Micronutrient deficiencies in Ethiopia and their inter-relationships

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Micronutrient deficiencies in Ethiopia and their inter-relationships

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STELLINGEN

I

The belief that anaemia is common in the ensete staple areas is not true because ensete is always eaten in conjunction with kale which is rich in iron. (dit proefschrift)

II

The high prevalence of vitamin A deficiency in the grain staple areas (cropping zone) could be reduced by encouraging the cultivation and consumption of vitamin A-rich foods. (dit proefschrift)

III

Relief food in Ethiopia should be checked for its nutritional adequacy and measures taken to correct any shortcomings. (dit proefschrift)

IV

More schools for the blind should be opened in Ethiopia and facilities in existing schools improved. (dit proefschrift)

V

The consequences of the high prevalence of iodine deficiency in Ethiopia are poorly understood. (dit proefschrift)

VI

Micronutrient deficiencies should not be approached in isolation from the problems of infection and infestation. (dit proefschrift)

VII

While the production and consumption of teff in the USA is increasing, it is paradoxical that the policy in Ethiopia is the opposite.

VIII

Ethiopia shall soon stretch out her hands unto God. (Psalm 68: 31)

IX

Ethiopia is a complex and beautiful country. The original garden of Eden, cradle of the human race, the oldest Christian country and the source of the Blue Nile ..... it is now blighted by famine and civil war. (Philip Marsden-Smedley, 1990)

X

Large and expensive projects funded by Northern countries are often not in the interest of people in the South but of the donors themselves.

XI

Dumping of radioactive and other industrial waste in developing countries is worse than a declaration of war because there is no end to the genocide.

XII

Human capital is a more important factor for achieving economic growth than physical capital. (Richard Jolly, 1989)

XIII

Peoples of developing nations should rely, as much as possible, on their traditional practices and norms to avoid dependency on others.

XIV

Half a century from now, will there still be a need for a commitment to eliminate micronutrient deficiencies in the world within a period of 10 years?

Proefschrift Zewdie Wolde-Gebriel
Mironutrient deficiencies in Ethiopia and their inter-relationships.
Wageningen, 7 April 1992.

To Yewediaset, Yilma, Simon and Brook

CONTENTS

PREFACE

After graduating from Gondar Public Health College and serving for three years in Health Centres of the Ministry of Health, I had the aspiration and determination to go to Medical School. However, I was contacted by the late Derek S. Miller of Queen Elizabeth College (now King's College again), University of London and was asked if I would be interested in joining a research project in Gondar. During this time, I became interested in research, in nutrition and the challenges they both offered. This lead to my Master's programme in nutrition at Queen Elizabeth College and to my subsequent position at the Ethiopian Nutrition Institute (ENI). During this time, I came in contact with many people working in the field of nutrition and amongst them were Professor Joseph Hautvast and Dr Clive West. During the course of discussions with Professor Hautvast, staff development at ENI was one of the major topics raised and as a result, a number of staff of ENI participated in courses organized by the International Agricultural Centre in Wageningen. Possibilities of admission of some of the senior staff to PhD courses in his Department were also raised. So, my gratitude to Professor Hautvast is not limited to his guidance and support during my current research work but also encompasses the long standing devotion and concern he has shown to the growth and development of ENI in particular and of nutrition programmes in Ethiopia in general. I am also grateful to his wife Marlou for her hospitality.

It is now over a decade since I have come to know you Clive. You can not imagine how I feel to be a student under the supervision of an old colleague. Not to mention how much I have learnt from you, I am one of your admirers for your being very hard working and openness. I believe that the momentum we have gathered now should be developed further and sustained for more research in the future. From the day I arrived in Wageningen to start my research work, I have received unlimited support and guidance from you for which I will always be very grateful. I am also very grateful to his family for allowing me to work with Clive on my research in the time which he should have been spending with them.

Despite the enormity of the task, the field work went smoothly and according to plan. The credit for this goes to all those who were actively involved in the various studies. I would therefore like to express my sincere appreciation and gratitude to the staff of ENI in general and to the following in particular: Haile Gebru and Asnakech Mekonnen of the Computer Unit; Amha-Selassie Tadesse, Getachew Zenebe, Petros Gabre, Yilma Habteyes, Chernet Aboye and Almaz Gonfa of the Laboratory Division; Tezera Fisseha and Bantirgu Haile Mariam of the Medical Division; Tsegnesh Tsegaye, Genet Gustavo, Zewdalem Asefa, Zemen Meshesha, Wossenie Zewdie of the Nutrition Division, and Tekle Yohanis Kuko, Sisay Tisasu, Bagegn Damtew, Eshetu Negash, Gebeyehu Tefera, Fekadu Demissie, Kenenessa Bedada and Baye Akale of the Administration Division.

Support has been received from the National Health Research Institute in the analysis of thyroxin-binding globulin and acquisition of supplies not forgetting the dry ice.

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I am very much indebted to the directors of schools for the blind and the schools where the intervention studies were carried out and their staff for the remarkable cooperation and assistance I received from them, and village elders and chiefs in Melkaye who gave me every assistance. I very much appreciated the cooperation of the children who took part in the studies and of their parents.

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I very much appreciate and thank Etetu Gudeta from ENI for typing some of the earlier manuscripts. I also thank Ben Hiddink, Wilma de Maar, Lous Duym, Grietje van der Zee and other members of the Department of Human Nutrition for their assistance. Some of the laboratory analyses were carried out in the Department of Human Nutrition in Wageningen. I am very grateful to those who helped me with the analyses and my special thanks go to Peter van de Bovenkamp, Jan L. Harryvan, Annet Rodenburg, Jannie Bos, Cock Germing-Nouwen. I also want to thank H. Tietmma of Hoechst Holland for the analysis of the immunoglobulin and serum proteins.

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Some of the laboratory analysis would have not been possible had I not received funds from the United States Aid for International Development for which I am very grateful.

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This work would have not reached the present stage if I had not had the support and encouragement of my wife, Yewediaset Zeleke; my brother, Yilma Wolde-Gebriel and my sons, Simon and Brook. I appreciate your determination and perseverance.

Wageningen, March 1992 Zewdie Wolde-Gebriel.

CHAPTER 1

Introduction

Amongst the features characteristic of developing countries, high rates of morbidity; high rates of infant, child and maternal mortality; poverty; and ignorance are very prominent. In the majority of these nations, there is a population explosion while food production is on the decline. In some, civil wars and recurrent droughts have exacerbated the situation and brought about the need for continuous food aid. Unfortunately, welfare and funding agencies from industrialized countries have often attached many strings to their aid programmes and shown limited interest in funding long term development programmes. The ever declining prices of raw materials and increasing cost of oil and manufactured goods resulting in economic recession, high debt and interest rates, and structural adjustments have made the situation worse in these countries over the last few decades. Nutritional deficiencies which are good indicators of the general health status of nations have become more prevalent in developing countries during this period. Next to protein-energy malnutrition, deficiencies of iodine and of vitamin A and nutritional anaemia are the commonest nutritional problems in these countries.

Ethiopia

Ethiopia is a highland country with an area of 1.2 million square kilometres of which 75% is more than 500 metres above see level. Based on the projection made after the 1984 census, the current population is estimated to be 52 million increasing at an annual rate of 2.9%. Crude birth rate is 44.7 per 1000, crude death rate 19.8 per thousand and infant mortality rate is 155 per thousand live births. Over 90% of the people live in rural areas with agriculture being the main activity. Illiteracy, infectious and nutritional diseases, unemployment, recurrent drought and civil strife are the primary problems of the country.

Vitamin A deficiency

Vitamin A is a fat soluble vitamin obtained from animal sources and also from provitamin A carotenoids of plant origin. It is involved in vision, cell differentiation, synthesis of glycoproteins and mucous secretions from epithelial tissues, reproduction, growth and immune processes. When there is deficiency of vitamin A, signs are manifested in the eyes and epithelial tissues.

Night blindness was recognized as early as 1500 BC and different ways of treating cases were recorded in ancient Egypt. According to the Papayrus Ebers and the London Medical Papyrus, night blindness was treated by squeezing cooked liver into the eyes. In ancient Greece both the topical application and the consumption of cooked liver was practised following the experience in Egypt (*85*).

In 1915 McCollum and Davis (*43*) showed that butter and egg yolk contained an essential growth factor for ıats and gave the name "fat soluble A" to this factor. During the same year, Osborn and Mendel (*59*) identified a similar fat soluble growth factor in cod liver oil and butter. In the 1920s, Moore (*54*) demonstrated that ß-carotene present in plant tissues was converted biologically to vitamin A and stored in the liver. During this same period the effect of vitamin A on appetite, growth and cell differentiation were also elaborated (*12,13,44,84*). In 1925, Fridericia and Holm (*26*) described the need for vitamin A for the regeneration of visual purple, while the visual recycling process was later worked out by Wald and co-workers (*20,81*).

Night blindness is the first symptom of vitamin A deficiency because of the role of vitamin A in light perception at low light intensity by the rod cells of the retina. As the deficiency state worsens, the epithelial layer of the cornea becomes dry and non-wettable but sometimes, this condition is not specific to vitamin A deficiency (*40,66*) as it can be manifested by other environmental factors. In 1860, Hubbenet (cited in *70*) described the occurrence of epithelial dryness and scaling of the conjunctiva and the cornea in night blind and malnourished subjects who responded positively to ingestion of beef liver. Later in 1863, Bitot (also cited in *70*) described white foamy patches which exist along with night blindness in the conjunctiva. As a result, these patches are now referred to as Bitot's spots and are one of the most important signs of vitamin A deficiency. Another sequela of vitamin A deficiency is decreased production of tear and goblet cells with subsequent keratinizing metaplasia and haziness of the cornea. The keratinized corneal tissue can also be a good growing medium for bacteria and viruses which can aggravate the process leading to keratomalacia and blindness. The keratinized cornea eventually becomes ulcerated and heals gradually resulting in a corneal scar or it perforates whereby the inner segments of the eye ball prolapse thus finally resulting in irreversible blindness.

Recent studies have demonstrated that vitamin A plays an important role in reducing morbidity, particularly of respiratory and diarrhoeal diseases, and of mortality (*2,10,52,62,67-69*). These effects are almost certainly mediated through the action of vitamin A on the immune response (*83*).

Vitamin A deficiency is exacerbated by low intake of other nutrients particularly protein and fat (*4,70*). Children who suffer from vitamin A deficiency are more likely to suffer from other nutritional deficiencies not only because nutritional deficiencies occur together but also because of the influence of vitamin A on the metabolism of other nutrients. As mentioned above, the two micronutrients most commonly deficient in developing countries in general, apart from vitamin A, are iodine and iron. Thus the inter-relationship between the nutrition and metabolism of vitamin A, iodine and iron are reviewed below while results of studies in Ethiopia on these nutrients are presented in subsequent chapters in this thesis.

Iodine deficiency disorders

Iodine deficiency disorders (IDD) comprise the subtle form of the enlargement of the thyroid gland commonly known as goitre and the more severe and serious conditions of cretinism characterized by neurological or myxoedematous defects (*30*).

The neurological defects include: impaired voluntary motor activity, usually involving paresis or paralysis of pyramidal origin, chiefly in the lower limbs, with hypertonia, clonus, and plantar cutaneous reflexes in extension; spastic or ataxic gait while in the severest cases walking or even standing is impossible, and strabismus. In the myxoedematous form, most cases exhibit major clinical symptoms of hypothyroidism characterized by dwarfism, myxoedema, dry skin, sparseness of hair, slow-growing nails, retarded production of sex hormones and sexual maturation, and abnormal naso-orbital configuration (*17*).

The principal aetiological factor in the development of IDD is inadequate intake of iodine. Iodine is required by the body for the synthesis of hormones by the thyroid gland. The daily requirement of iodine is estimated to be 100-150 μg for adults. Goitrogenic agents which interfere with the metabolism of iodine and formation of thyroid hormones are also important in the causation of IDD. The most important goitrogens are probably thiocyanates, either preformed or synthesized from other compounds. Goitrogens are found in a variety of foods such as cassava, millet, soya bean, vegetables of the genus *Brassica* including cabbage and turnip, and plants of the family *Cruciferae* (*27*). Involvement of some trace elements such as molybdenum, selenium and fluorine in goitre occurrence has also been reported (*28,86*). Contamination of drinking water with *Escherichia coli* and toxins from other microbes (*27,29*), and with urochrome, one of the products of human waste (*76*), has been implicated as another cause for goitre. In recent years, excess iodine has been shown to be a cause for the enlargement of the thyroid gland (*55*). Furthermore, nutritional factors including vitamin A deficiency and protein-energy malnutrition, have been reported as important factors in the occurrence of goitre (*3,35,39*).

Relationship between vitamin A and iodine nutrition

Information on the relationship between vitamin A and iodine nutrition has come from studies in experimental animals and humans. In 1929, Rabinowitch (*61*) tested the effect of mixture of vitamin A and D with iodized jecoleic acid on 12 cases of Grave's disease and another control group of 12 patients with the same disease who received Lugol's solution only. The rate of decrease of the basal metabolic rate was greater in the patients who received the vitamin and iodine mixture which led to the conclusion that vitamin A and D influence the course of exophthalmic goitre. In 1937, Fasold (*22*) treated seven pubertal girls with vitamin A every third day for 7-8 months, and observed that in four girls the goitre size decreased while the menstrual cycle was prolonged or menstruation ceased entirely. When the vitamin A treatment was discontinued, goitre reappeared in 3-4 weeks and the menstrual cycle became regular. This indicated that vitamin A has some influence on hormonal regulation of the thyroid and ovary at puberty.

In 1938, Lindquist (*41*) noted that the serum vitamin A level was low in Basedow's disease and that this returned to normal on iodine treatment or removal of the hyperthyroid gland. Serum vitamin A levels were higher in myxoedematous patients than in normal persons which indicated the involvement of the vitamin in thyroid physiology. Sadhu and Brody (*64*) in 1947 observed that rats treated with heavy doses of vitamin A had normal growth, depression of their basal metabolic rate and reduction in the size of the thyroid gland.

These same authors revealed that heavy vitamin A medication tended to neutralize the increased metabolic effect of thyroxin injection while potassium iodide decreased somewhat the metabolic rate of control rats but did not decrease that of the thyroxin-treated rats. They also reported that partly oxidized vitamin A reduced the size of the thyroid. Bukatsh *et al.* (*14*) in 1951 examined 377 goitrous patients and found that 22% had night blindness and 73% had decreased dark adaptation. Treatment with vitamin A combined with green and yellow vegetables decreased the size of the thyroid gland and resulted in alleviation of the symptoms of hyperthyroidism. In therapy resistant cases, elimination of foci of infection and improvement of fat absorption, combined with the above treatment produced clinical improvement.

