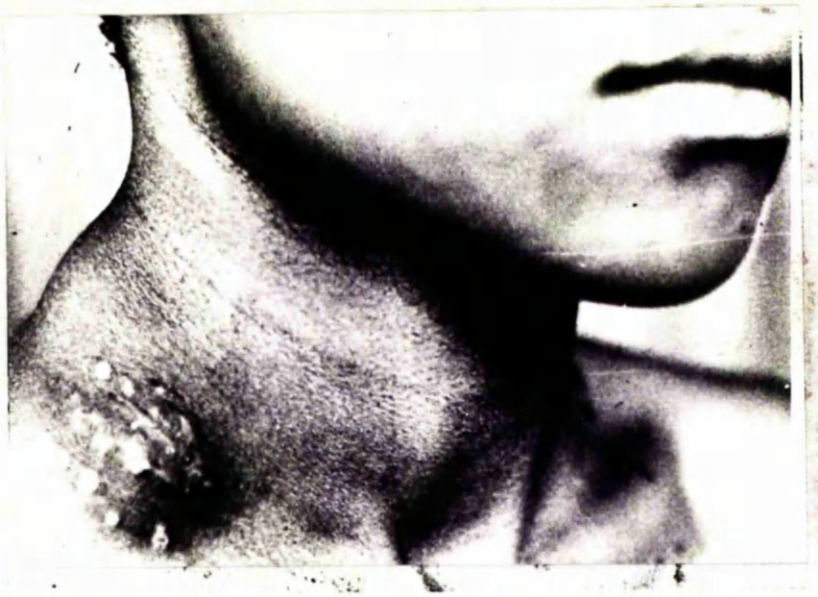


Fig. 23b. - Section from above biopsy. (H & E x 275)

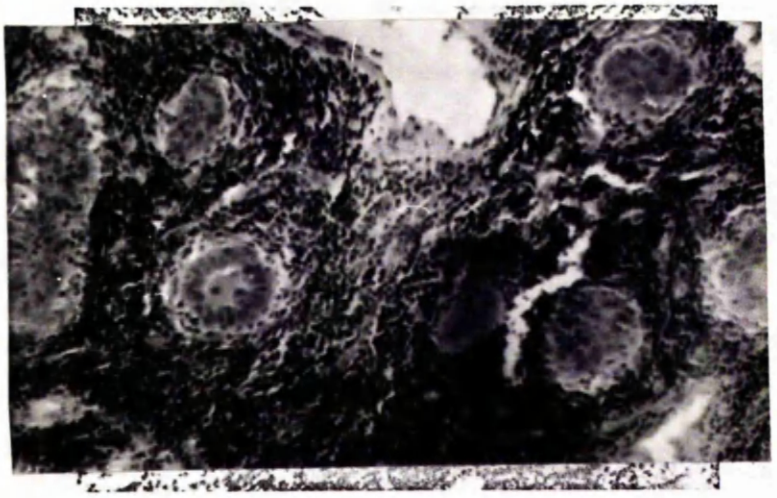


Fig. 23c. - Another section showing psamomma body. (H & E x 275)

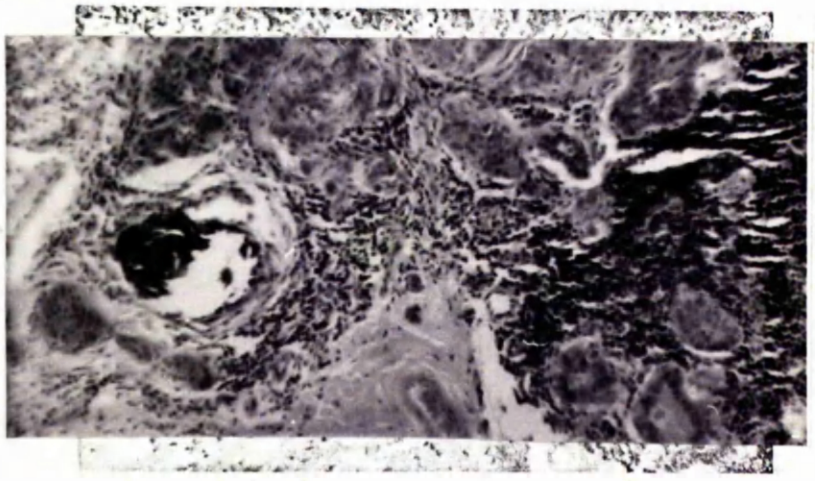


Fig. 24a. - Follicular carcinoma. Microfollicular pattern (H & E x 150)

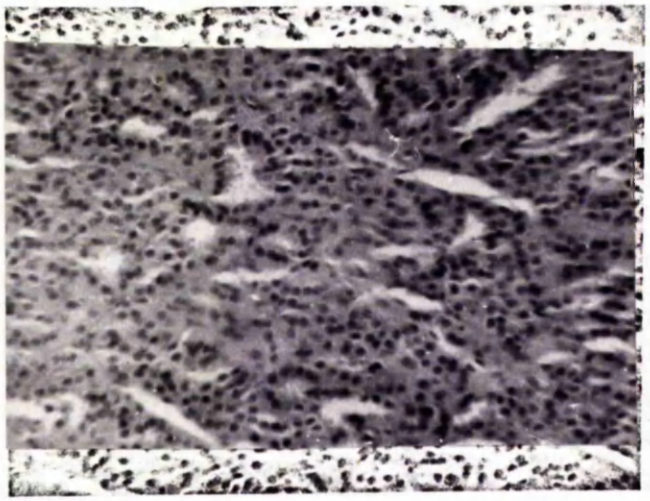


Fig. 24b. - Follicular carcinoma, microfollicles. (H & E x 225)

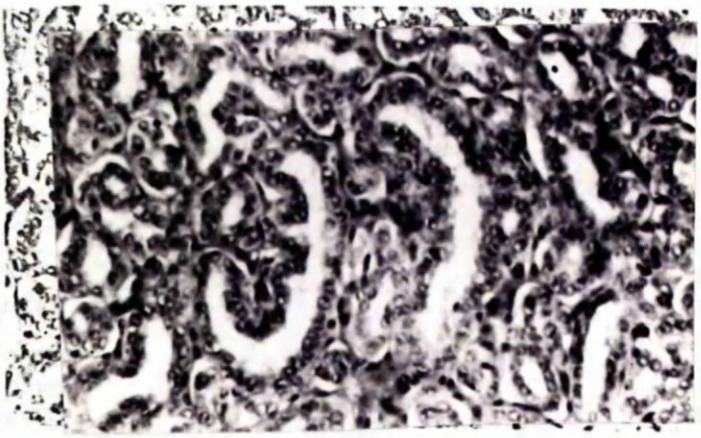


Fig. 24c. - Follicular carcinoma. Solid sheets of cells. (H & E x 375)

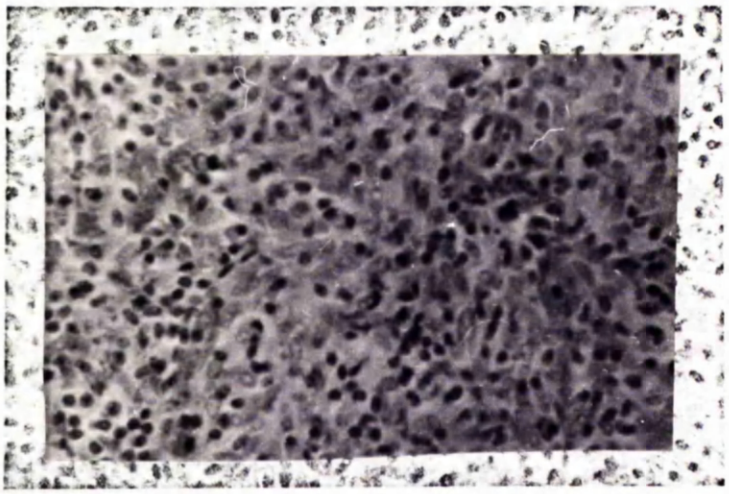


Fig. 25a. - Medullary carcinoma - positive stain for amyloid in stroma. (H & E x 375)

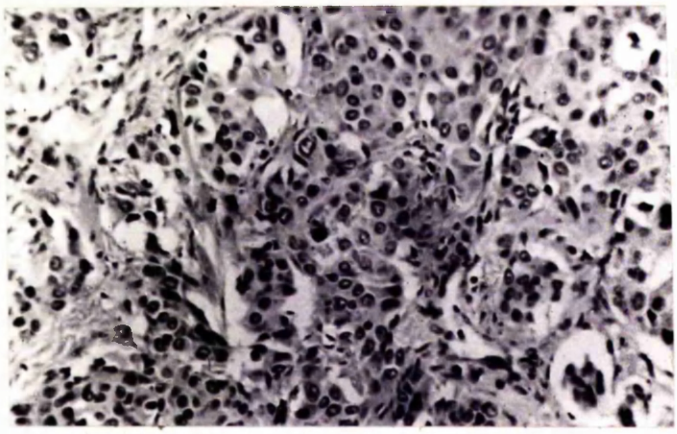


Fig. 25b. - Anaplastic carcinoma No. 18, table 22 (H & E x ——)