In 1958, Horvat and Maver (*33*) demonstrated from their study on the island of Krk in Yugoslavia that vitamin A has a role to play in the reduction of goitre size. The prevalence of goitre in a group of schoolchildren was decreased by 45% in those who received 3,000 IU vitamin A supplementation while it remained the same in a control group which was not supplemented. Differences in the consumption of cyanogenic glycosides and the iodine content of water could not explain the differences in goitre prevalence seen on the island. Frape *et al.* (*24*) observed that in pigs, the secretion of thyroxin increases at low level of vitamin A intake and tends to decrease with higher intakes of the vitamin. In 1961, Veil *et al.* (*78*) observed that supplementation of adult male Wistar rats with 5,000-30,000 IU/day of vitamin A decreased basal metabolism and urinary and faecal excretion of thyroid hormone. No effect on basal metabolism was observed when vitamin A was administered to thyroidectomized animals. Fabris and Bruscagnin (*21*) gave 50,000 units of vitamin A intramuscularly for 30 days to 12 hypothyroid and hyperthyroid individuals and on the 30^{th} day I^{131} was administered. The uptake of radioactive iodine was significantly decreased after vitamin A treatment in the normal as well as the hyper- and hypothyroid individuals.

More recent studies have also shown that vitamin A affects iodine metabolism. Thus Ingenbleek and De Visscher (*36*) conducted a study in Senegal in which they compared subjects in an area where the prevalence of goitre ranged between 40% and 50% with controls in Dakar. Serum levels of transthyretin, retinol-binding protein and retinol levels were lower in both the goitrous and non-goitrous subjects in the goitre area than in those from Dakar. The concentrations decreased progressively with increase in goitre size while serum albumin levels and urinary iodine excretion were low in the goitrous subjects. Ingenbleek (*37*) also observed in rats with vitamin A deficiency that thyroglobulin mannosylation was impaired with abnormal closure of bonds, reduced monoiodotyrosine and diiodotyrosine coupling reactions, and decreased production of thyroid hormones. Iodine deficiency alone did not induce the above mentioned glycosylation reaction but it did aggravate the effect produced by vitamin A deficiency. According to Oba and Kimura (*58*), the size of the thyroid gland in rats with vitamin A deficiency increases and the level of circulating thyroxin decreases to half that of control rats. Transthyretin was the major carrier of thyroxin in control rats while in the vitamin A-deficient rats the amount of thyroxin bound to transthyretin was reduced and the amount bound to thyroxin-binding globulin increased.

However, in 1942, Remington *et al.* (*63*) concluded from their study on rats that vitamin A deficiency was not an aetiological factor in development of simple goitre while the requirement for vitamin A increased in rats with thyroid hyperfunction and decreased in those which were thyroidectomized. One year after their initial study on the island of Krk, Horvat *et al.* (*34*) measured the uptake of radioactive iodine in the same population studied earlier. From this study they concluded that low intake of vitamin A was not a factor in the occurrence of goitre on Krk. Ascoll *et al.* (*5*) administered 5,000; 15,000 and 40,000 IU of vitamin A for a period 23, 17 and 13 days respectively to 78 children and did not observe any effect on hyperkeratosis or goitre. Similar conclusions were made by other investigators who did studies on guinea pigs and rats (*6,77*). Thus, the evidence published up until now on the role of vitamin A in iodine metabolism is somewhat conflicting.

Iron deficiency anaemia

Nutritional anaemia is caused by a lack of iron, folic acid and/or vitamin B_{12}. Iron is needed as a component of haemoglobin. Thus iron deficiency leads to the production of hypochromic normocytic red blood cells. Folic acid and vitamin B_{12} are required for the synthesis of DNA. Thus deficiency of the vitamins prevents mitotic division and thus the red blood cells produced are normochromic but hypercytic. Anaemia can also be caused by loss of blood through haemorrhage and infestations from hookworm and schistosoma; by malaria which causes haemolysis of red blood cells; and by thalassaemia and sickle cell in certain populations. Iron deficiency anaemia is a medical and public health problem of prime importance, causing few deaths but contributing to ill health, weakness and substandard performance of many people in the world. Iron deficiency anaemia is produced by inadequate absorption of iron from the diet resulting from a low iron content, the presence of inhibitors of iron absorption or the lack of promoters of iron absorption in the diet. Inclusion of haemoglobin in the diet increases iron absorption not only because of its iron content but also because it stimulates the absorption of non-haem iron. Iron deficiency anaemia is commonly observed amongst infants, young children and women of childbearing age. Infants have almost no haem iron in the diet as they are mainly fed on milk which lacks haem iron. After this age the amount of haem iron starts to increase depending on the type and amount of food fed. Poor absorption from the predominantly vegetarian diets of most people in developing countries is an important cause of iron deficiency. Anaemia leads to lethargy and decreased work performance (*7,65,79*) not only because of the inhibition of transport of oxygen from lungs to tissues and of carbon dioxide in the reverse direction but also due to impaired cognitive function and mental performance probably associated with inadequate iron in the brain. Anaemia also causes decreased resistance to infection (*16,73*), impairment in body temperature regulation (*8*) and increased risk from lead poisoning (*82*). On the other hand, high body iron stores cause liver damage and increase the risk of hepatocellular carcinoma (*72*).

Relationships between vitamin A and iron

Evidence that vitamin A can contribute to nutritional anaemia comes from studies in both man and laboratory animals. In 1922, Findlay and Mackenzie (*23*) reported that rats fed a diet deficient in vitamin A developed patches of gelatinous degradation in bone marrow and that in those animals which survived longest, most of the haematopoietic tissue was replaced by fibrous stroma. Such marked changes were not seen by Wolbach and Howe in 1925 (*84*) although they did see a reduction in the number of haematopoietic cells. In 1926, Koessler *et al.* (*38*) observed anaemia in early vitamin A deficiency which proceeded to increases in haemoglobin levels and haematocrit counts as the severity of vitamin A deficiency developed. Similar early changes were also observed by Sure *et al.* in 1929 (*74*) and Frank in 1935 (*25*) and later by Amine *et al.* (*1*) and O'Toole *et al.* (*60*). Koessler *et al.* (*38*) also pointed out that, as vitamin A deficiency progresses, rats become dehydrated thus giving rise to haematoconcentration. Other workers have also shown that there is a decrease in extracellular water in vitamin A deficiency (*15,42,46*). When McLaren *et al.* (*45*) investigated haematological changes in rats at the stage of vitamin A deficiency when growth retardation was beginning to become apparent, they found that there was an increase in haematocrit which could be attributed to lack of growth rather than an effect on haematopoietic tissues. Other studies in chickens, rats and horses (*18,47,57*) have shown that vitamin A deficiency results in anaemia while Staab *et al.* (*71*) have demonstrated an accumulation of iron in the liver in vitamin A-deficient rats.

Studies in children in the mid-1930s showed that vitamin A deficiency results in anaemia and haemosiderosis in the liver and spleen (*9,75*). In 1940 Wagner (*80*) conducted a study on experimental vitamin A deficiency in a group of ten human subjects. After 188 days the subjects showed signs of vitamin A deficiency and during this period haemoglobin and haematocrit values fell, and poikilocytosis and anisocytosis were seen. Wagner concluded that haematopoiesis was impaired. Hodges and Kolder (*31*) reported a similar clinical study in 1971 with 8 human volunteers who were maintained on very low vitamin A intakes for 357 to 771 days. Moderate anaemia developed which was refractory to medicinal iron but responsive to vitamin A.

As a result of this finding, Hodges *et al.* (*32*) reviewed the results of studies carried out on non-pregnant and non-lactating women in developing countries, including Ethiopia, where the intake of iron was 14 mg per day or more. They found a strong relationship between serum levels of vitamin A and blood levels of haemoglobin. In a similar analysis of data from studies carried out at INCAP in Guatemala, Mejía *et al.* (*48*), found a positive correlation between serum iron and blood haemoglobin levels in children with adequate intakes of vitamin A but not in those with inadequate intake. In the programme in Guatemala in which sugar was fortified with vitamin A, Mejía *et al.* (*49,50*) were able to show after six months of fortification that increased levels of vitamin A were associated with increased levels of serum iron and total iron-binding capacity while levels of serum ferritin declined during this period. Thus, the authors suggested that vitamin A deficiency increases stores of iron and that administration of vitamin A stimulates the synthesis of transferrin which would increase the availability of iron for haematopoiesis. However, it may well be that there is a direct effect of vitamin A on haematopoiesis itself as Douer and Koeffler (*19*) have shown that retinoic acid enhances the growth of human erythroid progenitor cells.

The beneficial effects of vitamin A on anaemia have been demonstrated in a number of trials. Reddy's group in Hyderabad in India (*53*) reported a study in 1977 in which a daily supplement of 8 mg retinyl palmitate was given to vitamin A-deficient children for two to three weeks. This resulted in a significant increase in haemoglobin, haematocrit and serum iron. More recently Mejía and Chew (*51*) have carried out a study in which children aged 1-8 years received vitamin A, iron, both of these, or a placebo. Vitamin A supplementation produced significant elevations in the serum levels of retinol, blood haemoglobin, haematocrit, erythrocyte count, serum iron, and percent saturation of iron but had no effect on total iron-binding capacity or serum ferritin. In three studies in Thailand, Bloem *et al.* (*11*) have investigated the relationship between iron and vitamin A status. The first study was a cross sectional study of 1060 children aged 1-8 years in which it was found that retinol was associated significantly with haematocrit, serum iron, transferrin, ferritin, and saturation of transferrin. In order to obtain further information as to whether this relationship was causal, two intervention studies were carried out in which 78 children were randomly allocated to two groups which were given a single dose of either vitamin A or a placebo. In the first of the intervention studies, there were significant differences between the two groups in the levels of retinol, retinol-binding protein, serum iron, and transferrin saturation one and two months after supplementation. However after 4 months, there were no significant differences between the two groups because the effect of the single vitamin A dose had worn off. In Bloem's second intervention study, short-term effects were also seen. A study has been reported from National Institute of Nutrition in Hyderabad (*56*) in which pregnant women were dosed with iron either with or without vitamin A and a positive effect of vitamin A on iron status was seen.

Outline of the thesis

The following chapters in this thesis present results from studies conducted in Ethiopia and cover four broad areas: a) the prevalence of vitamin A deficiency, IDD and nutritional anaemia, b) inter-relationships between these three deficiency diseases, c) the effects of interventions, and d) the staple food, ensete. **Chapters 2 and 4** deal with national surveys on xerophthalmia and on goitre. **Chapter 3** elucidates causes of blindness in the six schools for the blind as a basis for the detection of the importance of vitamin A deficiency in the causation of blindness in the country. **Chapter 5** describes the situation in a severe vitamin A-deficient area illustrating the severity of the problem in certain pocket areas of the country especially where relief-food aid has been distributed for a long time. **Chapters 6, 7 and 8** describe intervention studies on the impact of vitamin A on iodine and iron metabolism. In **Chapter 9**, the findings of the various studies and their practical implications are discussed and recommendations for future action programmes are presented. In **Annexes 1 and 2**, agro-economic as well as food and nutrition aspects of ensete (*Ensete ventricosum*), one of the staple foods of Ethiopia and on which over 10 million people depend, are described.

The maps of Ethiopia used in this thesis are based on the 14 Administrative Regions and one local Administration (Assab) which were in existence prior to September 1989.

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CHAPTER 2

Xerophthalmia in Ethiopia: a nationwide ophthalmological, biochemical and anthropometric survey*

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Summary

A total of 6636 children, aged from 6 months to 6 years and selected throughout the country using a multistaged stratified sample design, were examined for signs of xerophthalmia. The concentrations of retinol and of ß-carotene were measured in 742 children, including those with xerophthalmia and every twentieth of the remaining children. Anthropometric measurements were made on 2971 of the children. Bitot's spots were seen in 1.0% of all children, with a higher prevalence in the pastoral (1.6%) and cropping (1.1%) agro-ecological zones than in the zones characterised by cash crops (0.4%) and "ensete" (false banana,(*Ensete ventricosum*) (0.0%). One case of corneal xerosis and 2 cases of corneal scar were also seen. Serum retinol levels were in the "deficient" range (< 0.35 μmol/l) in 16% and "low" (0.35 - 0.69 μmol/l) in 44% of children. Serum retinol and clinical signs did not show any correlation with occupation and education of head of household, household size or anthropometric measurements. More stunting than wasting was observed with peak prevalence of these signs of malnutrition being observed in the second year of life.

Introduction

Vitamin A deficiency is one of the major nutritional problems in Ethiopia (*4,5,9,14,21*) as in many other developing countries. In spite of the potential to produce a wide variety of fruits and vegetables containing ß-carotene, most people do not consume them. Onions, garlic, potatoes, and to a lesser extent, tomatoes, lemons, oranges and bananas, all of which contain no or very little ß-carotene, are the principal fruits and vegetables consumed. Kale (*Brassica carinata*), consumed during the rainy season in most areas, and dried red pepper (*Capsicum annuum*) are the main sources of (pro)vitamin A in the diet. The limited consumption of green leafy vegetables and provitamin A-rich fruits such as mango and papaya can probably be attributed to a number of factors: lack of appreciation of their nutritional value, avoidance because of beliefs and taboos, non-availability in markets, and price. The situation is exacerbated by the long periods of fasting of 150 days each year observed by Coptic Christians when they avoid meat, dairy and poultry products (*12*).

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In Ethiopia, there are terms in the major languages for night blindness: "dafent" in Amharic, "he'ma" and "gahmi" in Tigrignia and "bebereti" in Oromegna. Treatment of night blindness with fresh animal liver is also widely carried out in the areas where these languages are spoken. Thus, vitamin A deficiency is a well-recognized problem in the country. Previous reports of its magnitude have been confined to specific areas of the country or to specific groups and area not representative of the country as a whole. They have shown that vitamin A deficiency is a problem in Ethiopia (*4,9*). Thus it was decided to carry out the present study which was designed with the following aims:

- to assess the vitamin A status of preschool children across the whole of Ethiopia and to assess the prevalence of ocular signs of vitamin A deficiency,
- to provide data on the distribution of the problem in the different agro-ecological zones, and
- to provide baseline data in order to be able to evaluate future intervention programs.

The study was carried out in the period between March 1980 and July 1981.