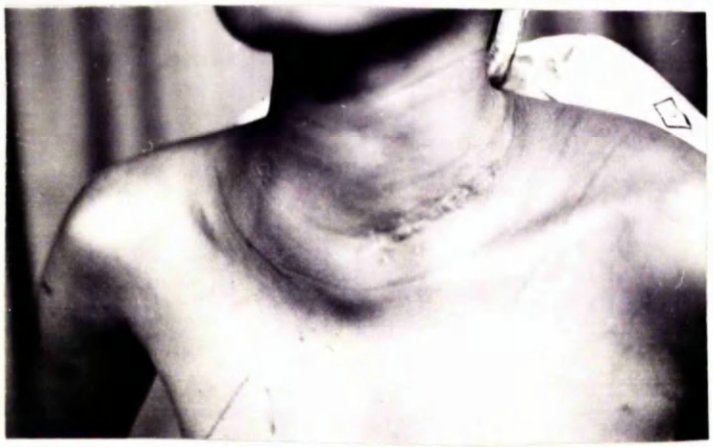
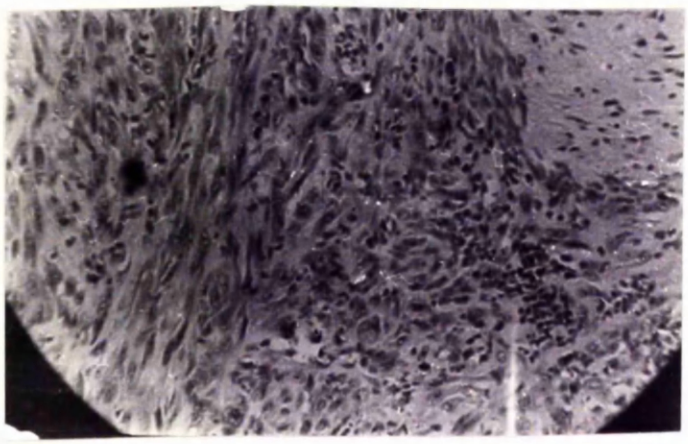


Fig. 25c. - Anaplastic carcinoma, spindle cell pattern from above. (H & E x 150)



tumour which microscopically is formed of a mixture of papillary and follicular elements in varying proportions (figures 22 a, b, c). Using the classification of Woolner et al. (1961) all tumours with both papillary and follicular elements have been designated PAPILLARY CARCINOMA including those with a predominantly follicular architecture. It is now clear that the presence of follicular elements does not alter the biological behaviour of this neoplasm which metastasises to regional lymph nodes (figure 23a, b and c), has a low grade malignancy and generally a good overall prognosis.

Follicular Carcinoma.

A slowly-growing histologically differentiated tumour which may occur in two histopathological types.

1) The localised follicular carcinoma, firm, solitary, well encapsulated, is often indistinguishable to the naked eye from a benign adenoma. However, neoplastic invasion of the capsule or capsular sinuses distinguishes this tumour from the benign adenoma. The invasion may be minimal only and multiple blocks must be examined.

2) The invasive follicular carcinoma may originate from a benign adenoma and the encapsulated or localised follicular carcinoma may be one stage in its development. Usually presenting as a multinodular goitre or as a hard fixed mass in relation to the thyroid, the frequent vascular invasion leads to distant metastases in bones and lungs which are often the presenting clinical feature. As expected those with extensive capsule invasion and distant metastases carry a worse prognosis than the papillary variety or the encapsulated localised tumour. Microscopically the architecture varies from a predominant microfollicular pattern to solid sheets of cells, a mixture of both being common (figures 24a, b and c).

No.	*Sex*	*Age*	*Tribe*	*Clinical Features*	*Histology*	*Treatment*
1	F	50+	Kikuyu	Pathological fracture L. femur. Thyroid nodule	Follicular	No treatment. Metastases in lungs, liver, pelvic and femoral bones. Died.
2	M	17	Abaluhya	Diffuse firm goitre	Follicular	Total thyroidectomy. Thyroxine.
3	F	48	Kikuyu	Multinodular goitre. Skull metastases	Follicular	Radio-iodine. Thyroxine. No follow up.
4	M	60+	Meru	Metastases L. pelvic bone.	Follicular	Radio-iodine. Thyroxine. Died April 1970
5	F	25	Somali	Multinodular goitre	Follicular	Total thyroidectomy. Thyroxine.
6	F	24	Kikuyu	Hard multinodular goitre	Follicular	Inoperable. Radio-iodine. Thyroxine. No follow up.
7	F	50+	Kikuyu	Pathological fracture L. hip. Nodular goitre	Follicular	Thyroxine. No follow up.
8	F	22	Kikuyu	R. lobe nodule	Follicular	R. lobectomy. Thyroxine.
9	F	40+	Kikuyu	Bilateral cervical lymphadenopathy. Thyroid nodule	Papillary	Inoperable. Thyroxine. No follow up.
10	M	50+	Kikuyu	Cervical lymphadenopathy. Hard nodular goitre	Papillary	Inoperable. Thyroxine. No follow up.
11	M	39	Chaga	Ulcerated tumour L. mandibular region. Thyroid normal	Papillary	Inoperable. Radio-iodine. Thyroxine. No follow up.
12	F	17	Kikuyu	Nodule thyroid isthmus	Papillary	Sub-total thyroidectomy. Thyroxine. No follow up.
13	F	29	Kamba	Multinodular goitre	Papillary	Inoperable. Thyroxine. No follow up.
14	F	22	Kikuyu	Cervical lymphadenopathy	Papillary	Total thyroidectomy. Lymph node dissection.
15	F	32	Luo	Multinodular goitre	Papillary	Total thyroidectomy. Thyroxine.
16	F	50+	Kikuyu	Cervical lymphadenopathy. Nodular goitre	Papillary	Total thyroidectomy. Lymph node dissection.
17	F	26	Kikuyu	Central thyroid nodule	Papillary	Sub-total thyroidectomy. Thyroxine.
18	F	50+	Kikuyu	Hard goitre. Respiratory obstruction.	Anaplastic	Died, post thyroidectomy.

Table 22 Details of carcinoma patients.

Medullary Carcinoma.

A slow-growing solid tumour which may metastasise to regional lymph nodes, lungs and liver. Derived from the interstitial cells (C cells) of the thyroid and noted for the production of calcitonin and other hormones. Abundant hyaline stroma usually gives a positive stain for amyloid. Histologically the tumour consists of small round or spindle cells lacking pattern but easily distinguished from the rapidly growing and invasive Anaplastic Carcinoma which is also composed of rapidly dividing spindle or round cells. (figures 25 a, b and c).

Group I.

The clinical and pathological details which comments on treatment of the 18 patients with carcinoma of the thyroid gland are shown in table 22.

There were four males and 14 females and their ages ranged from 17-60 years. The numbers are insufficient for comparison of the ages in each group of patients, but it is notable that four patients with follicular carcinoma were aged 25 years or less. The majority of the patients belonged to the Kikuyu tribe from the Central Province of Kenya, the area served by the Kenyatta National Hospital.

Follicular Carcinoma.

Eight patients had follicular carcinoma; surgical treatment was possible in three patients (2, 5, 8); four patients had metastases to bone and one patient had an inoperable local tumour at presentation (1, 3, 4, 6, 7). Three patients had undergone some form of thyroid surgery in the past. They clearly demonstrated the aggressive nature of untreated or inadequately treated follicular carcinoma and are described briefly below.

Fig. 26. - Patient No. 1. Metastatic follicular carcinoma, left hip and pelvis.

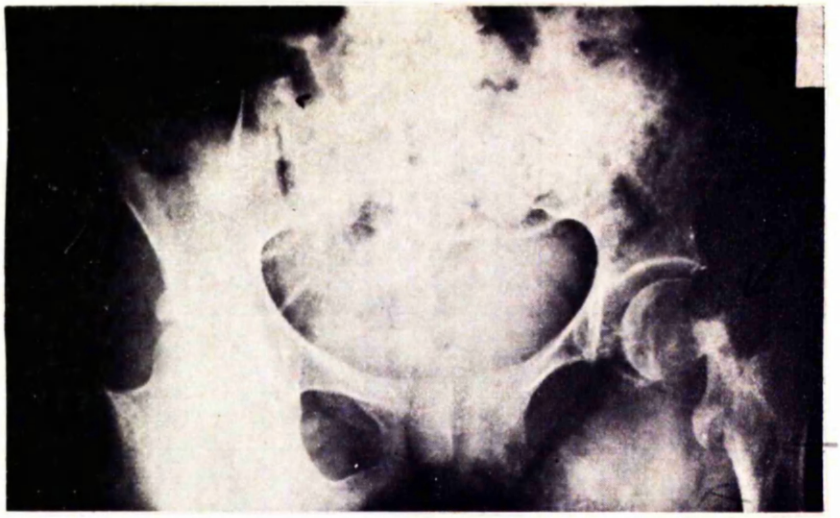


Fig. 27a. - Patient No. 3. Follicular carcinoma with metastases.

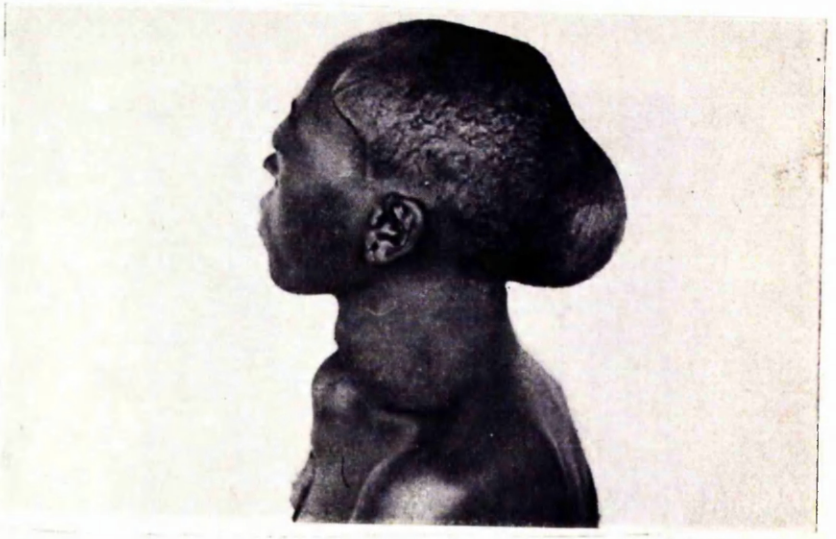


Fig. 27b. - Patient No. 3. Deposits in skull.

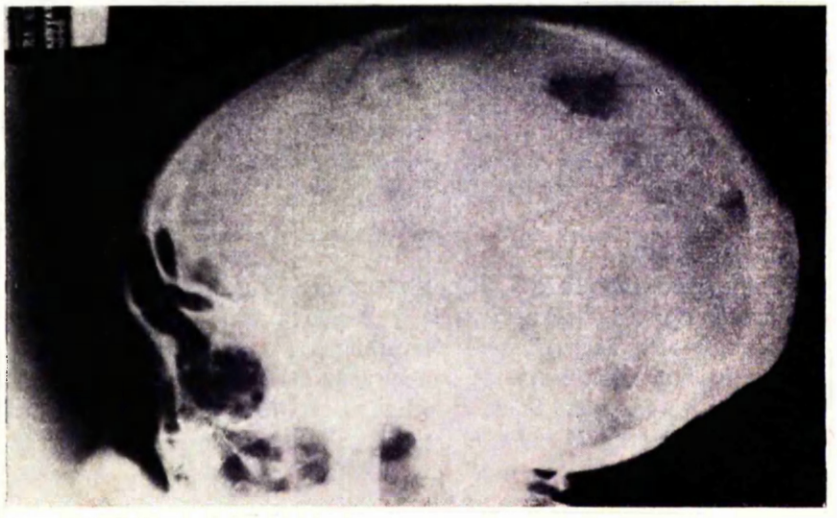


Fig. 28 a. - Patient No. 4. Angiograph of pelvic tumour, showing vascular supply and bone erosion.

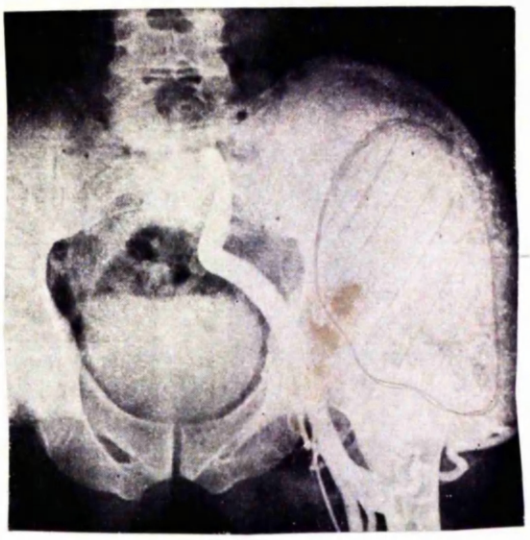


Fig. 28b. - Metastatic follicular carcinoma from above tumour - architecture resembles a benign nodule. (H & E x 150)

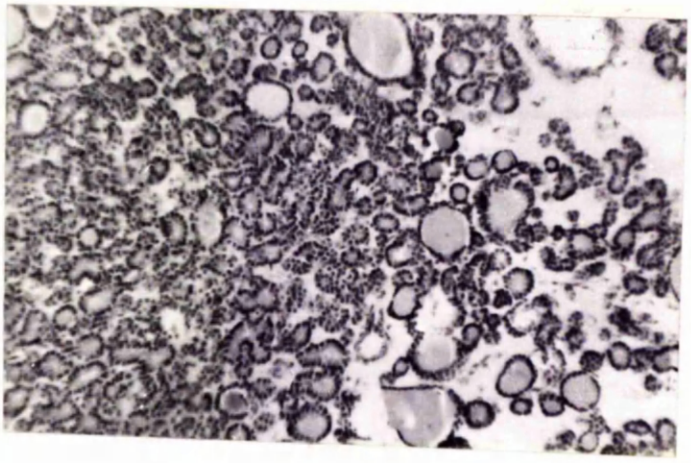


Fig. 28c. - Recut of original (1962) biopsy showing invasion of capsule and sinuses. (H & E x 150)

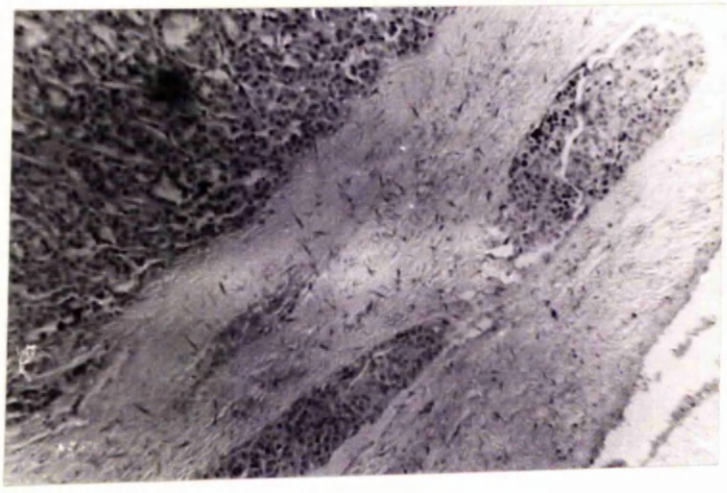
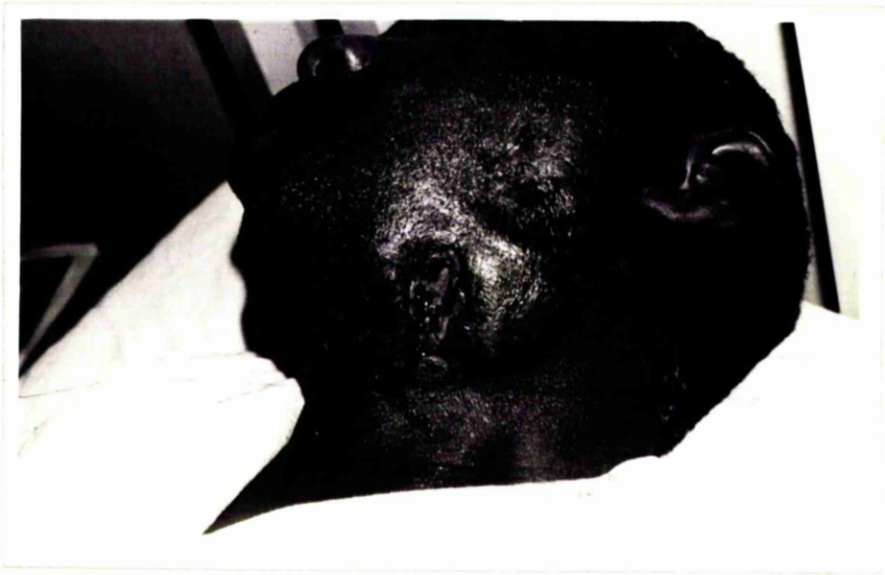


Fig. 29 - Secondary papillary carcinoma.



Patient No. 1 presented with a pathological fracture of the left femur, and almost complete destruction of the left ischial ramus in October 1968 (figure 26). A hard nodule was palpable in the thyroid region of the neck. Thyroidectomy had been performed two years previously in a district hospital; attempts to obtain records of this operation and the pathological report were unsuccessful. The patient died shortly after the development of rapid liver enlargement and ascites. At the post-mortem examination, metastatic deposits from a primary follicular carcinoma were present in the liver, lungs, pelvic bones, left femur and right scapula.

Patient No. 3 presented in November 1969 with a hard craggy thyroid mass, and a large occipital tumour (figure 27a). Thyroidectomy had been performed elsewhere in 1966 for unknown reasons. Osteolytic lesions were visible on skull x-ray (figure 27b). Biopsy of the thyroid tumour confirmed follicular carcinoma and treatment with radio-iodine was commenced.

Patient No. 4 had an apparently benign adenoma of the thyroid gland removed in 1962. In October 1969 he presented with a huge pelvic tumour involving the left iliac crest (figure 28a). Biopsy confirmed metastatic follicular carcinoma (figure 28b). The neck was free of tumour and the thyroid gland impalpable. Sections of the original thyroid specimen were re-examined, and fresh sections cut from the available blocks. The original histological diagnosis of "foetal adenoma" was changed to localised follicular carcinoma when a breech in the capsule and vascular invasion in the freshly cut sections were found. (figure 28c). This case highlights a difficulty which may be encountered in differentiating the benign from the malignant thyroid neoplasm. The tumour concentrated a tracer dose of radio-iodine

and treatment with radio-iodine was begun.

Papillary Carcinoma.

There were nine patients with papillary carcinoma. No active surgical treatment was undertaken in four patients who presented with inoperable lesions (9, 10, 11, 13). Papillary carcinoma presenting in two young women as a single thyroid isthmus nodule was treated by subtotal thyroidectomy (12, 17). Total thyroidectomy and block dissection of cervical glands was performed on two patients (14, 16) and total thyroidectomy alone in one patient (15).

Papillary carcinoma is usually a slow-growing tumour of low-grade malignancy, often compatible with long life even without active treatment (Crile 1960). Occasionally papillary tumours assume aggressive properties after a long period of indolence. (Rawson and Leeper 1968). This unfavourable progression is an ominous sign and is usually associated with the appearance of spindle-cell or giant-cell metaplasia, as illustrated by the following case.