Materials and Methods

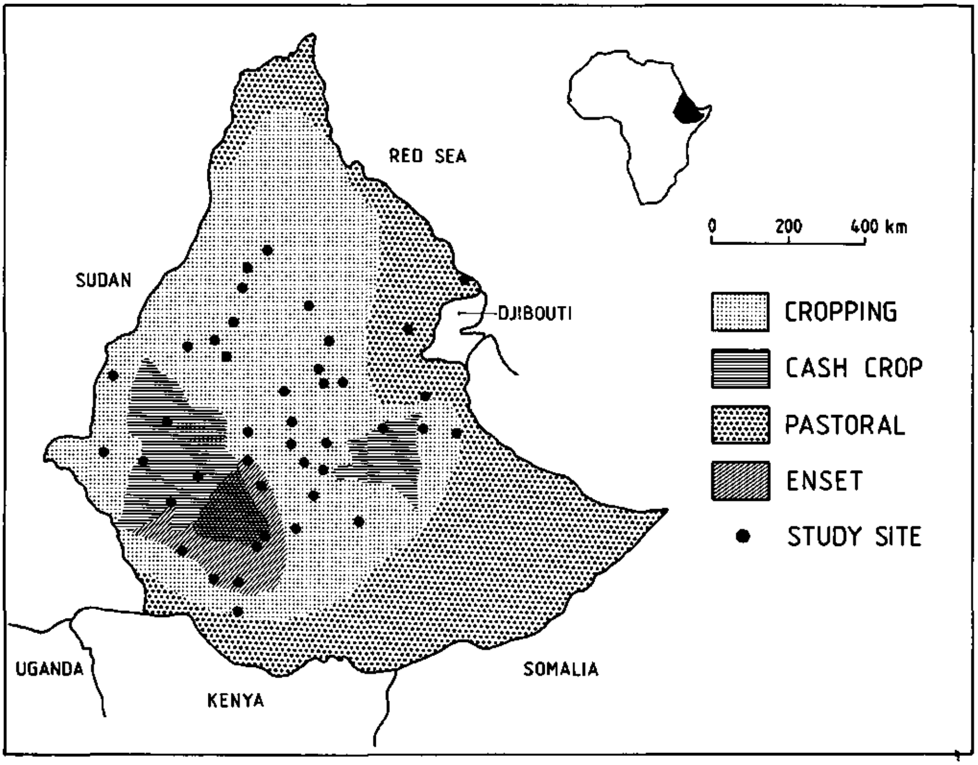
Sampling of the population

To obtain a representative sample for the survey, a multistaged stratified sample design was adopted. The country was divided into four ecological zones based on the type and amount of the various crops cultivated, the main source of income and the number and purpose of the livestock held. These factors determine to a large extent, the dietary habits and practices of the people who reside in the areas. The four ecological zones used in this survey were: **cropping**, involving cereals and pulses; **pastoral**, involving animal husbandry; **cash crop**, involving coffee and khat (*Khat edulis*, a green leafy herb chewed as a stimulant); and **ensete** (*Ensete ventricosum*, false banana).

A list of semi-urban and urban areas with populations over 2500 people was prepared for the four ecological zones and for each of the administrative regions except Eritrea and Tigrai which were excluded for reasons of security. From this list, several urban and semi-urban areas were selected at random from each of the ecological zones and in proportion to the number of children below the age of 6 years. A total of 42 semi-urban and urban centres were selected comprising 24 cropping, 8 pastoral, 7 cash crop and 3 ensete sites. Of the total of 6636 children, 3827 (57.7%) were from the cropping, 1215 (18.3%) from the pastoral, 1114 (16.8%) from the cash crop and 480 (7.2%) from the ensete agro-ecological zones. These numbers correspond to the proportions of people in the zones on a nationwide basis. In terms of dietary habits and of demographic and socio-economic characteristics, the semi-urban areas are very similar to the rural areas where 90% of the population live and reflect the country as a whole. As can be seen in Figure 1, the survey sites were evenly distributed throughout the country. Before carrying out the survey, a census of all families with children below 6 years of age was conducted at each site in order to produce a list of target households.

From this sampling frame, 160 households were selected at random at each survey site and all the children in each of these households were included in the survey. However, it was not possible to examine all children at each site except in the ensete area because some mothers did not wish to cooperate.

Figure 1 Map of Ethiopia showing study sites



Ophthalmological examination
Before the survey, the two health officers who carried out all of the ophthalmological examinations (ZWG and TD) were trained by an experienced ophthalmologist and diagnostic methods were standardized during a pilot study at four of the sites included in the study. During the survey, the results obtained by each observer were checked by the other observer in order to maintain standardization. Clinical signs of xerophthalmia were recorded according to the WHO (*22*) classification except that night blindness and xerophthalmia fundus were disregarded because of the difficulty in diagnosis. Rose bengal was applied to both eyes of all children to assist in the recognition of Bitot's spots and xerosis and also to evaluate its reliability in diagnosing vitamin A deficiency.

Measurement of serum retinol and β-carotene
Blood was collected from all children with clinical signs of vitamin A deficiency, from those who were rose bengal positive and from every 20th child without eye signs. Venous blood was taken without anticoagulant from 784 subjects but analysis was not possible on 43 samples because insufficient blood was drawn or because it was haemolyzed. Serum was separated by centrifugation and frozen using a gas-operated field refrigerator and samples were transferred to the laboratory in Addis Ababa in flasks containing dry ice. The concentrations of retinol and of ß-carotene were measured by ultraviolet spectrophotometry after extraction (*2*). Subjects were classified with respect to their vitamin A and ß-carotene status following ICNND (*10*).

Anthropometry
Weight and height were measured on all children at about half of the study sites. At the remaining sites, measurements were not possible for logistic reasons. A total of 3423 children were measured but data were incomplete for 514 of them. Weight was measured to the nearest 100 g using a hanging scale (Salter) calibrated with a 5 kg weight at regular intervals throughout each day. Height was measured to the nearest 0.5 cm using a height stick with movable head piece and a flat wooden base. For small children, length was measured to the nearest 0.5 cm in a recumbent position with a length board. An effort was made to record age in months as exactly as possible through structured interviews of mothers with reference to a calendar of national and local events. The standard deviation scores (Z-scores) were calculated with the help of software (CASP) developed by WHO (*23*) and the National Center for Health Statistics (NCHS) (*6,7,16*). ZWH score of 2.00 or -2.00 means that the child is 2 SD above or below the median weight-for-height respectively while a ZHA refers to the Z score for height-for-age. Based on these scores, children were classified as normal (ZWH > -2.00 and ZHA > -2.00), wasted (ZWH < -2.00 and ZHA > -2.00), stunted (ZWH > -2.00 and ZHA < -2.00), or wasted and stunted (ZWH < -2.00 and ZHA < -2.00).

Statistics
Chi-square analysis was used to test for statistical significance of differences. If the data were not normally distributed, Mann-Whitney procedure was used.

Results

Clinical signs of xerophthalmia
Conjunctival xerosis and Bitot's spots were seen in 4.8 and 1.0% of the children respectively (Table 1). Conjunctival xerosis was more prevalent in the cropping and pastoral zones (> 5%) compared with the cash crop (1.9%) and the ensete zones (0.8%) and the difference between cropping and cash crop zones was significant (P<0.001). Similar significant differences were found for Bitot's spots with prevalence rates of 1.1% in the cropping and 1.6% in the pastoral zones, compared with 0.4% in the cash crop and no cases in the ensete zone.

Table 1 Distribution of clinical signs of xerophtalmia in children aged 6 to 72 months in four agro-ecological zones in Ethiopia

Clinical signs	Number of children with clinical signs in each zone (percent)				
	Cropping	Pastoral	Cash crop	Ensete	Total
Conjunctival xerosis (X1A)	227 (5.9)*	65 (5.3)	21 (1.9)*	4 (0.8)	317 (4.8)
Bitot's spot (X1B)	43 (1.1)	20 (1.6)	4 (0.4)	0 (0.0)	67 (1.0)
Corneal xerosis (X2) & corneal scar (XS)	3 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.1)
Total examined (100%)	3827	1215	1114	480	6636

Statistically significant (Chi square) from cropping zone: *$P < 0.001$.

Only one case of corneal xerosis and two cases of corneal scar were seen and these children were all from the cropping zone. Conjunctival xerosis and Bitot's spots were twice as common ($P<0.001$, Chi-square) in boys as in girls and this trend was apparent for all age groups (Table 2).

Concentrations of retinol and β-carotene in serum

Serum retinol levels were "deficient" (as defined by ICNND (1963), < 0.35 μmol/l) in 16%, "low" (0.35-0.69 μmol/l) in 44%, normal (0.71-1.75 μmol/l) in 39% and high in only 1% of children. The median serum retinol levels were marginally low, 0.62 μmol/l (25^{th} and 75^{th} percentiles, 0.44 and 0.86 μmol/l) for all ecological zones. As shown in Table 3, the serum retinol concentrations were significantly higher in children in the cropping zone than in their counterparts in the pastoral cash crop and ensete zones.

Table 2 Distribution of children in Ethiopia with different clinical signs of xerophtalmia grouped by age

Clinical signs months	Sex	Number of children with clinical sign in each age group in						
		< 12	12-24	24-36	36-48	48-60	60-72	Total
Conjunctival xerosis (X1A)	M	1	11	23	42	63	80	220
	F	0	8	11	19	27	32	97
	M+F	1	19	34	61	90	112	317
Bitot's spots (X1B)	M	2	2	3	10	10	19	46
	F	1	0	2	5	4	9	21
	M+F	3	2	5	15	14	28	67
Corneal xerosis (X2) & corneal scar (XS)	M	0	0	3	0	0	0	3
	F	0	0	0	0	0	0	0
	M+F	0	0	3	0	0	0	3
Total eye lesions	M	3	13	29	52	73	99	269
	F	1	8	13	24	31	41	118
	M+F	4	21	42	76	104	140	387
Total examined	M	182	359	408	713	754	922	3338
	F	189	340	382	683	771	933	3298
	M+F	371	699	790	1396	1525	1855	6636

Table 3 Serum retinol and ß-carotene concentrations in children aged 6 to 72 months in four agro-ecological zones in Ethiopia

Zone	Number	Concentration (µmol/l)[a]	
		Retinol	ß-carotene
Cropping	477	0.65 (0.44 - 0.94)	0.89⁺ (0.63 - 1.25)
Pastoral	138	0.62* (0.42 - 0.78)	0.86⁺ (0.50 - 1.30)
Cash crop	91	0.53* (0.38 - 0.78)	0.90⁺ (0.56 - 1.31)
Ensete	36	0.50* (0.39 - 0.66)	1.30 (0.94 - 0.19)

[a] Concentration expressed as median with 25^{th} and 75^{th} percentiles within parentheses.
1 µmol/l is equivalent to 28.6 µg/dl of retinol or 53.7 µg/dl of ß-carotene.

Significantly different (Mann-Whitney test): *, from cropping zone ($P < 0.02$); ⁺, from ensete zone ($P < 0.01$).

Median serum retinol values were low in most age groups and both sexes. No significant differences were observed between age groups or between the sexes. ß-carotene was within the normal range in older children and low in those children below the age of two years (Table 4).

About 22% of children with Bitot's spots had serum retinol levels < 0.35 µmol/l which is regarded as "deficient" while 57% had "low" levels of 0.35-0.69 µmol/l and 21% had normal values (Table 5).

The levels in children with Bitot's spots were significantly lower (median 0.50 µmol/l: 25[th] and 75[th] percentiles, 0.37 and 0.65 µmol/l: $P<0.001$) than those without Bitot's spots (median 0.63 µmol/l: 25[th] and 75[th] percentiles, 0.44 µmol/l and 0.87 µmol/l). As far as conjunctival xerosis is concerned, about 15% of children had serum retinol levels < 0.35 µmol/l and 42% had serum retinol levels 0.35-0.69 µmol/l (Table 5).

Table 4 Serum retinol and ß-carotene concentrations in boys and girls aged from 6 to 72 months in Ethiopia

Age group (months)	Sex	n[a]	Median serum concentrations, µmol/l (25th and 75th percentiles)	
			Retinol	ß-carotene
< 12	M	17	0.62 (0.29-0.76)	0.68 (0.41-0.79)[b]
	F	22	0.62 (0.43-0.74)	0.73 (0.50-1.22)[b]
12-23	M	42	0.69 (0.41-1.01)	0.54 (0.38-0.81)[b]
	F	35	0.59 (0.31-0.94)	0.70 (0.36-0.94)[b]
24-35	M	46	0.66 (0.47-0.89)	0.85 (0.58-1.27)
	F	41	0.71 (0.51-0.91)	0.89 (0.41-1.34)
36-47	M	85	0.63 (0.44-0.82)	0.95 (0.53-1.28)
	F	55	0.56 (0.41-0.81)	0.88 (0.53-1.36)
48-59	M	110	0.62 (0.47-0.94)	0.93 (0.68-1.39)
	F	65	0.59 (0.42-0.84)	1.00 (0.68-1.46)
60-72	M	138	0.62 (0.43-0.86)	1.03 (0.73-1.39)
	F	83	0.59 (0.41-0.87)	1.00 (0.75-1.41)
Total	M	438	0.62 (0.44-0.87)	0.89 (0.60-1.28)
	F	301	0.62 (0.41-0.84)	0.91 (0.62-1.31)

[a] Three children were not included because their sex was not known
[b] Values significantly lower (Mann-Whitney) than those of the older age groups, $P < 0.001$

Table 5 Distribution of children in Ethiopia with various concentrations of serum retinol and ß-carotene presented per ecological zone and clinical sign

Ecological zone	Clinical sign[a]	Serum retinol concentration (μmol/l)[b]			Serum ß-carotene concentration (μmol/l)				
		< 0.35 n (%)	0.35 - 0.69 n (%)	≥ 0.70 n (%)	< 0.37 n (%)	0.37 - 0.74 n (%)	0.75 - 1.84 n (%)	≥ 1.85 n (%)	Total n (100%)
Cropping	X1A	29 (13.6)	86 (40.2)	99 (46.3)	18 (8.4)	58 (27.1)	118 (55.1)	20 (9.3)	214
	X1B	7 (17.9)	24 (61.5)	8 (20.5)	2 (5.1)	12 (30.8)	23 (59.0)	2 (5.1)	39
	X2+XS	1 (33.3)	2 (66.7)	0 (0.0)	0 (0.0)	2 (66.7)	1 (33.3)	0 (0.0)	3
	No signs[c]	35 (15.8)	81 (36.7)	105 (47.5)	24 (10.9)	59 (26.7)	123 (55.7)	15 (6.8)	221
Pastoral	X1A	11 (18.0)	26 (42.6)	24 (39.3)	9 (14.7)	18 (29.6)	25 (41.0)	9 (14.7)	61
	X1B	6 (30.0)	9 (45.0)	5 (25.0)	4 (20.0)	6 (30.0)	10 (50.0)	0 (0.0)	20
	No signs	8 (14.0)	26 (45.6)	23 (40.4)	10 (17.6)	12 (21.1)	31 (54.5)	4 (7.0)	57
Cash crop	X1A	6 (30.0)	10 (50.0)	4 (20.0)	2 (10.0)	8 (40.0)	9 (45.0)	1 (5.0)	20
	X1B	1 (25.0)	3 (75.0)	0 (0.0)	0 (0.0)	1 (25.0)	3 (75.0)	0 (0.0)	4
	No signs	12 (17.9)	31 (46.3)	24 (35.8)	8 (11.9)	15 (22.4)	40 (59.7)	4 (6.0)	67
Ensete	X1A	0 (0.0)	3 (75.0)	1 (25.0)	0 (0.0)	1 (25.0)	0 (0.0)	3 (75.0)	4
	No signs	6 (18.8)	19 (59.4)	7 (21.9)	0 (0.0)	4 (12.5)	21 (65.6)	7 (21.9)	32
Total	X1A	46 (15.4)	125 (41.8)	128 (42.8)	29 (9.7)	85 (28.4)	152 (50.8)	33 (11.0)	299
	X1B	14 (22.2)	36 (57.1)	13 (20.6)	6 (9.5)	19 (30.2)	36 (57.1)	2 (3.1)	63
	X2+XS	1 (33.3)	2 (66.7)	0 (0.0)	0 (0.0)	2 (66.6)	1 (33.3)	0 (0.0)	3
	No signs	61 (16.2)	157 (41.6)	159 (42.2)	42 (11.1)	90 (23.9)	215 (57.0)	30 (8.0)	377
		122 (16.4)	320 (43.1)	300 (40.4)	77 (10.4)	196 (26.4)	404 (54.5)	65 (8.8)	742

[a] X1A, conjunctival xerosis; X1B, Bitot's spots; X2, corneal xerosis; XS, corneal scars.
[b] 1 *μmol/l is equivalent 28.6 μg/dl retinol or 53.7 μg/dl ß-carotene.*
[c] Serum retinol and serum ß-carotene levels of randomly selected children with no clinical signs.