Patient No. 2 presented with an ulcerated soft tissue tumour overlying the left mandible (figure 29). He claimed that this "lump" had been present for about 15 years. There had been no discomfort until a rapid increase in size and ulceration in the previous six months forced him to seek medical attention. Biopsy revealed mixed papillary, follicular and spindle-cell patterns. The thyroid gland felt normal to palpation; x-ray of the left mandible was normal. Two months after the administration of radio-iodine (80 mCi) to destroy normal thyroid tissue, no uptake of radio-iodine could be demonstrated over the thyroid gland or the tumour. For this reason a second dose of radio-iodine was not administered.

HISTOLOGICAL CLASSIFICATION OF THYROID CARDINOMA IN 63 CASES ENCOUNTERED BETWEEN 1964 AND 1969 INCLUSIVE

Type	Cases	
	No.	per cent
Papillary	32	51 %
Follicular	25	40 %
Medullary	1	1.5%
Anaplastic	5	7.5%
TOTAL	63	100%

Fig. 24.

SEX DISTRIBUTION OF PATIENTS WITH THYROID CARCINOMA

SEX	TYPE OF CARCINOMA			
	Papillary	Follicular	Anaplastic	Medullary
Female	24	21	4	0
Male	8	4	1	1
TOTAL	32	25	5	1

Fig. 25.

TRIBAL DISTRIBUTION OF PATIENTS WITH THYROID CARCINOMA

(The figures in brackets indicate the per cent of the total population of each tribal group according to the 1962 population census -

Type of Carcinoma	Kikuyu (20%)	Luo (13%)	Abaluhya (13%)	Kisii (4.6%)	Kalengin (6%)	Kamba (11%)	Coast tribes (7%)	Total
Papillary	10	6	4	0	1	3	2	26
Follicular	9	2	3	2	4	0	0	20
Anaplastic	2	0	0	1	0	0	0	3
TOTAL	21	8	7	3	5	3	2	49

Fig. 26

Fig. 30. - Geographical Distribution of follicular carcinoma in Kenya.

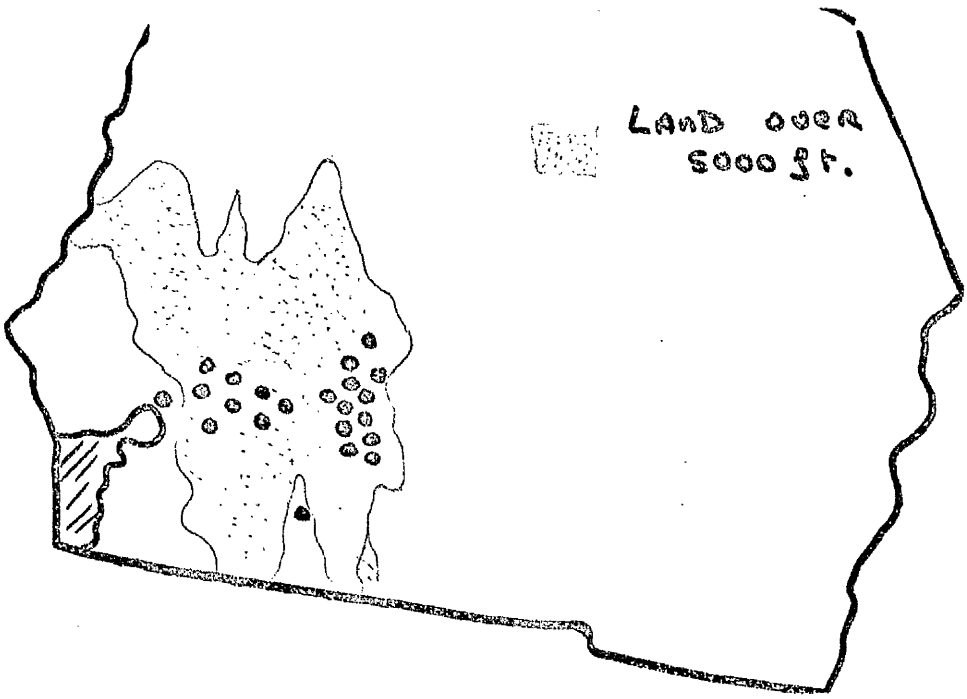
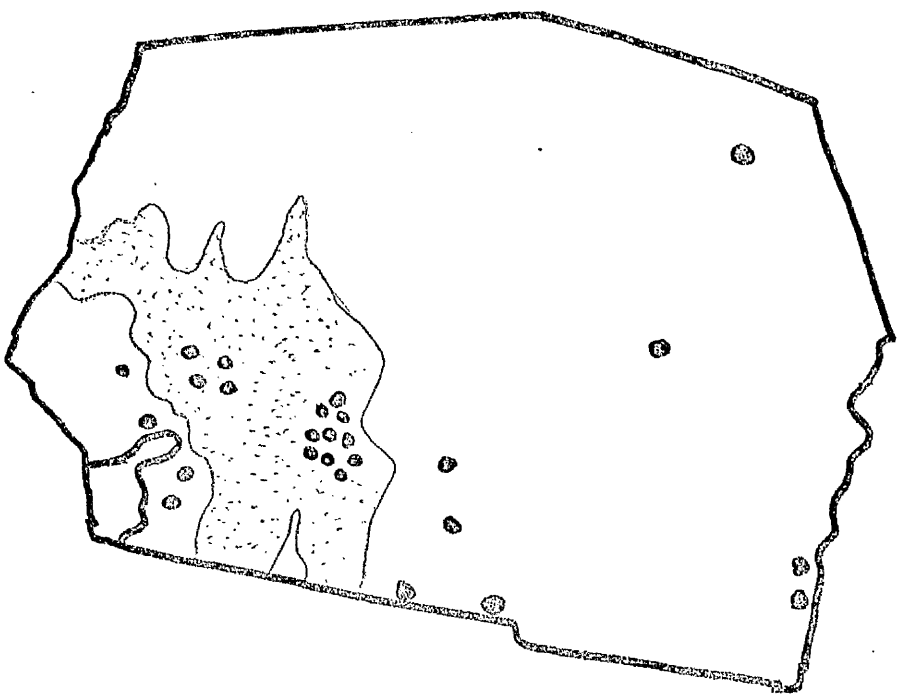


Fig. 31. - Geographical distribution of papillary carcinoma in Kenya.



Group Two.

The Histological Distribution of thyroid cancer is shown in table 23. The majority of tumours are histologically differentiated with an almost equal distribution between the follicular and papillary varieties. There were five cases of anaplastic carcinoma and one of medullary carcinoma in the series. Two cases of Burkitt's lymphoma involving the thyroid gland were found but are not included in this series. No examples of primary lymphosarcoma of the thyroid were found.

The Sex Distribution is shown in table 24. The female/male ratio was approximately 5/1 for all histological types.

The Tribal Distribution of 49 patients is shown in table 25. The percentage figures in brackets beside each tribal group refer to the percentage of that tribe of the total population of Kenya in the 1962 population census.

The largest number of tumours and the highest incidence were found in the Kikuyu tribe, which is the largest tribal group in Kenya. The remaining tumours are distributed among the other tribes but the numbers are probably too small to allow firm conclusions to be made. However, the following observations are worth making. Follicular tumours were found mainly in the highland tribes (Kikuyu, Kisii, Kalenjin), who live in areas where endemic goitre is known or presumed to exist. The tribal distribution of papillary carcinoma was more widespread, and in "lowland" tribes it was the predominant histological variety. The location of residence of each patient was plotted on a map of Kenya.

The Geographical Distribution of follicular carcinoma is indicated on figure 30, and of papillary carcinoma on figure 31. Follicular carcinoma occurred almost exclusively in areas when endemic goitre is known or presumed to exist. The geographical distribution of papillary carcinoma was more widespread.

DISCUSSION

The large majority of patients in my personal series presented late in the course of their disease with clinically obvious or suspect carcinoma and no diagnostic difficulty was encountered. Two patients had a clinically single thyroid nodule unresponsive to thyroxine therapy and hence carcinoma was suspected clinically (No. 8 and 12 table 22). One patient (No. 2, table 22) had a diffuse goitre, apparently simple clinically, suspected malignant surgically and confirmed so on histological examination. All but one patient with follicular carcinoma had locally invasive or metastatic disease; three had undergone some form of thyroid surgery in the past and one of these, at least, had an unrecognised localised follicular carcinoma at initial presentation. (No. 4, table 22). The sinister nature of the localised follicular carcinoma lies in its ability to masquerade as a benign adenoma and its true nature may only be revealed on the reappearance of local tumour or the appearance of distant metastases after a variable time interval. The clinical difficulty in differentiating the benign adenoma from the localised follicular carcinoma is matched by the difficulty found by the pathologist in deciding whether or not a particular adenoma is malignant. The margin of error will be reduced if the pathologist is fully informed of the clinical history, particularly anything suggestive of malignancy, and if a wide dissection is undertaken to include the capsule of the tumour. In addition invasion of blood vessels, particularly veins at the margin of the nodule may be the sole evidence of malignancy and will only be detected if multiple sections are taken for histological examination. When there is histological doubt one should try to ensure adequate long-term follow-up.

Carcinoma of the thyroid gland is not common.

Between 1957 and 1963, 44 malignant thyroid tumours were recorded by the Kenya Cancer Registry accounting for about one per cent of all malignant disease (Linsell, 1967). Elsewhere in Africa the reported incidence is comparable; 1.7 per cent in Kampala, Uganda (Davies 1961) and 1.3 per cent in Ibadan, Nigeria (Jackson and Reeve 1961). The incidence in the United Kingdom is about one per cent (Riddel 1958). In The present series of 66 cases occurred over a six year period, and is the largest yet reported from Africa. Shepherd and Manthy (1963) recorded 25 cases from Mulago Hospital, Kampala, collected between 1953 and 1962, and 37 cases were recorded in the University Teaching Hospital in Ibadan, Nigeria between 1960 and 1967 (Taylor 1968).

Although the same histological types of malignant thyroid tumours described in Europe and the United States of America are encountered in Kenya, Uganda and Nigeria, there appear to be differences in the frequency of the various histological types. The incidence of follicular carcinoma is highest in the African series (table 26). Variation in histological classification criteria may be responsible. In the Kenyan series every effort has been made to distinguish between papillary and follicular varieties, and to include all mixed tumours in the papillary group.

Aetiological factors in carcinoma of the thyroid gland are obscure and controversial, particularly the association between non-toxic goitre and carcinoma. In the past, an association between endemic goitre and thyroid carcinoma was considered important. Wegelin (1928) observed that thyroid cancer was ten times more common at autopsy in Berne, Switzerland, an endemic goitre area, whereas in Vienna and in Prague, areas of modest endemicity, the incidence of

INCIDENCE (%) OF VARIOUS HISTOLOGICAL TYPES OF PRIMARY MALIGNANT TUMOURS OF THE THYROID.

Centre	Number of Patients	% Papillary Carcinoma	% Follicular Carcinoma	% Medullary Carcinoma	% Anaplastic Carcinoma	% Malignant lymphoma	Other tumours
Kenya (Present Series)	63	51	40	1.5	7.5	-	
Uganda (Kampala) (1)	16	5	45	0	50		
Nigeria (Ibadan) (2)	37	35	54	0	11		
London (3)	243	38	24	6	25	-	7
Athens (4)	171	59.1	22	2.9	9.4		0.4
Helsinki (5)	321	44	26	4	25	1	
Aberdeen (6)	127	44	7.9	-	39.3	8.7	
Mayo Clinic (7)	885	61.1	17.7	6.5	14.7	-	-
Cali, (Columbia) (8)	113	42	33	4	18		

1. Shepherd and Manthy (1964)
2. Taylor (1968)
3. Taylor (1969)
4. Koutras (1971)
5. Lanberg (1971)
6. Stewart et al. (1972)
7. Woolner et al. (1961)
8. Wahner et al. (1966)

malignant thyroid tumours was intermediate. An apparent decrease in the incidence of thyroid cancer was observed in Switzerland, following the introduction of iodised salt (Wynder 1952). Benign and malignant thyroid tumours have been observed in experimental animals following prolonged periods of thyrotrophic hormone stimulation (T.S.H.) induced by a low iodine intake (Axelrad and Leblond 1953) and subtotal thyroidectomy (Doniach and Williams 1962). Moreover, clinical observation indicates that the suppression of endogenous T.S.H. by exogenous thyroxine may limit growth of differentiated thyroid carcinoma (Crile 1960: Balme 1964).

Recently, however, the widely held belief that nodular non-toxic goitre predisposed to the development of thyroid carcinoma has been modified. Pendergrast (1961) has shown that the marked fall in the incidence of goitre in the United States of America since the First World War, after the introduction of iodised salt has not been accompanied by a decrease in the mortality or morbidity from thyroid cancer. Moreover Saxen and Saxen (1954) had already reported thyroid cancer to be equally prevalent in goitrous and nongoitrous areas of Finland. Following the introduction of iodised salt in Berne, Switzerland, thyroid cancer has not decreased in incidence although the pattern has changed: a decrease in the incidence of follicular carcinoma was accompanied by a rise in the incidence of papillary carcinoma leaving the overall incidence unchanged (Walthard, 1961).
Wahner et al. (1966) have produced evidence of an association between follicular thyroid carcinoma and nodular endemic goitre in Cali, Columbia, South America and a clear lack of correlation between papillary carcinoma and endemic goitre. These observations suggest a possible positive correlation between follicular thyroid carcinoma and endemic goitre, a relationship which seems to be true in Kenya.

where follicular carcinoma was observed almost exclusively in subjects living in areas where endemic goitre is known or presumed to exist. An additional beneficial effect of the distribution of iodised salt in Kenya may be a reduction in the incidence of follicular carcinoma of the thyroid gland.

The definitive surgical treatment which offers the best chance of cure was not possible in many patients particularly those with follicular carcinoma, because of advanced metastatic disease at initial presentation. All patients received a maximum tolerable dose of thyroxine to suppress pituitary T.S.H. Those with papillary carcinoma may respond well to this treatment alone (Crile 1960). Radio-iodine may be used to limit the growth of metastatic deposits of follicular carcinoma in bone. Normal thyroid tissue must be totally removed either by surgery or an ablative dose of radio-iodine. The expense involved, mainly in transportation of the radio-iodine, to a developing nation with a limited health budget may be prohibitive.

THYROTOXICOSIS.

Introduction.

Thyrotoxicosis is considered to be rare among the indigenous population of Africa. During the past decade, approximately 50 cases were recorded in the world literature. Trowel (1960) saw two indigenous African patients with thyrotoxicosis in 30 years of medical practice in East Africa. Gelfand (1962) reported the first Rhodesian African patient in whom he was certain of the diagnosis. Thyrotoxicosis is rare among the indigenous populations of Uganda (Patel 1964), Nigeria (Davey and Ogunlesi 1963), South Africa (Dancaster 1970) and Zambia (Lowenthal 1971). In Kenya, thyrotoxicosis was thought to be extremely rare until Wright (1967) described eight cases. Taylor (1968) and Dancaster (1970) have suggested that the rarity of thyrotoxicosis in the African is an immunological phenomenon related to an inability of the African to produce autoimmune antibodies. This problem has not been adequately studied because of the small numbers of patients encountered by each observer, and the total lack of data on auto-antibody formation in African thyrotoxic patients.

Thirty one African patients with thyrotoxicosis were reviewed at a thyroid clinic in Nairobi (table 1). In 25 patients thyroid auto-antibodies have been measured. In addition the thyroid glands of 30 Africans with thyrotoxicosis and 30 appropriately matched Caucasians have been assessed for the histological features of auto-immune thyroid disease (lymphocyte and plasma cell infiltration).

Patients.

All African patients were investigated and treated at the Kenyatta National Hospital, Nairobi. The diagnosis was established in all patients using the "clinical diagnostic index" described by

Crooks et al. (1959) and by the clinical response to antithyroid drugs. Confirmation of the diagnosis was obtained in 23 patients by estimation of the serum protein bound iodine (P.B.I.). The characteristic histological appearances of toxic diffuse goitre (Graves's disease) confirmed the clinical diagnosis in two patients in whom the P.B.I. was not estimated. Additional investigations in eight patients included the measurement of the 4 and 48 hour thyroid gland uptake of radio-iodine or the thyroid clearance rate (Wayne 1960). The sex and age of each patient was noted (in about one third of patients the age was not known; in these cases the age was "assessed"). Goitre consistency (diffuse or nodular) was assessed by palpation and its duration recorded. The presence of ocular signs was noted, using the criteria described by Crooks et al. (1959).

There were 24 female and seven male patients whose ages ranged from eight to 60 years. Most were aged between 25 and 45 years. Twenty five patients (20 female and five male) were considered to have Graves's disease (toxic diffuse goitre) on the basis of having a diffuse goitre of recent onset (< 2 years). Unequivocal exophthalmos was present in six female and four male patients with toxic diffuse goitre. One female patient had pretibial myxoedema and exophthalmos.

Four female patients had a long standing (> 5 years) multinodular goitre; all were more than 50 years of age, and two presented with cardiac failure resistant to therapy with digoxin and diuretics. One elderly male patient who had a solitary thyroid adenoma ('hot' nodule) developed atrial fibrillation and sustained a fatal cerebral embolism. After courses of antithyroid drug therapy, lasting between three and twelve months, subtotal thyroidectomy was

performed in ten patients. One female patient had recurrent thyrotoxicosis following thyroidectomy two years previously - detailed case histories are included in the appendix.

Immunological Studies.

Serum was obtained from 25 patients before and during treatment with antithyroid drugs. In Nairobi all sera were tested for antibody to thyroglobulin by a tanned red blood cell haemaglutination method, using Burroughs Wellcome reagents and a microtiter apparatus (Goldin et al. 1965). The sera were frozen and sent by air to the Department of Pathology, Western Infirmary, Glasgow, and tested for antibody to thyroglobulin (Fulthorpe et al. 1961) and antibody to thyroid microsomes (Holborow et al. 1959).

Histological Studies.

Thyroid tissue was available for study from ten patients in this series who had undergone subtotal thyroidectomy and from 20 African thyrotoxic patients similarly treated at the Kenyatta National Hospital, Nairobi, between 1963 and 1967. Sections of thyroid tissue from 30 Caucasian thyrotoxic patients were obtained from the Department of Pathology, Royal Devon and Exeter Hospital, Exeter, Devon. The patients were matched with the above African group for sex, and as closely as possible for age, duration of antithyroid drug therapy before surgery, exophthalmos and consistency of goitre. Round-cell infiltration (figure 30) was assessed in all cases by counting the number of low power fields containing round-cell aggregates out of 50 fields for each gland (Buchanan et al. 1962).

Fig. 32. - Round cell infiltration on a thyrotoxic gland.