However, no differences were seen between the average serum retinol in those with conjunctival xerosis (median 0.65 μmol/l: 25th and 75th percentiles, 0.44 μmol/l and 0.94 μmol/l) and those with no clinical signs (median 0.62 μmol/l: 25th and 75th percentiles, 0.42 and 0.84 μmol/l). For the children without eye lesions, 16.2% had "deficient" levels and 41.6% marginal (or "low") serum vitamin A. In the three children with more severe eye lesions, the values for serum retinol were below 0.35 μmol/l in one and 0.35-0.69 μmol/l in the others.

As far as serum ß-carotene levels are concerned, 10.4% were in the "deficient" range (as defined by ICNND (*10*) < 0.37 μmol/l), 26.4% were "low" (0.37-0.74 μmol/l), 54.4% normal (0.75-1.84 μmol/l) and 8.8% high (≥ 1.85 μmol/l) (Table 5). Children from the ensete zone had significantly higher ($P<0.05$) serum ß-carotene concentrations than in all other zones. There were no differences in the distribution of levels of ß-carotene between children with and without the different eye lesions. The values were significantly lower ($P<0.001$) in children aged less than two years than in older children of the same or different sexes (Table 4). No association was established between either serum vitamin A level or with serum ß-carotene level with occupation of the head of household, household size and sex of children.

With rose bengal staining, it was observed that 80.5% of those with Bitot's spots, 45.3% of those with conjunctival xerosis and 29.7% of those with no clinical signs stained positively. Thus, the specificity of rose bengal staining for detecting eye lesions was very low. Positive staining of eyes with rose bengal was not associated with low serum retinol levels (data not shown). Rose bengal staining was positive in 16.6% of children with serum retinol level < 0.35 μmol/l and 23.6% with levels between 0.35 and 0.69 μmol/l.

Anthropometry
The degrees of wasting and stunting were similar in all ecological zones with more stunting alone (30.2-35.4%) than stunting and wasting together (5.3-11.1%) and wasting alone (3.2-6.0%) (Table 6). No relationship was observed between nutritional status as assessed by anthropometry and serum retinol level or clinical manifestations of vitamin A deficiency.

Table 6 Proportion of children according to nutritional status by ecological zone

Ecological zone	Nutritional status			
	Normal	Wasted	Stunted	Wasted and stunted
Cropping	830 (61.7)	54 (4.0)	421 (31.3)	40 (3.0)
Pastoral	423 (53.6)	47 (6.0)	279 (35.4)	40 (5.1)
Cash crop	401 (64.5)	20 (3.2)	188 (30.2)	13 (2.1)
Ensete	89 (58.2)	6 (3.9)	54 (35.3)	4 (2.6)

Discussion

This study presents the results of the first proportionally-sampled country-wide survey of vitamin A deficiency and xerophthalmia in Ethiopia. Earlier studies have demonstrated that vitamin A deficiency is one of the nutritional problems of the country. Postumus (quoted in *9*), recorded a prevalence of Bitot's spots as high as 6% in primary school children in Gondar while in the ICNND (*9*) survey carried out in 1957, the average prevalence of Bitot's spots was found to be approximately 1.5% with higher prevalence in Addis Ababa and lower in Harar, Jimma, Eritrea and Axum. This compares with the overall rate of Bitot's spots found in the present survey of 1.0% with rates as high as 1.6% in the pastoral zone and no cases were found in the ensete zone. A prevalence rate of Bitot's spot of 0.5 percent is regarded as representing vitamin A deficiency of public health significance (*22*). In the present study this prevalence rate was exceeded except in the ensete area.

In the present large-scale survey, the overall prevalence of conjunctival xerosis was 4.8%. Relatively high rates were noted in the cropping (5.9%) and pastoral (5.3%) ecological zones and low rates in the ensete (0.8%) and cash crop (1.9%) zones. As conjunctival xerosis is not very specific sign, it is not a reliable criterion for establishing whether vitamin A deficiency is a problem of public health significance. Prevalence rates of Bitot's spots, above 0.5%; corneal xerosis/ulceration/ keratomalacia above 0.01%; and corneal scars, above 0.05% are used for this purpose (*22*). These rates were exceeded for Bitot's spots (1.0%) and corneal xerosis/ulceration/ keratomalacia) (0.03%, n=3) for the population as a whole while the proportion of Bitot's spots was higher in the cropping (1.1%) and pastoral zones (1.6%) but below the cut-off point in the cash crop (0.4%) and ensete (0%) zones. All the three corneal lesions were found in the cropping zone (0.08%). The extent of vitamin A deficiency is confirmed by the finding that 16 percent of children had serum retinol levels less than 0.35 µmol/l. WHO (*22*) set 5 percent with under 0.35 µmol/l as a criterion for indicating that vitamin A deficiency is a problem of public health significance. The children with Bitot's spots had significantly lower levels of serum vitamin A than those without eye lesions but mean serum retinol concentrations were similar in children with conjunctival xerosis and those from the randomly selected group. In this population, conjunctival xerosis therefore is not specific for vitamin A deficiency. Other environmental factors such as flies, dust, high temperature and low humidity may also be factors contributing to conjunctival xerosis and perhaps even to other forms of xerophthalmia. Although serum retinol concentrations in children with Bitot's spots were lower than in children without eye lesions, serum retinol levels were not good predictors of clinical signs.

This confirms the findings of an earlier study in school children in Addis Ababa in which no relationship was found between Bitot's spots and serum vitamin A (*3,18*). In the cropping zone, the mean retinol concentation was higher than that in the pastoral and cash crop zones even though all of the corneal xerosis and corneal scars and the highest prevalence of Bitot's spots were found in this ecological zone.

Conversely, apart from conjunctival xerosis, there were no clinical eye signs of xerophthalmia in the ensete area even though the mean serum retinol concentration was not significantly different from that in the other three ecological zones. In fact, it was lower than all of the others, albeit not significantly. No significant difference in serum retinol levels between children of various ages were observed although ß-carotene levels were significantly higher in children older than two years than in their younger counterparts ($P<0.001$). It is interesting to note that the concentration of serum ß-carotene was about 50% higher in the ensete zone indicating a higher intake, at least in the short term, of ß-carotene-rich foods (*11*). Vitamin A status depends on the stores of retinol in the body and an indirect indicator of these stores superior to serum retinol levels, such as the relative dose response, is required (*1,8,15*).

The low prevalence of xerophthalmia in the ensete zone can be attributed to the intake of kale, reflected in the high serum ß-carotene level, and of cheese which are eaten together with ensete (Z. Wolde-Gebriel and C.E. West, in preparation). On the other hand, the higher prevalence of vitamin A deficiency in the cropping zone can be attributed to the mono-crop culture as also suggested by De Sole *et al.* (*5*). Although children in the pastoral zone consume dairy products, the concentration of retinol and ß-carotene in such products may be low because of a low level of ß-carotene in the fodder consumed by the animals due to the arid nature of the environment. The distribution of dairy products is also likely to be uneven.

In the present study, positive rose bengal staining was not correlated with either clinical signs or with serum retinol levels. Although some earlier studies did suggest its usefulness (*17,19*), Kusin *et al.* (*13*) and Sommer (*20*) have demonstrated that rose bengal staining is not specific for vitamin A deficiency.

More than half of the children measured were classified as normal in terms of weight for height and height for age. More stunting than wasting was observed in all ecological zones. However, the anthropometric measurements did not correlate with eye signs or with serum retinol levels.

In a review of 188,737 out-patient medical records over a 5-year period in two major hospitals with paediatric and ophthalmic services in Addis Ababa, a total of 685 (0.36%) cases of hypovitaminosis A were identified (*4*). Of these, 74.4% were diagnosed as vitamin A deficiency, 19.4% as Bitot's spots and 6.3% as keratomalacia. Out of 116 children admitted with measles to Gidole hospital in Gamo Gofa Administrative Region, one case with corneal ulcer and xerosis and two cases of keratomalacia were diagnosed (*14*). A community survey in the same area showed that 22 children out of a total of 406 (5.4%) had Bitot's spots, one had corneal xerosis and another had corneal ulceration with keratomalacia (0.5%). In Lumibilbilo and Assasa subdistricts of Arssi, and Dodola and Adaba subdistricts of Bale Administrative Regions, Bitot's spots were seen in 5.0%, corneal xerosis and ulceration with keratomalacia in 0.8% and corneal scar in 0.5% of children aged between 6 months and six years (*5*). These findings and those presented in this paper indicate that vitamin A deficiency is a problem of public health significance in Ethiopia especially in the cropping and pastoral ecological zones. It calls for a concerted control programme.

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CHAPTER 3

Causes of blindness in children in the blind schools of Ethiopia*

Zewdie Wolde-Gebriel, Haile Gebru and Clive E. West

Summary

A total of 721 children in the six schools for the blind in Ethiopia were studied. In 1988-1989 histories were taken to ascertain the predisposing factors and ophthalmological examinations and records were used to determine the causes of blindness. Ninety-five per cent of those examined had bilateral blindness, 12% did not know how they had become blind and, of those who provided information on how they became blind, 21% knew that they were born blind, 30% implicated measles as being responsible, and 13% implicated "mitch" which is an Amharic term used to describe a very wide range of non-specific and vague illnesses of which measles probably constitutes a significant proportion. Seventy per cent of the blindness was due to either corneal opacity or phthisis bulbi. Of those with non-congenital bilateral corneal opacity or phthisis bulbi, 40% were preceded by measles and 17% by mitch. A study of 66 adults in the handicraft and skill-training centres attached to the blind schools indicated that the principal predisposing factors of blindness were mitch (30%), smallpox (15%), cataract (12%), and traditional eye medicine (11%). Seventy percent had corneal scars or phthisis bulbi and 14% cataract.

Introduction

It is estimated that the rate of blindness in Ethiopia is 1.5 ± 0.2% (*2*) which corresponds to three quarters of a million blind persons out of the 1990 projected population of 50 million (*11*). Of this blindness, it is estimated that about 80% is preventable or curable. Limited surveys have been conducted in one of the schools for the blind, and in the population at large. From these surveys, the main causes of blindness in the population as a whole were stated to be senile cataract, blinding corneal lesions of childhood, glaucoma, trachoma, smallpox, measles, chickenpox, and drinking of traditional medicine against tapeworm (*3,7,14,15*). Onchocerciasis, which is prevalent in the south-western part of the country is regarded as a rare cause of blindness (*12*).

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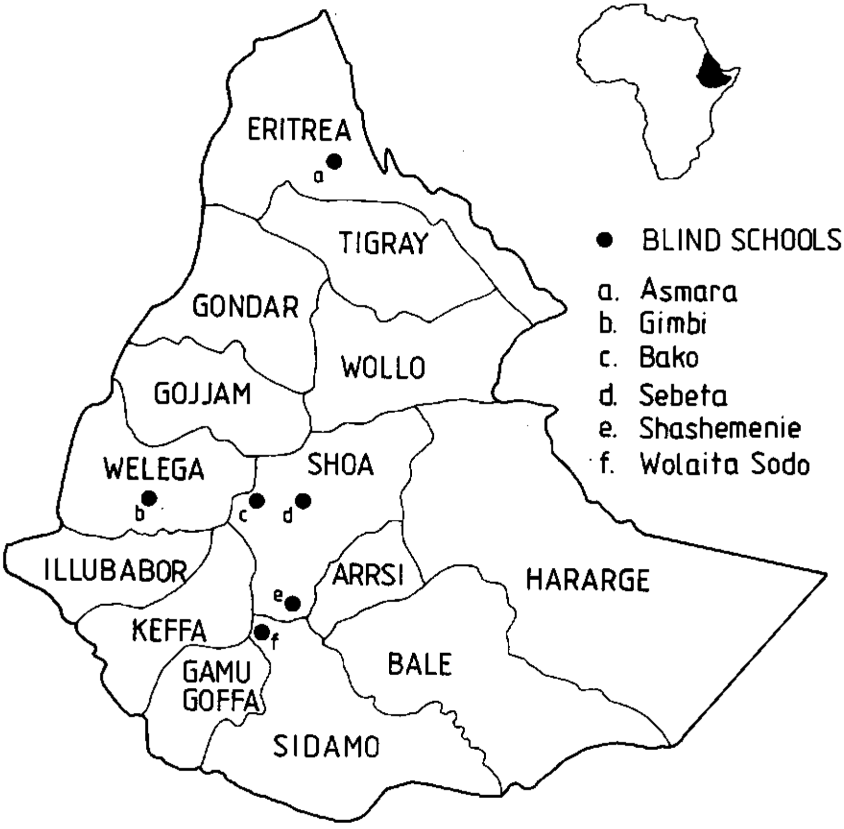
The purpose of this study was to identify the causes of blindness amongst children in the six blind schools in the country as such information could assist in the design of blindness prevention programmes.

Subjects and methods

A predesigned questionnaire was used to collect data on a total of 721 subjects (476 males and 245 females) in the six blind schools in Ethiopia (Figure 1) between July 1988 and February 1989.

Figure 1 Map of Ethiopia showing the location of the six schools for the blind.



In each school, eyes of subjects were examined using a hand light, direct ophthalmoscopy without dilatation of the pupils, loupe (magnification x 2.5) and Snellen's chart when necessary for children with visual acuity over 3/60. In this study, blindness was defined as the inability to count fingers at a distance of 3 metres with the better eye (*23*). Results of the ophthalmic examinations were checked against clinical records of subjects which included a report of a thorough eye examination by an ophthalmologist except in Bako and Gimbi schools where no records were available. In almost all cases our findings were the same as those of the ophthalmologist. Whenever there was doubt, the diagnosis of the ophthalmologist was recorded. Examination was conducted in rooms with sufficient light during the day.

Information on the questionnaire comprised name, age, sex, place of birth by region, age affected, predisposing illness, period between onset of illness and blindness, measures taken at the time, the number of other family members affected, the general nutrition condition of the subject at the time of onset of blindness, whether admitted to hospital or not at the time of onset of blindness, and the social condition of the family. The information obtained from the children was cross-checked with that on records which had been elicited from parents or guardians.