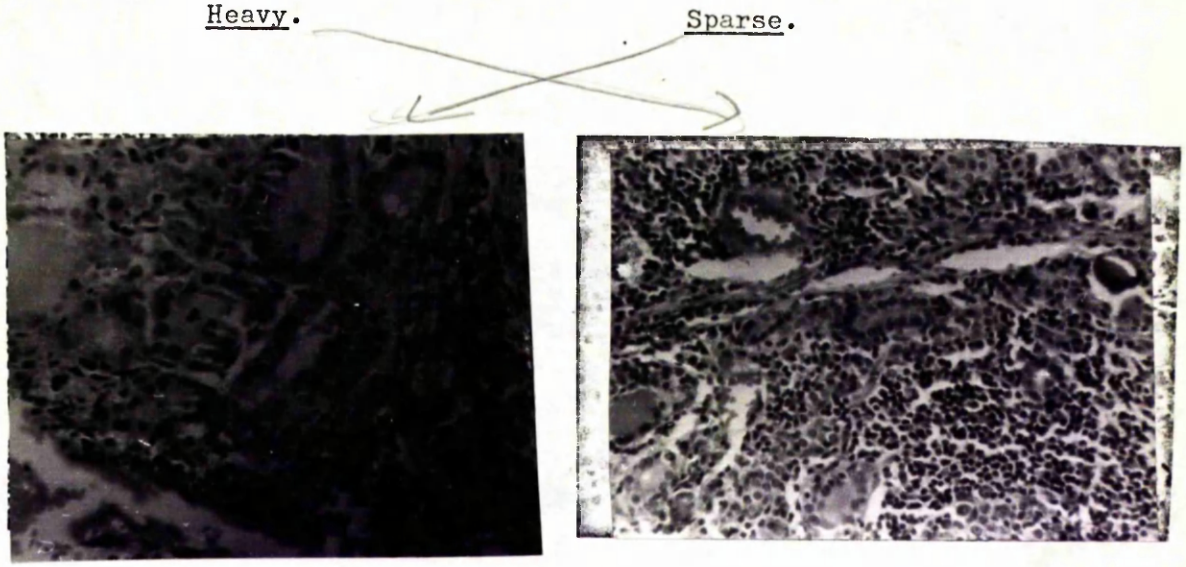
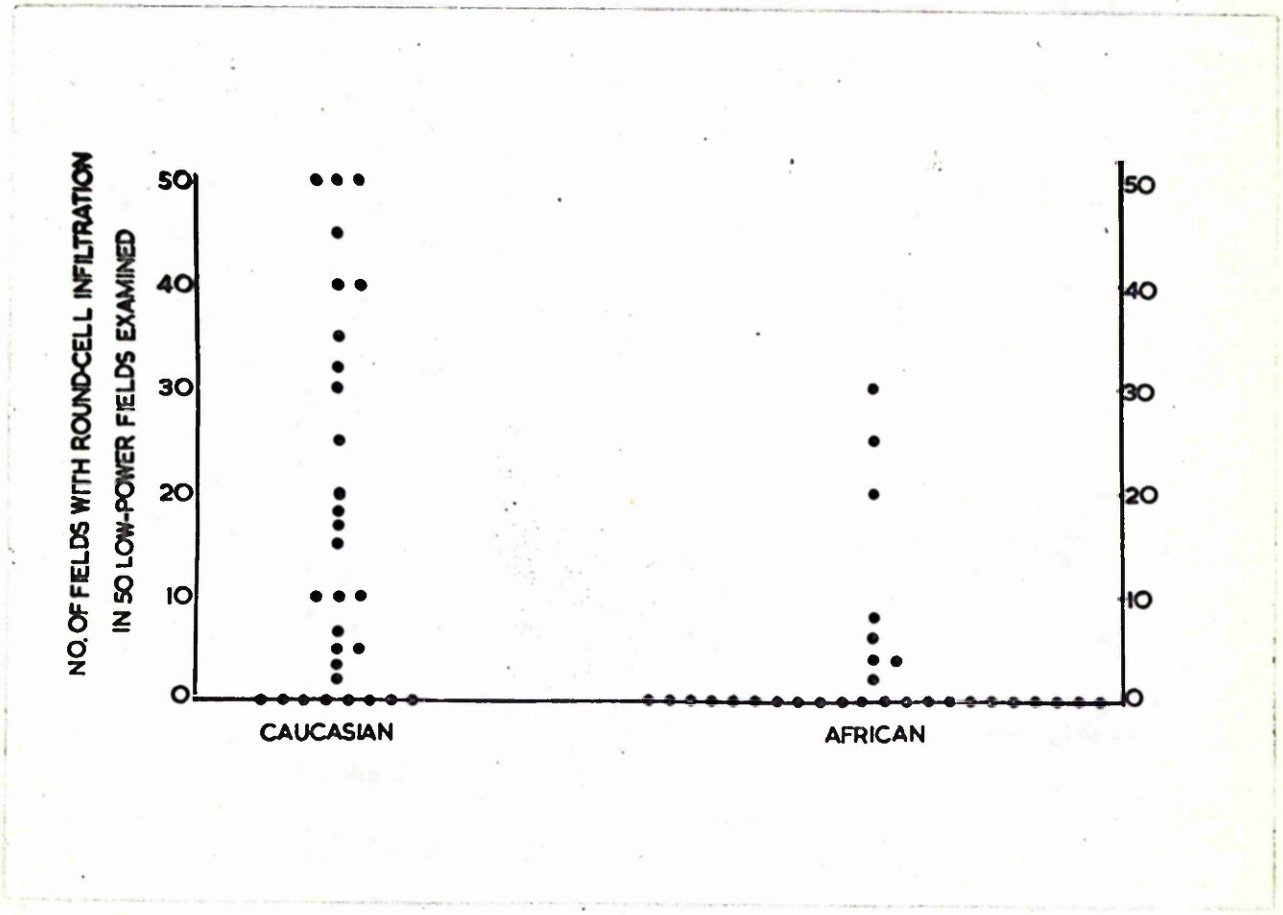


Fig. 33. - Round cell infiltration of the thyroid gland in 30 Caucasian and 30 African thyrotoxic subjects.



Results

Antibody to thyroglobulin was detected in the serum of one patient and antibody to thyroid microsomes in the serum of four patients. In two patients with 'microsomal' antibody, no round-cell infiltration was present in post-operative thyroid gland sections. Round-cell infiltration was present in the thyroid gland sections of 22 (70 per cent) Caucasian patients and in eight (27 per cent) African patients (figure 31).

Discussion.

In no patient was the diagnosis in doubt. Thyrotoxicosis was associated with a diffuse goitre in 26 patients and a nodular goitre in five patients. Exophthalmos was present in 50 per cent of patients with toxic diffuse goitre and was accompanied by pretibial myxoedema in one patient. Thyrocardiac disease (congestive cardiac failure, atrial fibrillation) occurred only in elderly patients with toxic nodular goitre. No unusual symptoms or signs were recorded. Thus in the African the clinical manifestations of thyrotoxicosis are similar to those observed in other races.

In Durban, Natal, thyrotoxicosis is 30 times more common in the Indian and Caucasian populations than in the Bantu (Dancaster 1970) and in Southern Rhodesia, it is confined almost exclusively to the Caucasian race (Shee and Houston 1963). Although the experience of 31 patients within two years represents a considerable increased incidence over the reported incidence from elsewhere in Africa, it is clear that thyrotoxicosis is still an uncommon disease among the indigenous populations of Kenya.

Reasons for the racial differences in the incidence of thyrotoxicosis must be related to the pathogenesis which although not completely clarified seems to be related to a disturbance of immune tolerance. The presence of thyroid auto-antibodies and round cell infiltration of the thyroid gland in a high proportion of Caucasian thyrotoxic patients and the close clinical and immunological associations between thyrotoxicosis and other auto-immune diseases indicate that auto-immunisation plays an important part in the aetiology of thyrotoxicosis. (Anderson et al. 1964). In addition the abnormal thyroid stimulator (L.A.T.S.) found in the serum of a high proportion of patients with Graves's disease, may be an auto-antibody to the thyroid (McKenzie 1967).

In the present study the incidence of thyroid round cell infiltration in the Caucasian group was similar to the incidence reported by other workers (Roitt and Doniach 1960, Buchanan et al. 1962). The incidence and degree of thyroid round cell infiltration was significantly lower in the African group than in the Caucasian group. Circulating thyroid auto-antibodies were detected in 16 per cent of African patients, in contrast to the reported incidence of between 40 per cent and 70 per cent in series of Caucasian thyrotoxic patients (Roitt and Doniach 1960, Bastenie et al. 1967).

These studies indicate that the predisposition to form thyroid auto-antibodies is weak in the African thyrotoxic patient. In this context it is worth noting that all varieties of auto-immune diseases are considered to be uncommon or rare among indigenous African populations (Greenwood 1968) and auto-immune thyroiditis (spontaneous myxoedema and Hashimoto's thyroiditis) seem to be extremely rare. As already noted, 600 consecutive thyroidectomy specimens from Kenya African patients were studied for round cell

infiltration and in one case the histological features of Hashimoto's disease were observed: 550 African patients with a variety of thyroid disorders were reviewed by observers experienced in thyroid disease over a two year period (with access to P.B.I. estimations and with facilities for the estimation of anti-thyroglobulin and performing radio-iodine tests) and no cases of spontaneous myxoedema or Hashimoto's disease were detected. Clearly the immunological system of the indigenous African is at present either resistant to or is not exposed to antigenic stimuli which initiate and maintain auto-antibody formation.

Studies in the Caucasian race have demonstrated that the tendency to develop auto-immune thyroid disease is familial and probably genetically determined. For example the relatives of patients with Hashimoto's disease (Hall et al. 1960, Roitt and Doniach 1967) and of patients with thyrotoxicosis (Saxen 1965, Evans et al. 1967) have a high incidence of thyroid antibodies. Hashimoto's disease (Irvine et al. 1961, Zaino and Cerra, 1964) and thyrotoxicosis (Hassan et al. 1966) have been reported in monozygotic twins. It is therefore possible that the rarity of auto-immune thyroid disease and indeed auto-immune disease in general, is solely the result of a genetically determined racial characteristic. Trotter (1962) has suggested that the cause of thyrotoxicosis will be found in a combination of genetic and environmental factors. The observation that auto-immune thyroid disease is equally common in the black and white races of North America would seem to support the role of an environmental factor, which might either act to provoke the emergence of auto-immune disease in western societies, or be a factor which prevents the emergence of auto-immune disease in indigenous African communities.