Blind adults working in handicraft or participating in skill-training centres attached to the schools at Bako (n = 22), Wolaita Sodo (13) and Gimbi (31) were also interviewed and examined. Information on age, sex and factors predisposing to blindness were collected from these adults. Free and informed consent was obtained from all subjects, school directors and the Ethiopian National Association for the Blind.

Results

Of the 721 children admitted to the blind schools, 681 (95%) had bilateral blindness, 11 (1.5%) had bilateral visual impairment with visual acuity greater than 3/60 and 27 (3.7%) monocular blindness. Information on the visual acuity of two of the students was lacking. The age of the children in the six blind schools was 12.1 ± 4.1 years (mean ± SD) with more than half of the children aged between 10 and 16 years (Table 1). The mean ages of the children in each of the schools were similar except for the children in Shashemenie who were younger with a mean age of 8.1 ± 3.0 years. There were more males (n = 476, 66%) than females (n = 245, 34%) admitted to the blind schools and no girls were admitted to Bako school. When subjects or their parents were asked which factors predisposed to blindness, 12% did not know how they had become blind. Factors in those for whom information was available were: congenital blindness, 21%; measles, 30% and before the age of 8 years in 85% of cases; "mitch", 11%; trauma and related factors, 6.9%; exposure to surface-reflected sunlight, 4.9%; epidemic eye diseases, 3.3%; smallpox, 2.2%; and trachoma, 2.0%.

Table 1 Classification of subjects by school, age and sex

School	Sex	Age (years)				Total	Age (mean ± SD)
		4-9	10-15	16-19	>20		
Asmara	M	14	53	6	0	73	12.3 ± 2.5
	F	6	19	3	0	28	
Gimbi	M	1	27	9	2	39	14.2 ± 3.7
	F	2	17	6	1	26	
Bako	M	5	22	18	0	45	14.0 ± 3.4
	F	0	0	0	0	0	
Sebeta	M	16	94	22	1	133	13.0 ± 2.8
	F	8	50	19	0	77	
Shashemenie	M	86	34	2	1	123	8.1 ± 3.0
	F	59	19	1	0	79	
Wolaita	M	2	26	26	9	63	15.8 ± 4.1
	F	0	21	13	1	35	

Mitch is an Amharic term used to describe a very wide range of non-specific and vague illnesses with 94% of subjects reporting febrile illness immediately prior to the onset of blindness accompanied by a range of other symptoms such as vomiting, headache and muscular pains, or eye disease with reddening of the conjunctiva, excessive lacrimation and sometimes itching. Traditional medicines were reported to have been used in 12% of the subjects who had experienced mitch. Trauma and related factors include not only perforation of the eye but also damage due to foreign bodies and explosions. The expression "exposure to surface reflected sunlight...." may be some traditional view of the aetiology of blindness since on examination, all subjects involved had corneal scar/s or phthisis bulbi.

In Table 2, causes of blindness and visual impairment of both schoolchildren and adults are presented. About 70% of the blindness in children was due to corneal opacity or phthisis bulbi. Of the 304 non-congenital bilateral corneal opacity or phthisis bulbi cases, 123 were said to be preceded by measles (40%) and 51 by mitch (17%) while 91% of subjects who reported measles, had bilateral blindness.

When subjects were asked about the length of time between the onset of the predisposing illness and the commencement of blindness, 66% did not know.

Table 2 Causes of blindness

	Schoolchildren				Adults	
	Right eye		Left eye			
	n	%	n	%	n	%
Corneal scar	294	40.9	294	40.9	25	37.9
Phthisis bulbi	202	28.1	208	28.9	21	31.8
Optic atrophy	71	9.9	69	9.6	6	9.1
Cataract	9	5.8	43	6.0	9	13.6
Retinopathy	27	3.8	24	3.4	1	1.5
Microphthalmus	24	3.3	26	3.6	0	0.0
Glaucoma	13	1.8	14	1.9	1	1.5
Uveitis	13	1.8	12	1.7	0	0.0
Other	17	2.4	18	2.5	3	4.6
Sighted	16	2.2	11	1.5	0	0.0
Total	719	100.0	719	100.0	66	100.0

Where it was possible to obtain information, blindness or visual impairment came in less than a week for 26%, 1-4 wk for 20%, 1-3 mo for 31% and in 4-6 mo for 11%. Four subjects reported that they went blind after drinking traditional medicine against tapeworm and 2 against rabies. All six subjects had optic atrophy. Ten percent of subjects stated that other family members were also blind or visually impaired while 11% said that other members of the community were affected.

As far as the study of the adults is concerned, a total of 66 subjects (48 men and 18 women) aged 37.6 ± 14.1 years (mean ± SD) were included (Table 2). From the interview, the predisposing factors were mitch (n = 20, 30%), smallpox (n = 10, 15%), cataract (n = 8, 12.1%), traditional eye medicine (n = 7, 11%), trachoma (n = 5, 7.6%), measles (n = 3, 4.5%), congenital (n = 2, 3.0%) trauma or explosion (n = 2, 3.0%), glaucoma and degenerative myopia (one each, 1.5%) and unknown (n = 7, 11%). On examining the eyes, 46 of the adults (70%) had corneal scars or phthisis bulbi, 9 (14%) had cataract of which one was surgically treated and had regained his sight, 6 (9.1%) had optic atrophy, 2 (3.0%) had trichiasis, and the remaining three subjects had glaucoma, retinopathy or degenerative myopia. Of the 46 adults with corneal scars or phthisis bulbi, 2 (4.3%) reported measles, 20 (43%) mitch, 8 (17%) smallpox, 4 (8.7%) trachoma, 3 (6.5%) eye infection or epidemic eye disease, and 2 (4.3%) trauma or explosion immediately prior to the onset of blindness.

The age of onset of blindness was under 6 yr in 19 subjects (29 %) excluding the two with congenital blindness (3 %), 6-10 yr in 20 subjects (30 %), 11-25 in 11 subjects (17 %), 26-50 yr in 9 subjects (14 %) and over 50 yr in two subjects while it was unknown to three subjects (4 %).

Discussion

Based on a survey of adults, Budden (*2*) estimated that 53 per 100,000 people in Ethiopia had bilateral corneal scarring originating in childhood. Assuming that half of these people are under the age of 20 yr, and that corneal scarring accounts for 70% of childhood blindness (Table 2), this would represent about 18,000 blind persons under the age of 20 yr and about 12,000 school-age children in the country. Thus, the total number of children admitted to the blind schools is probably only about 5% of children eligible to attend. It is interesting to note that 27 (3.7%) of the children in the schools had sight in one eye (Table 2) and this highlights the need for expert examination of subjects prior to admission. The high proportion of boys compared with girls (almost two-fold) is probably attributable more to the restraint of sending blind girls away from home than to a higher prevalence of blindness among boys compared with girls.

Measles has been shown to play an important role in corneal blindness in African children (*4,5,6,8,9,13,16,17*). In the present study, it was given in the history as the predisposing factor in 40% of bilateral corneal blindness cases but this is probably an underestimate. Some may not have connected a prior attack of measles to the onset of corneal ulceration as it often occurs after the fever and rash of measles have passed (*20*). In addition the role of mitch has to be considered. It is an Amharic term meaning literally "slap on the face by spirits" and has equivalents in other languages in Ethiopia. For example, it is referred to as "rukutá" in Oromigna which is spoken in Welega, Sidamo, Illubabor, Arssi, Hararge and Bale where it was commonly reported as being a problem. Mitch was reported as responsible for 17% of bilateral corneal blindness cases and it may well be that half of the mitch cases were in fact measles. If this is so, the 40% of bilateral corneal blindness cases now attributed to measles can probably be increased to about 50%.

In the adults in the handicraft and skill-training centres attached to the blind schools, 43% gave mitch as a predisposing factor while only 4% quoted measles. The lower proportion of measles and higher proportion of mitch as predisposing factors in adults compared to the children might be due to the increasing consciousness of the symptoms of measles and exact diagnosis of cases by medical personnel for the children as opposed to the adults who may have been inclined to include most of the measles cases as mitch.

The precise role of measles in corneal ulceration has been the subject of many studies (*4,5,6,9,13,16,17,21*). More recently, the involvement of vitamin A in this relationship has become clearer as a result of two studies in Tanzania. Foster and Sommer (*5,6*) showed that the primary cause of post-measles eye lesions could be attributed to vitamin A deficiency in 50%, measles keratitis in 12.5%, herpes simplex in 20.8%, and to traditional medicines in 16.7% of cases while Pepping *et al.* (*13*) found that the mean serum retinol level was significantly lower in children with corneal lesions compared with those with normal corneas. The causative effect of measles in reducing the concentration of serum retinol has been demonstrated using an animal model system by Sijtsma *et al.* (*19*).

In the 19 blind schools in Tanzania, Sauter (*18*) found that 291 of the 426 children studied (68%) had xerophthalmia of which 156 (37%) had a history of measles.

In the present study, it was found that mitch is often treated with traditional medicines particularly to the eyes. Thus damage to the eyes brought about by measles would be exacerbated by such medicines. A large number of plants are used in the treatment of eye complaints in Ethiopia (*10*). Although, many are known to be toxic, no systematic study has been made. However, it is known that the seeds of the "kosso" tree (*Hagenia abyssinica*), which are used to prepare a traditional anti-tapeworm medicine produce eye complications leading to blindness (*15*). In describing the eye medicines used, some subjects referred to treatment with the seeds of "feto" (*Lepidium sativum*) and to treatment with goat or sheep faeces which are mixed with butter or milk and the leaves of the creeping plant "aregresa" (*Zehneria scarba*). Contamination of affected eyes with pathogenic microorganisms, particularly from faeces, would no doubt aggravate the situation.

Smallpox was reported as a predisposing factor in 16 children (2.2%) and 10 adults (17%) in the handicraft centres. The rate was higher in the adults than in children signifying the importance of the disease as a predisposing factor prior to 1976 when it was declared that the disease was eradicated (*22*). The youngest subject who reported smallpox as a predisposing factor was 15 years old at the time of interview which meant that the subject was three years of age when smallpox was declared eradicated in 1976. This lends credence to the reliability of the interviews. Furthermore in subjects who reported smallpox as a factor, facial scars were observed. In the study carried out in the Luapula Valley in Zambia in 1962-1964 (*1*), 15% of the cases were attributed to smallpox which is very comparable to the value found in the adults in the present study.

Trauma and damage due to foreign bodies and explosions were found to be responsible for 6.9% of blindness. This is much higher than the 0.7% reported by Sauter (*18*) in his study of children in blind schools in Tanzania.

Over two thirds of the bilateral blindness seen in children in the present study is due to corneal opacity resulting from diseases or conditions which are preventable. In order to minimize the number of children who become blind in the future, the problems associated with the preventable diseases and conditions should be addressed by the Government and all those concerned. Since about half of the preventable bilateral blindness occurs in children under the age of 4 yr, particular attention should be directed to blindness prevention in programmes for mother and child health care including the control of vitamin A deficiency. Community participation in such programmes is essential for their success.

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CHAPTER 4

Goitre in Ethiopia*

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Summary

A stratified goitre survey was conducted on 35,635 school children and 19,158 household members in all Regions of Ethiopia except Eritrea and Tigrai. The gross goitre prevalence (mean of male and female values) among school children and household members was 30.6% and 18.7% respectively while that of visible goitre was 1.6% and 3.2% respectively. Prevalence was higher in females (27.3% in household members and 36.1% in school children) than in males (10.1% in household members and 25.1% in school children) and increased with age more in females than in males. The prevalence rates at higher altitudes were higher than those at lower altitudes in both school children and household members. Using an epidemiological model the consequences of iodine deficiency, including cretinism and maternal wastage, have been estimated.

Introduction

Iodine deficiency disorders (IDD) encompass a variety of conditions including goitre, mental disorders and milder psychomotor defects, abortions, stillbirths, and increased perinatal and infant mortality. Goitre was known to the Hindus as early as 2000 B.C., to the Egyptians by 1500 B.C., and in Western Europe in the 1st century A.D. (*21*). In Ethiopia, there is a lack of written documentation on the occurrence in the past of goitre as is the case for many other diseases. Nevertheless, early travellers in the country and physicians during the Italian invasion of Ethiopia in the Second World War reported cases of goitre in various parts of the country (*18*). More recent studies demonstrated that goitre is one of the nutrition diseases of public health significance in certain areas in the country (*5,13,16,23,29*). The primary objective of the present study was to estimate the prevalence of goitre throughout the country. A second objective was to estimate the prevalence of other manifestations of IDD based on epidemiological models relating the prevalence of these manifestations to that of goitre.

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Material and Methods

Sampling

The study was conducted in the period between March 1980 and July 1981. Data on the population of urban and semi-urban areas, altitude, and agro-ecological zones were obtained from the Central Statistical Authority, Mapping Authority, and Ministry of Agriculture respectively. All Administrative Regions of the country were studied except Eritrea and Tigrai which were excluded for security reasons. First stage stratification was based on the population of the urban and semi-urban areas while subsequent stratification was based on Administrative Region and altitude, since 89% of the population of the country live in areas more than 1400 m above sea level (*19*). School children and household members were studied (see Figure 1).

In towns where there was more than one government primary school, one was selected in consultation with the educational authorities in order to ensure that those selected for the survey of school children were representative of all sectors in the area. All children present on the day of examination were included. Through such a procedure, a total of 35,635 school children (19,159 boys and 16,476 girls) were enroled in the study.

In the household survey, a total of 19,158 subjects (7,649 males and 11,509 females) were examined in 42 urban and semi-urban settings. The study sites were in 38 provinces with a population of over 19 million out of the total of 85 provinces in the country which has a population of 50 million (*25*). All households in smaller semi-urban settings or in two "kebeles" (urban dwellers' associations) in larger towns were registered by personnel employed for the purpose. From this list of households, 160 households were selected at random. All members of the selected households were requested to come to one central area, usually the kebele office or the local health institution for physical examination. The enumerators went to the houses when subjects did not report on time. Despite this effort, it was not easy to contact all adult males because of their preoccupation with their daily routine and reluctance to undergo health examination. A predesigned questionnaire was used to register members of households, their ages, sex, relationship to head of household, goitre grade and duration of stay in the area. On the same questionnaire, data on staple diet, frequency of consumption of kale, availability and type of latrine and source of drinking-water were also collected to determine whether there was any relationship between these variables and the occurrence of goitre. Consumption of goitrogens in foods including kale and faecal contamination of drinking water are putative goitrogenic factors (*8*).

Physical examination

The physical examination of all subjects was carried out by two of the authors (ZWG, TD). Goitre classification was compared and standardized at the start of examinations at each new study site and at regular intervals throughout the survey. The thyroid gland was examined and graded according to techniques recommended by Perez *et al.* (*28*) and modified by Delange (*4*) where grade 0 corresponds to no goitre, IA is palpable but not visible, IB is goitre easily visible with the neck extended, II is visible without extension of the neck, and III is large goitre visible from a distance.

When the goitre grading was in doubt, the lower stage was always chosen. In this study gross goitre includes stages IA, IB, II and III while visible goitre includes stages II and III. Whenever nodular goitre was diagnosed, this was noted along with the goitre grade.

Estimation of IDD rates

Cretinism was estimated from an epidemiological model based on existing data from Asian countries, Zaire and Ecuador (*2,12*). The symbols used have been modified for the sake of clarity:

$$c_g = \exp(b_0 + b_i g + b_{ii} g^2)/[1 + \exp(b_0 + b_i g + b_{ii} g^2)]$$

where c_g = prevalence (proportion) of cretinism estimated from the prevalence of gross goitre,
g = prevalence (proportion) of gross goitre,
b_0 = -9.3939,
b_i = 15.796,
and b_{ii} = -8.8026.

The rates (proportion of live births) of reproductive losses namely, neonatal death, stillbirth and miscarriage/infertility were estimated as follows:

$$l_n = m_n c_g$$

where m_n = multiplier for l_n,
c_g = prevalence (proportion) of cretinism estimated from the prevalence of gross goitre,
l_i = rate of neonatal deaths (m_i = 0.602),
l_{ii} = rate of stillbirths (m_{ii} = 0.656),
and l_{iii} = rate of miscarriage/infertility (m_{iii} = 0.883).

Mild developmental handicaps, namely developmental delays, psychomotor defects and reduced mental performance, were estimated by multiplying prevalence of cretinism by three (*2,12*). The calculations were carried out using the prevalence of goitre from the household survey since similar data were used in deriving the equations. The goitre rates for both sexes together were calculated by taking the mean of the rates for males and females. The 1990 population projection was based on the 1984 census of Ethiopia (*25*) while the crude birth rates were from the 1984 Regional census (*26*). The national crude birth rate used in the calculations was a weighted mean of the regional rates taking into account the number of household members examined in each Region.

Statistics

Chi square test and multiple regression analysis were used for determining the significance of differences and correlations respectively.

Results

School survey

The prevalence of goitre among school children at the different study sites by administrative regions of Ethiopia is shown in Table 1. The prevalence (mean of rates for boys and girls) of gross goitre among school children was 30.6% while that for visible goitre was 1.6% (Table 1).

The prevalence of goitre was higher in school children living at higher altitudes than those at lower altitudes. The prevalence predictions have not been normalised for altitude. The slope and intercept of the linear regression of gross goitre (%) on altitude (m) with standard error in parentheses is: ($n = 41$; $r = 0.37$; $s = 0.0114$ (0.0046); $i = 6.03$ (9.37)).

More girls were found to have goitre than boys (Tables 1 and 2). The difference between the sexes became more pronounced with age (Table 2). In boys the prevalence dropped from about 25% for those 18 years of age and younger to less than 10% for those 19 years of age and older. In girls, the prevalence continued to increase with age from 20% in girls 0 - 5 years to over 42% in those 19 years of age and over. The sex (male:female) ratio for gross goitre was 1:1.3 for the age group 6-12 y, 1:1.6 for 13-18, and 1:5.3 for those above 19 years of age. From among those with visible goitre, 21 (5.7%) had nodular goitre.

Household survey

In the household survey, an overall gross goitre prevalence of 10.1% in males and 27.3% in females (mean of rates for males and females, 18.7%) was found (Table 3). Visible goitre prevalence was 0.34% in males and 5.9% in females (mean of males and females, 3.1%). The rate of visible goitre was lower than 4% in males in all regions while in females, a rate as high as 32.9% was seen in Gondar town. Of those with visible goitre, only 31 or 4.4% had nodular goitre which was seen at 15 of the study sites. Assuming that the sample population is representative for the whole country, 2.5 million males and 6.8 million females would have goitre while 85,000 males and 1.5 million females would have visible goitre (data from Table 3). Prevalence did not differ between males and females in the 0-5 y age range (4.1% in both), but was significantly higher ($P<0.001$) in females than in males thereafter (Table 4). Of the males aged 13-18 years, 30% were found with goitre while 45% females of the same age group had goitre. The sex difference was even more marked in the age group 19 years and older where the prevalence in males had decreased to 6.4% while in females it had increased to 46.0%. The sex ratio of goitre was 1.0 for under 5 y old children, 1:1.2 for the 6-12 y old, 1:1.5 for the 13-18 and 1:7.2 for the 19 y and above age group.

As for the school children, the prevalence of goitre was higher in household members living at higher altitudes than those at lower altitudes. The regression of gross goitre (%) on altitude (m) with standard error in parentheses was: ($n = 41$; $r = 0.41$; $s = 0.0083$ (0.0035); $i = 3.52$ (6.41)).

Figure 1 Map of Ethiopia showing Administrative Regions and study sites.

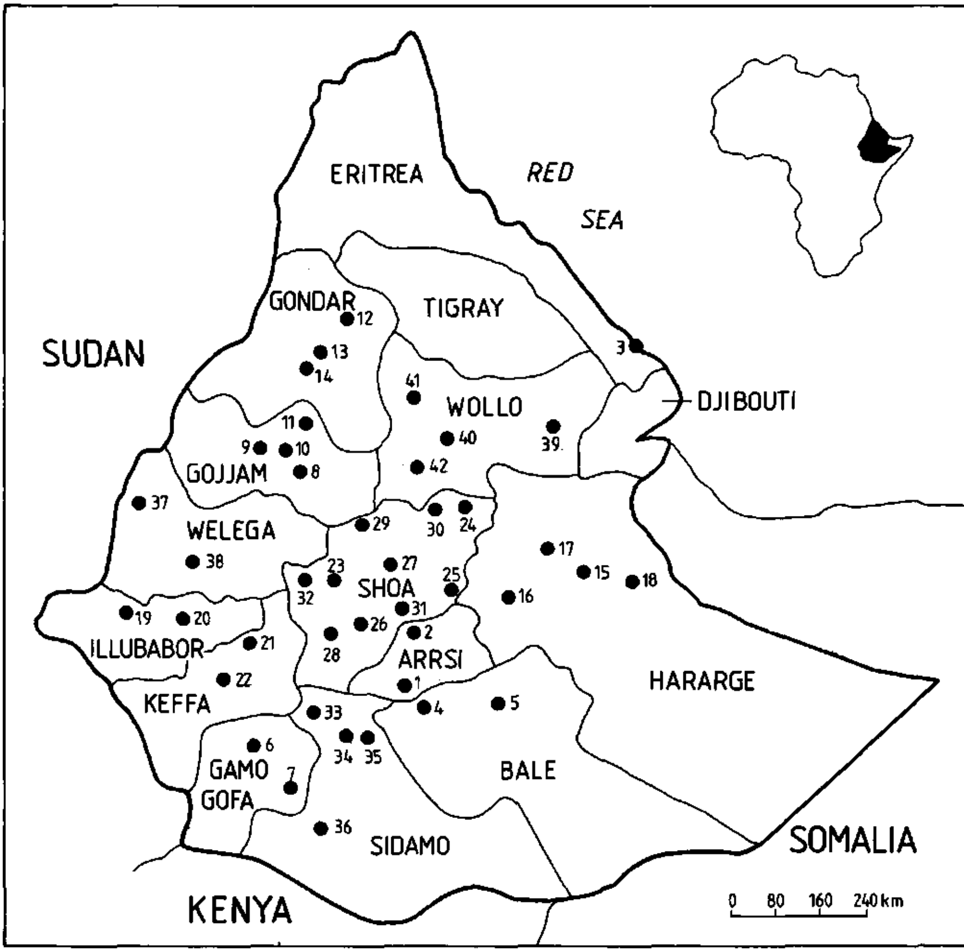

Table 1 Prevalence of goitre in school children at various study sites in Ethiopia

Region	Study site No.[a]	Study site Name	Altitude (m)	Examined Male	Examined Female	Goitre prevalence Male Gross		Male Visible		Female Gross		Female Visible	
				n	n	n	%	n	%	n	%	n	%
Arssi	1.	Bekoji	2835	566	437	204	36.0	1	0.5	252	57.7	7	1.6
Arssi	2.	Dierra	1780	443	340	49	11.1	0	0.0	58	17.1	0	0.0
Assab	3.	Assab	170	619	544	34	5.5	0	0.0	65	11.9	0	0.0
Bale	4.	Adaba	2420	445	480	236	53.0	2	0.4	288	60.0	9	1.9
Bale	5.	Ghinir	1970	520	621	70	13.5	0	0.0	116	18.7	3	0.5
Gamo-Gofa	6.	Felegeneway	1430	513	264	295	57.5	44	8.6	207	78.4	51	19.3
Gamo-Gofa	7.	Gidole	2090	768	448	54	7.0	1	0.1	115	25.7	6	1.3
Gojjam	8.	Burie	2200	384	327	176	45.8	11	2.9	188	57.5	27	8.3
Gojjam	9.	Chagnie	1690	515	550	261	50.7	1	0.2	336	61.1	3	0.5
Gojjam	10.	Injibara	2640	386	263	134	34.7	1	0.3	142	54.0	4	1.5
Gojjam	11.	Tis-Abay	1720	229	208	64	24.9	0	0.0	89	42.8	0	0.0
Gondar	12.	Debarek	2850	490	529	237	48.4	12	2.4	340	64.3	22	4.2
Gondar	13.	Gondar	2250	1427	1472	887	62.2	40	2.8	1107	75.2	121	8.2
Gondar	14.	Koladuba	1890	321	395	101	31.5	1	0.3	166	42.0	7	1.8
Hararge	15.	Alemaya	2030	140	114	6	4.3	0	0.0	5	4.4	0	0.0
Hararge	16.	Bedessa	1790	355	339	65	18.3	2	0.6	116	34.2	7	2.1
Hararge	17.	Idora[b]	920	-	-	-	-	-	-	-	-	-	-
Hararge	18.	Jijiga	1690	492	485	18	3.7	0	0.0	18	3.7	1	0.2
Illubabor	19.	Gambella	520	487	281	52	10.7	2	0.4	60	21.4	9	3.2
Illubabor	20.	Gore	2025	629	639	156	24.8	5	0.8	216	33.8	5	0.8
Kefa	21.	Agaro	1770	816	872	95	11.6	0	0.0	159	18.2	3	0.3

Table 1 (continued) Prevalence of goitre in school children at various study sites in Ethiopia

Kefa	22.	Bonga	1800	385	368	70	18.2	0	0.0	108	29.3	4	1.1
Shoa	23.	Ambo	2120	854	785	166	19.4	0	0.0	269	34.3	7	0.9
Shoa	24.	Ataye	1500	361	355	16	4.4	0	0.0	37	10.4	0	0.0
Shoa	25.	Awash	1015	243	221	0	0.0	0	0.0	2	0.9	0	0.0
Shoa	26.	Butajira	2090	425	310	101	23.8	7	1.6	114	36.8	7	2.3
Shoa	27.	Chancho	2510	286	263	68	23.8	6	2.1	115	43.7	17	6.5
Shoa	28.	Emdibir	2125	886	420	84	9.5	0	0.0	87	20.7	1	0.2
Shoa	29.	Gohatsion	2520	342	266	145	42.4	2	0.6	151	56.8	9	3.4
Shoa	30.	Mehalmeda	3060	404	365	27	6.7	1	0.2	67	18.4	1	0.3
Shoa	31.	Mojo	1850	417	424	8	1.9	0	0.0	32	7.5	1	0.2
Shoa	32.	Sheboka	1820	418	192	140	33.5	3	0.7	77	40.1	1	0.5
Sidamo	33.	Boditi	2100	254	111	29	11.4	2	0.8	10	9.0	0	0.0
Sidamo	34.	Dilla	1760	570	491	54	9.5	0	0.0	71	14.5	5	1.0
Sidamo	35.	Hagereselam	2790	269	177	27	10.0	0	0.0	35	19.8	0	0.0
Sidamo	36.	Yavello	1320	397	285	3	0.8	0	0.0	7	2.5	0	0.0
Wellega	37.	Assosa	1680	305	284	97	31.8	3	1.0	140	49.3	4	1.4
Wellega	38.	Guye	2030	297	86	169	56.9	19	6.4	41	47.7	1	1.2
Wollo	39.	Assaita	460	282	254	43	15.2	0	0.0	54	21.3	0	0.0
Wollo	40.	Haik	1990	441	410	116	26.3	5	1.1	135	32.9	9	2.2
Wollo	41.	Lalibela	2470	357	318	171	47.9	5	1.4	189	59.4	8	2.5
Wollo	42.	Wereillu	2685	421	483	76	18.1	1	0.2	161	33.3	8	1.7
Total				19159	16476	4804	25.1	177	0.9	5945	36.1	368	2.2

[a] Numbers indicated on map to show study sites.
[b] School survey not conducted.

There was a high correlation between gross goitre prevalence in school children and household members ($r=0.897$, $P<0.001$). Data on gross goitre in household members were used to estimate other forms of IDD in the population of the areas surveyed. For the more severe forms in survivors, the rate of cretinism was estimated to vary from 0.09 to 16 per 1,000 of the population. Assuming that the population surveyed was representative for the country, the number of cretins in Ethiopia in 1990 was estimated at 59,000 (1.17 per 1,000) while three times as many, 176,000 persons (3.51 per 1,000) may show some degree of developmental and neurological function impairment attributable to iodine deficiency. The estimated annual national toll in 1990 (rates per 1,000 live births) of reproductive losses attributable to iodine deficiency were as follows: neonatal deaths, 13,600; stillbirths 14,800; and infertility/miscarriage 20,000.

From the data collected on whether excreta was disposed of in a pit latrine, water-flushed toilet or in the open air, no relationship was seen with goitre size. Neither was a relationship seen with kale consumption, seasonally or all year round, or with the source of drinking water from pipe, well, spring or river.

Discussion

Studies carried out in the past have demonstrated that IDD existed in Ethiopia (*5,13,16,18,23,29*) and that in certain pocket areas, the prevalence may be as high as 71% (*23*). However, the present study is the first which has been designed to provide a representative overview of the severity and extent of IDD in the country. The goitre prevalence in school children found in this survey was 30.6% which is regarded as severe according to the classification of Hetzel (*11*). This rate is not as high as that reported from other African countries such as Tanzania with 47.8% (*17*). However, many surveys have not been as representative as the present survey which was stratified and covered the whole country. The present survey showed that in school children in particular and in household members in general, the prevalence of goitre increased with age and reached its peak in the prepubertal and pubertal age in both sexes but diminished in adulthood in males and plateaued after a slight decrease in females. These findings are in agreement with observations made elsewhere such as in Sudan and Tanzania (*6,17*). In the household study group of the present survey, the sex ratio for goitre prevalence was 1:1.5 in subjects aged 13-18 years and 1:7.2 in those 19 years of age and over.

Studies from other areas of the world have suggested that goitre prevalence is associated with soils of Pre-Cambrian origin (*30,32*), suboptimal iodine intake (*1*), excessive iodine intake possibly leading to autoimmune thyroiditis (*24*), high calcium, magnesium and fluorine consumption (*3,8,21*), selenium deficiency (*31*), goitrogenic components in the diet (*7,20,27*), bacterial contamination of drinking water (*8*) and malnutrition (*9,14,15*). The results of this study could find no associations with kale consumption, availability and type of latrine or source of drinking water but a relationship was found with altitude.