It is tempting to invoke the stresses and strains of modern civilisation as an important factor. While it is acknowledged that the onset of thyrotoxicosis is often preceeded by a period of emotional stress it has not been established that "stress" is responsible for the onset of thyrotoxicosis. Moreover emotional stress is not the prerogative of western society.

The second possibility that a factor present in the African environment acts to prevent the emergence of auto-immune disease is an intriguing possibility. Epidemiological surveys have suggested an association between parasitic infection and a low incidence of auto-immune disease (Greenwood 1968 b), and Greenwood et al. (1969 a, b) have demonstrated prolonged suppression of spontaneous auto-immune disease of N.Z.B. and (N.Z.B. x N.Z.W.) hybrid mice, and adjuvant arthritis in rats, (Greenwood et al. (1969 b) following infection with malaria. In humans, chronic infection with malaria is associated with immunological phenomena, which may produce disease. For example immune complex nephritis has been described in association with chronic infection with P. malariae (Allison et al. 1969) and malaria is an important aetiological factor in Burkitt's lymphoma. Although the role of malaria in this disorder has not been precisely defined it may act by suppressing the immune responses of the host and allow a virus (the E. B. virus) to assume an oncogenic role, (Burkitt 1969). Malaria has in the past been used empirically as a treatment for a variety of conditions, notably the connective tissue disorders and beneficial results are still claimed (Corelli 1968) although generally this form of treatment has fallen into disrepute. It seems possible, therefore, that repeated parasitic infections, particularly malaria, may contribute to the apparently low incidence

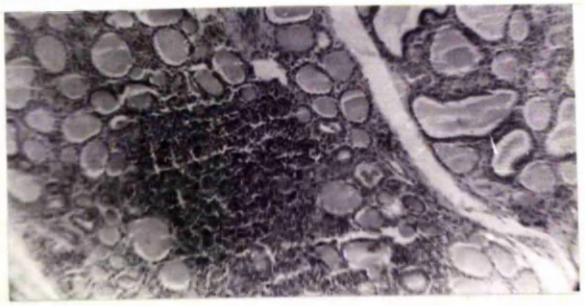
of auto-immune disease in the indigenous African. The effects of chronic exposure to malaria are generally undesirable. A beneficial effect is, perhaps, freedom from auto-immune disease.

If there is any truth in this hypothesis a rise in the standard of living with a concomitant reduction in parasitic disease may be followed by a gradual increase in the indidence of auto-immune disorders, including thyrotoxicosis. However a more immediate rise in the incidence of thyrotoxicosis may occur in Kenya and this rise may be a direct result of the introduction of iodised salt for the prophylaxis of endemic goitre. A suspicious rise in the incidence of thyrotoxicosis occurred in the U.S.A. following the distribution of iodised salt (Hartsock, 1926, McClure 1934) and a rise in the incidence of toxic nodular goitre has been recently observed in Tasmania, following the iodisation of bread. (Connolly et al. 1970). Elsewhere, endemic goitre may predispose to the development of toxic nodular goitre (Saxen and Saxen 1954), but not in Kenya, where toxic nodular goitre is rare at present.

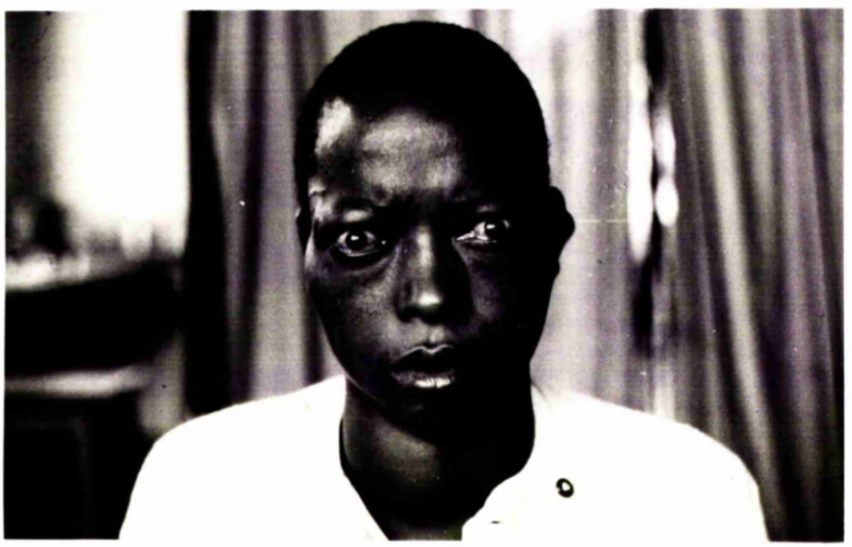
The treatment of thyrotoxicosis in Kenya should be along conventional lines with antithyroid drugs in all patients initially. Unfortunately treatment with radio-iodine is limited by post-radiation hypothyroidism which is a serious disadvantage in situations where adequate long term follow up of patients is difficult. However the low incidence of lymphoid infiltration of the thyroid tissue of Africans with thyrotoxicosis suggests that the incidence of post-operative hypothyroidism may be low in African patients.

THYROTOXICOSIS -- CASE REPORTS.

Patient Mansur S. Thyroid Clinic No. 482. Male Arab. 39 years of age. Graves's disease. Score + 34. Serum P.B.I. 11.0 ug./100 ml. Positive thyroid antibodies: (++ c.f.). Partial thyroidectomy. Histology - lymphocytic infiltration.

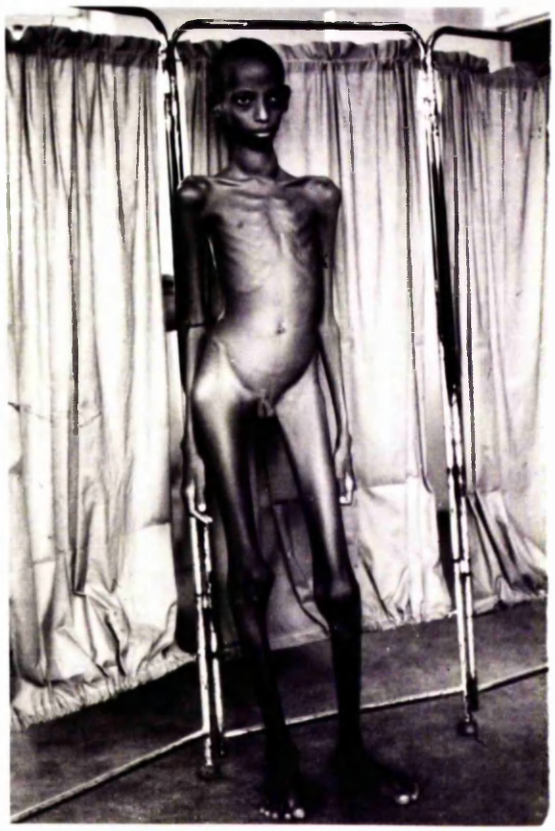


Lymphocytic Infiltration.

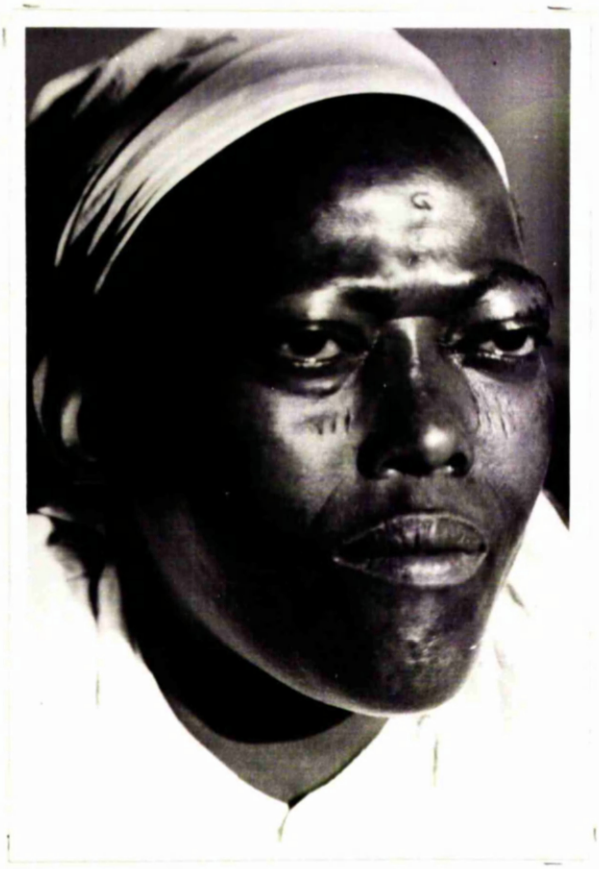


Patient Margaret N. Thyroid Clinic No. 381. Kikuyu female. 40 years of age. Graves's disease. Score +20. P.B.I. 12.0 ug./100 ml. Thyroid clearance 870 ml./hr. Negative thyroid antibodies. Treatment - antithyroid drugs for six months. No relapse following withdrawal after one year.

Patient Usuf. Thyroid Clinic No. 322. Boran male, 14 years of age. Graves's disease. Score + 32. P.B.I. 21.6 /ug./100 ml. Negative thyroid antibodies. Thyroidectomy. Negative lymphocytic infiltration.