Table 2 Distribution of goitre grades amongst school children by age and sex

Sex	Age (yr)	Number examined	Goitre grade											
			0		IA		IB		II		III		Total goitre	
			n	%	n	%	n	%	n	%	n	%	n	%
Male														
	0 - 5	19	14	73.7	5	26.3	0	0.0	0	0.0	0	0.0	5	26.3
	6 - 12	13406	10002	74.6	2495	18.6	832	6.2	77	0.6	0	0.0	3404	25.4
	13 - 18	5390	4023	74.6	901	16.7	369	6.8	92	1.7	5	0.1	1367	25.4
	19+	344	316	91.9	20	5.8	5	1.5	3	0.9	0	0.0	28	8.1
	Sub-total	19159	14355	74.9	3421	17.9	1206	6.3	172	0.9	5	0.0	4804	25.1
Female														
	0 - 5	30	24	80.0	3	10.0	3	10.0	0	0.0	0	0.0	6	20.0
	6 - 12	11724	7732	66.0	2587	22.0	1252	10.7	149	1.3	4	0.0	3992	34.0
	13 - 18	4534	2667	58.8	1003	22.1	669	14.8	186	4.1	9	0.2	1867	41.2
	19+	188	108	57.4	32	17.0	28	14.9	18	9.6	2	1.1	80	42.6
	Sub-total	16476	10531	63.9	3625	22.0	1952	11.8	353	2.1	15	0.1	5945	36.1

Table 3 Prevalence of goitre in household members at various study sites in Ethiopia

Region	Study site No.[a]	Name	Population 1990 Male	Population 1990 Female	Birth rate[b] 1990	Examined Male n	Examined Female n	Goitre prevalence Male Gross n	Male Gross %	Male Visible n	Male Visible %	Female Gross n	Female Gross %	Female Visible n	Female Visible %
Arssi	1.	Bekoji	3141	3337	42.3	180	207	58	32.2	0	0.0	115	55.6	15	7.2
Arssi	2.	Dierra	2729	3146	42.3	167	254	6	3.6	0	0.0	27	10.6	4	1.6
Assab	3.	Assab	18035	18036	39.3	157	290	9	5.7	0	0.0	36	12.4	0	0.0
Bale	4.	Adaba	3487	4339	48.6	199	267	49	24.6	1	0.5	126	47.2	11	4.1
Bale	5.	Ghinir	5000	5202	48.6	230	345	18	7.8	0	0.0	52	15.1	6	1.7
Gamo-Gofa	6.	Felegeneway	4464	4471	45.9	153	207	28	18.3	2	1.3	97	46.9	50	24.2
Gamo-Gofa	7.	Gidole	4554	5417	45.9	175	254	12	6.9	0	0.0	61	24.0	15	5.9
Gojjam	8.	Burie	4319	5388	41.3	194	310	56	28.9	6	3.1	158	51.0	42	13.5
Gojjam	9.	Chagnie	4530	5466	41.3	196	306	54	27.6	1	0.5	168	54.9	56	18.3
Gojjam	10.	Injibara	544	1231	41.3	160	284	25	15.6	0	0.0	127	44.7	7	2.5
Gojjam	11.	Tis-Abay	1477	1927	41.3	179	256	45	25.1	0	0.0	129	50.4	23	9.0
Gondar	12.	Debarek	4214	5858	44.7	143	251	28	19.6	1	0.7	135	53.8	42	16.7
Gondar	13.	Gondar	34915	46946	44.7	155	225	37	23.9	3	1.9	127	56.4	74	32.9
Gondar	14.	Koladuba	2943	5173	44.7	110	196	6	5.5	0	0.0	68	34.7	13	6.6
Hararge	15.	Alemaya	3788	4203	43.7	190	308	3	1.6	0	0.0	12	3.9	0	0.0
Hararge	16.	Bedessa	4030	3869	43.7	191	244	5	2.6	0	0.0	42	17.2	5	2.0
Hararge	17.	Idora	703	837	43.7	68	107	0	0.0	0	0.0	1	0.9	0	0.0
Hararge	18.	Jijiga	12897	14625	43.7	140	258	0	0.0	0	0.0	10	3.9	1	0.4
Illubabor	19.	Gambella	2788	2544	37.9	168	264	5	3.0	0	0.0	23	8.7	4	1.5
Illubabor	20.	Gore	3539	4346	37.9	281	371	21	7.5	2	0.8	103	27.8	13	3.5

Table 3 (continued) Prevalence of goitre in household members at various study sites in Ethiopia

Kefa	21.	Agaro	11325	10950	41.6	232	331	5	2.2	1	0.4	80	24.2	15	4.5
Kefa	22.	Bonga	3373	4005	41.6	144	275	13	9.0	0	0.0	85	30.9	7	2.5
Shoa	23.	Ambo	9660	10906	38.2	212	326	27	12.7	0	0.0	62	19.0	11	3.4
Shoa	24.	Ataye	2463	3013	38.2	129	217	3	2.3	0	0.0	24	11.1	2	0.9
Shoa	25.	Awash	2349	2631	38.2	163	266	0	0.0	0	0.0	16	6.0	3	1.1
Shoa	26.	Butajira	7719	8529	38.2	251	323	27	10.8	4	1.6	111	34.4	38	11.8
Shoa	27.	Chancho	1466	2008	38.2	135	255	9	6.7	0	0.0	60	23.5	18	7.1
Shoa	28.	Emdibir	840	1107	38.2	183	308	16	8.7	0	0.0	86	37.9	10	3.2
Shoa	29.	Gohatsion	1538	2177	38.2	186	299	52	28.0	1	0.5	151	50.5	46	15.4
Shoa	30.	Mehalmeda	2406	2862	38.2	121	210	0	0.0	0	0.0	47	22.4	4	1.9
Shoa	31.	Mojo	7587	8967	38.2	165	250	0	0.0	0	0.0	30	12.0	1	0.4
Shoa	32.	Sheboka	1350	1798	38.2	215	293	19	8.8	0	0.0	76	25.9	3	1.0
Sidamo	33.	Boditi	2525	2701	38.6	144	215	9	6.3	0	0.0	37	17.2	8	3.7
Sidamo	34.	Dilla	14322	14092	38.6	245	288	6	2.4	0	0.0	37	12.8	6	2.1
Sidamo	35.	Hagereselam	1537	1641	38.6	185	269	0	0.0	0	0.0	22	8.2	3	1.1
Sidamo	36.	Yavello	3573	3533	38.6	208	296	0	0.0	0	0.0	10	3.4	1	0.3
Wellega	37.	Assosa	2480	2457	31.2	283	413	54	19.1	1	0.4	162	39.2	21	5.1
Wellega	38.	Guye	553	681	31.2	276	288	37	13.4	1	0.4	112	38.9	18	6.3
Wollo	39.	Assaita	4005	4139	39.6	164	284	0	0.0	0	0.0	42	14.8	5	1.8
Wollo	40.	Haik	2582	3419	39.6	262	397	19	7.3	2	0.8	109	27.5	11	2.8
Wollo	41.	Lalibela	2747	3382	39.6	136	244	12	8.8	0	0.0	99	40.6	54	22.1
Wollo	42.	Wereillu	2715	3445	39.6	174	258	3	1.7	0	0.0	72	27.9	11	4.3
Total						7649	11509	776	10.1	26	0.3	3147	27.3	677	5.9

[a] Numbers indicated on map (Figure 1) to show study sites.
[b] Birth rate, number of live births per 1000 population per year (*26*).

Table 4 Distribution of goitre grades amongst all household members by age and sex.

Sex	Age (yr)	Number examined	Goitre grade 0		IA		IB		II		III		Total goitre	
			n	%	n	%	n	%	n	%	n	%	n	%
Male														
	0 - 5	4079	3913	95.9	156	3.8	9	0.2	1	0.0	0	0.0	166	4.1
	6 - 12	1951	1521	78.0	369	18.9	55	2.8	5	0.3	1	0.1	430	22.0
	13 - 18	315	219	69.5	75	23.8	15	4.8	6	1.9	0	0.0	96	30.5
	19+	1304	1220	93.6	53	4.1	18	1.4	10	0.8	3	0.2	84	6.4
	Sub-total	7649	6873	89.9	653	8.5	97	1.3	22	0.3	4	0.1	776	10.1
Female														
	0 - 5	4106	3938	95.9	159	3.9	9	0.2	0	0.0	0	0.0	168	4.1
	6 - 12	2265	1645	72.6	483	21.3	114	5.0	23	1.0	0	0.0	620	27.4
	13 - 18	652	356	54.6	152	23.3	90	13.8	53	8.1	1	0.2	296	45.4
	19+	4486	2423	54.0	823	18.3	640	14.3	503	11.2	97	2.2	2063	46.0
	Sub-total	11509	8362	72.7	1617	14.0	853	7.4	579	5.0	98	0.9	3147	27.3

Thus, there was a positive correlation between goitre prevalence and altitude amongst school children as well as household members. The correlation was relatively stronger amongst the household members which may be related to a longer period of exposure to a fixed iodine intake.

Although goitre prevalence was correlated with altitude, there was variation of prevalence within the same range of altitude amongst the different study sites particularly in lowland areas. Thus the prevalence in household members in Felegeneway which lies at an altitude of 1430 m was 33% while it was less than 8% at all the other sites below 1500 m. It is also noteworthy that next to Gondar, the highest prevalence of visible goitre was observed here.

Although leaching of iodine from the highland areas might result in iodine deficiency at high altitudes, no assessment of iodine content of foods, water and soil was done during the present study. However, the iodine content of salt from the Red Sea is low when compared with that from more open oceans (*16* and report by a WHO consultant, P. Subrimanian: unpublished observations). The iodine content of food and soils from goitrous areas in Ethiopia has also been shown to be low (Z. Wolde-Gebriel and C.E. West, in preparation). Some people in highland regions obtain their food from iodine-rich areas and this will help to increase iodine intake. Other factors such as goitrogens may reduce the availability of iodine.

Assessment in school children is a simple and cheap method for determining the extent and magnitude of IDD in a community as children are readily accessible and representative. In the areas we surveyed, the school children were from different socio-economic groups of the society and ate at home and thus their general dietary pattern should reflect that of the community in which they live. In the present study, the prevalence rate of goitre in school children reflected that in household members. Very low or zero rates of goitre were observed both in school children and household members in certain areas such as Alemaya, Jijiga, Awash and Yavello while high prevalence rates were observed in both groups in other areas such as Gondar, Debarek, Tis-Abay and Felegeneway.

Furthermore, this study was conducted in semi-urban and urban areas where the inhabitants rely on food produced in the surrounding rural areas. Thus the iodine intake of the people surveyed may not be very different from that of those who live in the nearby surrounding areas. Since the sites sampled were evenly distributed throughout the country, we believe that the findings are representative.

Although an enlarged thyroid gland by itself does not affect a subject's health, except when the goitre is so large that it compresses the trachea, its aesthetic implications especially in girls has social implications in many rural areas. Thus many goitrous women said that they found it difficult to find husbands and that those with large goitres did not aspire to university after successfully passing their examination out of fear of comments from others.

With concern to the other manifestations of IDD, excellent reviews on brain development and reproductive disorders in relation to iodine deficiency and thyroid function have been prepared by Hetzel and his colleagues (*10,22*). Relationships between iodine deficiency and thyroid function on the one hand, and reproductive failures, poor educational performance and physical development on the other hand have been documented from many places. These developmental IDDs are very important problems of public health significance but are generally neglected by health professionals and decision makers. Applying previously developed epidemiological models to the results from the population studied which is assumed to be representative of the whole country, it is estimated that there are 59,000 cretins and 176,000 cretinoids in Ethiopia. Classically, as predicted from the epidemiological model presented, cretinism is regarded as a problem in areas where the prevalence of goitre is more than 50%. From the present study we know that there are certain pocket areas with such high rates and this could explain the existence of cretinism in such areas.

Thus IDD would appear to be a serious threat to the health and well-being of the people residing in goitre endemic areas. Cretins are social and economic burdens to the households and communities in which they live and to the nation as a whole. The estimates at least indicate the magnitude of the problem and highlight a very serious problem which deserves the attention of health professionals at the level of research, policy formulation and programme action and a commitment to intervention from government. As far as research is concerned, efforts should be made to overcome the paucity of data on the impact of iodine deficiency and iodine supplementation on maternal welfare. As far as programmes are concerned, the salt iodation effort which has been initiated should be encouraged so that iodated salt can reach all goitrous areas. In view of the difficult terrain and the poor transport, distribution and marketing infrastructure of the country, the use of iodized oil capsules in difficult and inaccessible areas should also be considered.

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CHAPTER 5

Vitamin A, iron and iodine status in children with severe vitamin A deficiency in a rural village in the Hararge Region of Ethiopia*

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Summary

A total of 240 children were examined for vitamin A deficiency in a village in Hararge Region of Ethiopia. Night blindness, Bitot's spots, corneal xerosis, corneal ulceration and corneal scars were observed in 69, 16, 2, 15 and 14 children, respectively, based on the most severe eye signs. Blood was collected from 76 children with eye signs and 9 other children selected at random. The concentration of retinol in serum was <0.35 µmol/l in 30.2% of children and the median serum retinol binding protein, iron, transferrin saturation and ferritin levels were low. Levels of IgG and IgM were elevated in 78.8% and 82.4% children, respectively, while C-reactive protein levels were elevated in 42.4% of children. There was a higher prevalence of wasting (33%) than stunting (10%) with an additional 8% of children being both stunted and wasted. In the two years prior to the study, there were 74 deaths of which 17 were reported to be associated with ruptured corneas. The community had been dependent on relief food aid for the previous six years.

Introduction

A health problem with eye involvement in children in a village in Hararge Region in eastern Ethiopia was reported to the Regional Health Department by CARE International in September 1988. The Ethiopian Nutrition Institute was requested to send a multidisciplinary team to conduct a survey in this area as it seemed likely that the problem was related to vitamin A deficiency. The village concerned was Melkaye (Farmers' Association No. 34) in Darolobo *Wereda* (District) of Habro *Awraja* (Province). The area in which the village is situated was dry and agriculturally very poor and the main products were sorghum, maize, teff (*Eragrostis teff*), coffee and chat (*Khat edulis*). The inhabitants had been dependent on food aid since 1982 because of insufficient food production as a result of crop failures due to the abnormal low rainfall in the area. Initially, food aid had been provided free but after three years, a food-for-work programme was initiated. The food aid comprised wheat flour, vegetable oil, butter-oil and beans.

**Submitted for publication*

Patients and methods

Conduct of survey

The village of Melkaye has its own community health agent and the nearest health station (a clinic run by a health assistant with 1-2 y of public health and medical training after 8 years of schooling) is 34 km away by dry weather road at Mecheta while the nearest health center is 84 km southeast at Gelemso. There are four other villages of similar population within 5 km of the village.