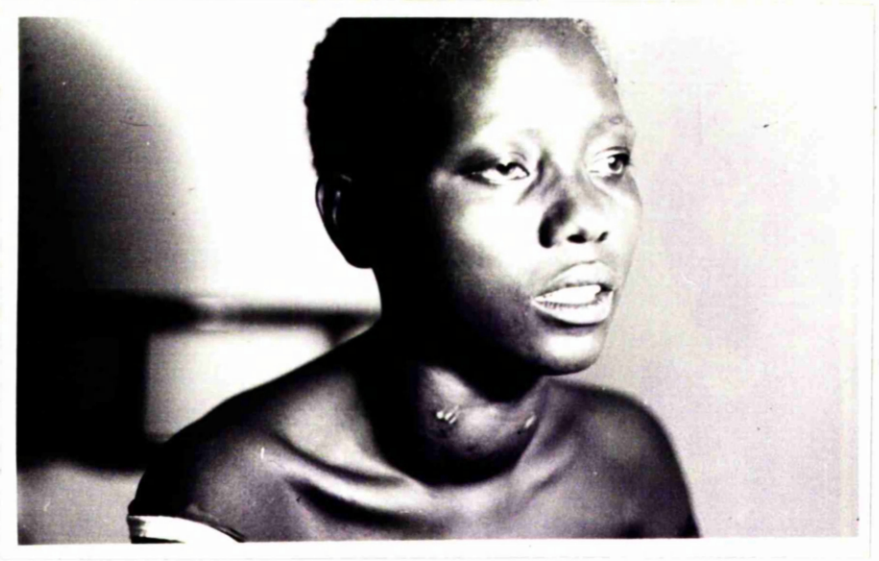
Patient N.K. Thyroid Clinic No. 85. Female Kikuyu. Age 30 years. Graves's disease. Score + 33. P.B.I. 9.5 µg./100 ml. Diffuse goitre, mild exophthalmos, pretibial myxoedema. Partial thyroidectomy. Negative thyroid antibodies, negative lymphocytic infiltration.



Patient Ruth C. Thyroid clinic No. 320. Female, 35, Nandi, Graves's disease. Bilateral exphthalmos, small diffuse goitre. Thyroid score + 20. Serum P.B.I. 8.4 µg./100 ml. Negative thyroid antibodies. Treatment - antithyroid drugs.

Patient Taabu D. Thyroid Clinic No. 100. Kikuyu female. 8 years of age. Graves's disease. Score + 30. P.B.I. 16 µg./100 ml. Relapse of thyrotoxicosis after one year antithyroid drug treatment. Negative thyroid antibodies. Negative lymphocytic infiltration. Partial thyroidectomy.

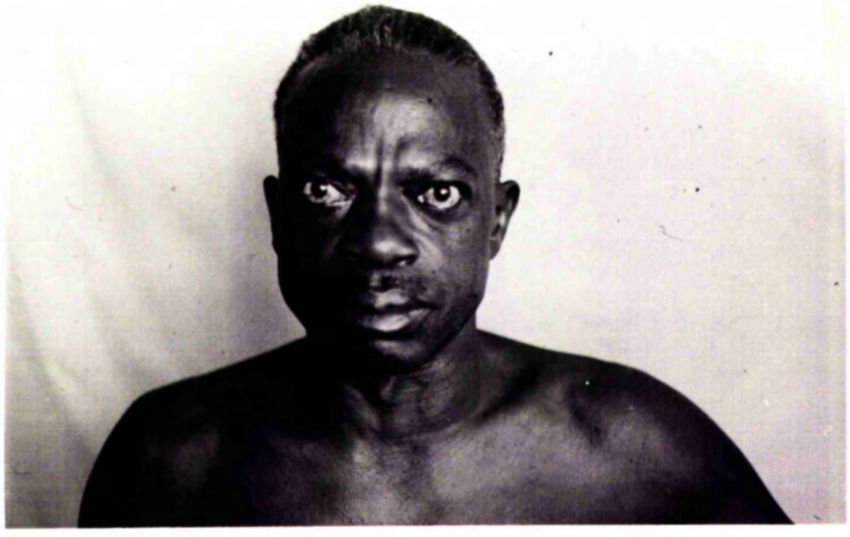
Patient Kavisu M. Mkamba female. 20 years of age. Graves's disease. Score + 23. P.B.I. 19.6 µg./100 ml. 4 hr. uptake 60 per cent. 48 hr. uptake 60 per cent. 48 hr. P.B.^{131}I, 1.04 per cent. Thyroid clearance 206 ml/hr. Negative thyroid antibodies. Treatment - carbimazole and thyroxine.



Patient Gatubu M. Thyroid Clinic No. 106. Kikuyu female. 32 years of age. Graves's disease. Score + 32. P.B.I. 8.5 µg./100 ml. Negative thyroid antibodies. Thyroidectomy. Negative lymphocytic infiltration.

Patient Joyce W. Thyroid Clinic No. 341. Kalengin female. 46 years of age. Toxic nodular goitre. Score + 20. P.B.I. 9.5 ug./100 ml. 4 hr. ^{131}I uptake 58 per cent. 48 hr. 55 per cent. P.B. ^{131}I at 48 hrs. 0.54 per cent. Negative thyroid antibodies. Thyroidectomy. Negative lymphocytic infiltration.

Patient M.W. Thyroid Clinic No. 340. Luhya male. 47 years of age. Graves's disease. Score + 15. P.B.I. 10.8 ug./100 ml. 4 hr. ^{131}I uptake 91 per cent. 48 hr. uptake 78 per cent. 48 hr. P.B.^{131}I, 0.6 per cent. Negative thyroid antibodies. Partial retrosternal goitre with venous obstruction. Good response to antithyroid drugs and thyroxine.



Patient Juliet C. Thyroid Clinic No. 306. Kikuyu Female. 40 years of age. Graves's disease. Unilateral (R) exophthalmos, (26 mm. (R), 19 mm. (L)). 50 g. diffuse goitre. Score + 29. P.B.I. 10.3 ug./100 ml. Thyroid clearance 162 ml./hr. Weakly positive immunofluorescence for complement fixing (c.f.) antibody. Treatment - antithyroid drugs.

THYROID DISEASE IN KENYA

SUMMARY

This thesis is essentially a general account of thyroid disease in Kenya based on a series of epidemiological, functional, clinical, pathological and immunological studies.

Simple goitre is the commonest variety of thyroid disorder in East Africa. In Kenya and in Tanzania the incidence reaches endemic proportions in certain highland communities. Studies of thyroid function and iodine nutrition in selected subjects living in communities with a high goitre incidence are reported in this thesis. The hallmarks of iodine deficiency, namely a low excretion of iodine in the urine and a high thyroidal uptake of radio-iodine were found in the goitrous and non-goitrous inhabitants of the endemic regions. Patients with simple goitre from the Central Province of Kenya attending a special clinic were studied and found to be in general moderately iodine deficient. However, a relatively low utilisation index (P.B.I./A.I.U. ratio) in goitrous subjects suggests that a defect in the utilisation of iodine by the thyroid may aggravate the effects of the iodine deficiency. The possibility that the defect is caused by an environmental agent is discussed.

Radiothyroxine studies confirmed that the amount of thyroxine degraded daily is low in endemic goitre subjects who have low serum P.B.I. values. The fractional turnover rate of thyroxine was increased in some subjects and the significance of this finding is discussed.

The management of patients who have established simple goitre should be conservative. A study is described in which the efficacy of thyroxine is confirmed. Surgery should be confined to those with pressure symptoms or signs, or where malignancy is suspected. The incidence of occult malignant disease was found to be highest in patients with a clinically single nodule. If careful

follow-up cannot be assured then the nodule should be removed for histological inspection.

A retrospective analysis of 593 surgical thyroid specimens confirmed macrofollicular colloid goitre as the dominant histological type of simple goitre. However, extensive areas of diffuse parenchymatous hyperplasia were found in about 30 per cent of glands examined. This appearance indicates ongoing stimulation by T.S.H., and is potentially reversible with inorganic iodine or thyroid hormone.

The clinical details of 18 patients with carcinoma of the thyroid gland, and the pathological features of 63 cases are described. The results of treatment were poor because patients in Kenya present late in the course of the disease usually with wide-spread metastatic deposits. The relatively high incidence of follicular carcinoma (40 per cent) may be due to the prevalence of endemic goitre.

The clinical manifestations of thyrotoxicosis are described in 25 African patients with toxic diffuse goitre (Graves's disease) and six with toxic nodular goitre. Antibody to thyroglobulin was detected in the serum of one patient and antibody to thyroid microsomes in four patients. Round cell infiltration of the thyroid gland was present in 27 per cent of 30 African thyrotoxic patients and 73 per cent of appropriately matched Caucasian patients. It is suggested that the low incidence of thyrotoxicosis in the African race is related to an inability to form thyroid autoantibodies, a phenomenon reflected in the rarity of Hashimoto's thyroiditis and spontaneous myxoedema in Africans.

CONCLUSIONS

1. The prevalent endemic goitre in the highland provinces of Kenya and in Nwezi, Tanzania is due mainly to iodine deficiency. In Kenya there may be an additional factor operating in some cases.

2. The management of established simple goitre should be conservative if possible. The single nodule must be carefully assessed and removed for histological analysis when follow-up cannot be assured.

3. Patients with thyroid carcinoma usually present with advanced disease and effective treatment is difficult. Follicular carcinoma may be more prevalent because of environmental iodine deficiency and endemic goitre.

4. Hashimoto's thyroiditis is rare and thyrotoxicosis uncommon in indigenous Africans in Kenya. The predisposition to form thyroid antibodies is low in Africans with thyrotoxicosis. When spontaneous remission does not occur thyroidectomy is the treatment of choice.

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