The total population of the village was 1147 persons in 110 households. A comprehensive questionnaire was designed specifically for the study. All households with children were registered and information on the children including age, sex and history of breast-feeding and illness were collected from heads of households. They were also asked to provide information, including cause of death, on all persons who had died in the previous 24 mo. This information was crosschecked with the death register of the community health agent. After registration, all children were examined by the physician (TF) and nutritionist (ZWG). Information is presented in this paper on the ocular symptoms and signs of xerophthalmia and the signs of trachoma. The WHO classification (*47*) for xerophthalmia was used: for brevity, night blindness is referred to as a sign rather than a symptom. A problem of public health significance exists when the prevalence of night blindness, Bitot's spots, corneal xerosis with corneal ulceration/keratomalacia, or corneal scars exceeded 1%, 0.5%, 0.01%, and 0.05% respectively. Where possible, blood was collected from those with clinical signs and symptoms of vitamin A deficiency and one in every 20 of the remaining children. Anthropometric data were collected on all children and qualitative dietary information was obtained from heads of households.

After completion of the survey vitamin A capsules, as recommended by WHO (*47*), were distributed to all children in Melkaye and the near-by villages. Those with clinical signs of vitamin A deficiency received three therapeutic doses on days 1, 2 and 7 while all other children received a prophylactic dose (200,000 IU for children over one year and 100,000 IU for children one year and younger).

A detailed report on the situation with recommendations for action was prepared and submitted to the Ministry of Health, Hararge Regional Health Office, Hararge Regional Relief and Rehabilitation Office, and CARE International.

Collection of blood and subsequent analysis

Blood (10 - 15 ml) was collected by venous puncture without anticoagulant using the Vacutainer system (Venoject; Terumo, Belgium) and centrifuged within 6 h, after transfer to the field laboratory established at the local clinic in Mecheta. The serum obtained was stored in the dark at -20°C until analysis. Vitamin A was analysed as follows. Serum (0.1 ml) was deproteinized by mixing with ethanol (0.4 ml, 90% v/v). The retinol concentration in an aliquot (50 μl) of the supernatant obtained after centrifugation was estimated spectrophotometrically at 325 nm by comparison with standards after separation by high performance liquid chromatography on a Sperisorb 5-ODS column (150 x 4.6 mm; Chrompak, Middelburg, The Netherlands).

The co-efficient of variation of standards was less than 3.4%. Further details of the method will be published elsewhere. Retinol-binding protein (RBP), transthyretin (TTR), transferrin, immunoglobulin A, G and M (IgA, IgG and IgM) and C-reactive protein (CRP) were analysed by immunonephelometry using a Behring Nephelometer and reagents supplied by Behringwerke AG, Germany as described by Fink *et al.* (*9*). Albumin was measured using the bromocresol green method of Doumas *et al.* (*8*). Total triiodothyronine (TT3), total thyroxin (TT4), thyrotropin (TSH) and ferritin were measured by radioimmunoassay using kits supplied by Amersham International, UK. Total iron-binding capacity (TIBC) and serum iron were measured as described by Schade *et al.* (*33*).

Anthropometry
Weight was measured to the nearest 100 g using a beam balance (Seca, Germany) for children over the age of 5 y and using a hanging scale (Salter, UK) for younger children. The scales were checked and calibrated with a known weight at the start of the day and at regular intervals throughout the day. Height was measured to the nearest 0.5 cm using a graduated height stick with a movable head piece while for children who could not yet walk, length was determined in a supine position using a calibrated measuring board. Arm circumference was measured to the nearest 0.1 cm with a measuring tape. The standard deviation scores (Z-scores) were calculated with the help of software (CASP) developed by WHO (*48*) and the National Center for Health Statistics (NCHS) (*25*). A ZWH score of 2.00 or -2.00 means that the child is 2 SD above or below the median weight-for-height, respectively, while a ZHA refers to the Z-score for height-for-age. Based on these scores, children were classified according to Waterlow (*41*) as normal (ZWH > -2.00 and ZHA > -2.00), wasted (ZWH < -2.00 and ZHA > -2.00), stunted (ZWH > -2.00 and ZHA < -2.00), or wasted and stunted (ZWH < -2.00 and ZHA < -2.00).

Dietary information
Information on feeding habits, food aid and distribution mechanisms was obtained from heads of households, community leaders and officials of governmental and non-governmental organisations. Samples of three plants which were being eaten but which are not normally consumed when food is readily available were collected for analysis of their ß-carotene content. They were identified by botanists of the Biology Department of Addis Ababa University.

Statistics
Chi square and Mann-Whitney for pair testing and Kruskal-Wallis for multiple parameter testing were used to compare significance of differences as the data were not normally distributed. Values of biochemical concentrations were checked for skewness and outside the range of -1 to +1 were regarded as skewed and data for the parameters were transformed to natural logarithms prior to correlation analysis. Ferritin values (skewness = 1.06) were transformed to square root before correlation analysis.

Results

Clinical examination

Of the 240 children examined, 116 (53.2% of the boys and 43.1% of the girls) had at least one recognised sign of vitamin A deficiency (Table 1). Data are presented for the eye with the most severe sign unless otherwise indicated. Night blindness (XN) was reported in 32.3% of the boys and 25.0% of the girls without other signs of xerophthalmia and in 12.9% of boys and 12.1% of the girls with more severe signs of xerophthalmia.

Table 1 Distribution of clinical symptoms and signs by age group and sex of children in Hararge

Symptoms/signs	Sex	Age (months)						
		< 24	24-47	48-71	72-95	96-119	120-150	Total
Night blindness	M	1	9	7	11	9	3	40
	F	0	8	5	5	6	5	29
	M+F	1	17	12	16	15	8	69
Bitot's spots	M	1/0[a]	0/2	0/1	1/1	0/1	0/1	2/6
	F	0/0	1/0	0/2	1/2	1/0	0/1	3/5
	M+F	1/0	1/2	0/3	2/3	1/1	0/2	5/11
Corneal xerosis	M	0/0	0/0	0/1	0/0	1/0	0/0	1/1
	F	0/0	0/0	0/0	0/0	0/0	0/0	0/0
	M+F	0/0	0/0	0/1	0/0	1/0	0/0	1/1
Corneal ulceration	M	0/0	0/1	1/2	0/2	0/0	1/3	2/8
	F	0/0	0/1	0/2	1/0	0/1	0/0	1/4
	M+F	0/0	0/2	1/4	1/2	0/1	1/3	3/12
Corneal scar	M	0/0	0/0	2/1	1/2	0/0	0/0	3/3
	F	1/0	0/0	2/0	3/0	1/1	0/0	7/1
	M+F	1/0	0/0	4/1	4/2	1/1	0/0	10/4
Total eye symptoms and signs	M	2	12	15	18	11	8	66
	F	1	10	11	12	10	6	50
	M+F	3	22	26	30	21	14	116
Total examined	M	20	27	18	24	23	12	124
	F	22	20	24	27	15	8	116
	M+F	42	47	42	51	38	20	240

[a] Monocular/binocular respectively.

Forty percent of children with night blindness reported that they had developed the symptom in the previous 12 mo while most of the remainder said that they could not remember when the symptom first appeared. The rate of Bitot's spots (X1B) without more serious signs was 6.5% in boys and 6.9% in girls while an additional 2.4% of boys and 0.9% of girls with such signs also had Bitot's spots in the other eye. For the more severe signs of active xerophthalmia including corneal xerosis (X2) and corneal ulceration/keratomalacia (X2 and X3), 9.7% of the boys and 4.3% of the girls exhibited these signs. The corneal ulceration (X3) was unilateral in three children and bilateral in 12 children while 14 of the 15 children exhibited ulceration covering more than one third of the corneal surface (X3B). Corneal scarring (XS) was observed in 14 children (6 boys and 8 girls; 5.8%) and in four of them it occurred in both eyes and involved more than one-third of the cornea which meant that they were blind. Twelve of these children with corneal scars (5%) were below the age of 8 years. No child was reported to have had a history of trauma or any other event which could have contributed to scarring of the cornea. Although not specific for xerophthalmia, 17 children exhibited conjunctival xerosis (X1A, data not shown in table). More than half of the ocular signs were observed in children aged 6 years and older while the sex ratio was 1.23. This male predominance was even more pronounced for the more severe signs of xerophthalmia with the exception of corneal scars. Trachoma was observed in 30 (12.5%) of all children.

Fifteen percent of the children were found to be suffering from either upper respiratory tract infection or diarrhea or both at the time of examination and in 60% of these children, the condition was reported to be at least of one month duration. Measles was reported in five children for the previous two-year period but had not resulted in corneal signs.

Biochemical parameters
Biochemical data are presented in Table 2. Of the children studied, 30.2% had serum retinol levels less than 0.35 µmol/l regarded as deficient (*12*), 58.0% between 0.36 and 0.69 µmol/l regarded as low (*12*) and the remaining 11.8% had levels of 0.70 µmol/l or above. Similar results were found for retinol-binding protein levels with 31.8%, 49.4% and 17.8%, respectively, having levels corresponding to the cut-off points representing deficient, low and adequate levels of retinol, respectively. In the sample of serum from one child, the concentration of retinol was below the detection limit of 0.04 µmol/l while for retinol-binding protein, 23 children had values below the detection limit of 0.26 µmol/l. Transthyretin levels were below the mean of the normal range (4.55 µmol/l) in all children. For albumin, 20.3% of the children had levels less than 507 µmol/l regarded as the lower limit of normal. The concentration of ferritin in plasma was not markedly depressed with only 4.1% of children having deficient values which are normally regarded as indicating depleted iron stores. The total iron-binding capacity of the children was extremely low with 96.6% having deficient levels. This is also reflected in the levels of transferrin (transferrin has a molecular weight of ca. 40,000 and two binding sites for iron). The proportion of children with low levels of circulating iron in plasma was much higher at 44.1%. The transferrin saturation which is the result obtained after dividing serum iron by total iron-binding capacity was found to be low in 15.3% of the children tested indicating iron-deficient erythropoiesis. Presence of infection was evident from the increased

Table 2 Median values of biochemical variables in serum

Biochemical variable (units)	Number	Median (25th & 75th percentiles)	Normal range	(source)[a]
Serum albumin (μmol/l)	74	565 (522 & 609)	507 - 797	(1)
Transthyretin (μmol/l)	85	2.96 (2.55 & 3.39)	1.82 - 7.27	(2)
Retinol-binding protein (μmol/l)	85	0.46 (0.26 &0.62)		(3)
Transferrin (g/l)	85	2.58 (2.44 & 2.90)	2.95 (2.0 - 4.0)	(2)
Retinol (μmol/l)	80	0.46 (0.29 & 0.55)	<0.35 deficient 0.35-0.69 low 0.70-1.05 adequate >1.05 normal	(4)
Total iron-binding capacity (μmol/l)	62	53.4 (49.9 & 58.5)	> 70.4	(5)
Ferritin (μg/l)	68	44.5 (38.4 & 58.8)	> 10	(5)
Serum iron (μmol/l)	68	11.8 (9.2 & 15.2)	10.7	(5)
Transferrin saturation (%)	62	23.0 (17.8 & 31.1)	> 16	(5)
Triiodothyronine (nmol/l)	70	1.72 (1.38 & 2.08)	0.80 - 2.69	(6)
Thyroxin (nmol/l)	70	137.1 (119.1 & 155.7)	61.8 - 164.7	(6)
Thyrotropin (μIU/ml)	69	1.90 (1.30 & 3.30)	1.00 - 5.50	(6)
IgA (g/l)	85	2.31 (1.72 & 3.06)	0.90 - 3.25	(2)
IgG (g/l)	85	18.4 (15.5 & 21.6)	8.0 - 15.0	(2)
IgM (g/l)	85	2.20 (1.69 & 2.81)	0.45 - 1.50	(2)
CRP (mg/l)	85	0.001 (0.001 & 1.81)	<0.005	(2)

[a] Source: 1, ref. *16*; 2, ref. *36*; 3, see values for retinol; 4, ref. *12*; 5, ref. *13*; 6, supplied by Amersham International, UK.

Presence of infection was evident from the increased immunoglobulin levels which were higher than normal in 49% of the boys and 61.8% of the girls in the case of IgA, in 96.5% of boys and girls for IgG and 80.4% and 88.2% in boys and girls for IgM, respectively. In addition, CRP was also higher than normal in 42.4% of the children.

No significant differences in the biochemical parameters between children with and without clinical signs of xerophthalmia signs were seen at the $P<0.01$ level which is the level of significance used to compare multiple values. There was, however, a positive correlation of age (data not shown) with the concentration of transthyretin ($P<0.01$); retinol ($P<0.01$); IgA ($P<0.05$); IgM ($P<0.001$) and almost with RBP ($P=0.08$) and IgG ($P=0.08$).

There were no significant differences in serum levels between the two sexes (data not shown) except that serum iron was higher in boys than in girls ($P<0.05$). There was a similar trend for transferrin saturation ($P=0.076$).

Correlations between the various biochemical parameters were analysed (Table 3).

Table 3 Coefficient of correlation (r) of interrelationships between biochemical and anthropometric parameters

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Serum albumin													
2. Transthyretin	.63‡												
3. Retinol-binding protein	.37‡	.75‡											
4. Transferrin	.34†	.34†	.18*										
5. Retinol	.55‡	.73‡	.74‡	.12									
6. Total iron-binding capacity	.43‡	.28*	-.05	.68‡	.16								
7. Ferritin	.09	.29†	.32†	-.43‡	.28*	-.52‡							
8. Serum iron	.18	.40‡	.36†	-.01	.42‡	.28*	.09						
9. Transferrin saturation	-.08	.18	.33†	-.38†	.29*	-.14	.26*	.90‡					
10 Total triiodothyronine	.47‡	.26*	.17	.44†	.21*	.31†	-.04	.10	-.04				
11. Total thyroxin	.13	.01	.11	.02	.11	.05	.12	.15	.17	.46‡			
12. C-reactive protein	-.51‡	-.38‡	-.16	-.22*	-.29†	-.28*	.04-	.35†-	.17	-.29†	-.18		
13. Weight/Age Z-score	.20*	-.00	.06	-.18	.12	-.07	-.07	.08	.05	.08	-.03	-.08	
14. Height/Age Z-score	.10	.27†	.30†	-.07	.25*	-.09	-.06	.19	.21	.17	.11	-.07	.59‡

Significantly correlated: *, $P < 0.05$; †, $P < 0.01$; ‡, $P < 0.001$.

Albumin levels which provide an indication of protein-energy status were related positively to transthyretin which responds more quickly to changes in protein-energy status; to retinol and retinol-binding protein which reflect vitamin A status; to triiodothyronine which reflects iodine status; and to TIBC and transferrin which are measures of the capacity to transport iron and of circulating iron, respectively. The concentration of retinol was related to that of its two carrier proteins retinol-binding protein and transthyretin; to the iron parameters of ferritin, serum iron and transferrin saturation but not transferrin itself; and to triiodothyronine which reflects iodine status. Serum iron was closely correlated with transferrin saturation, retinol-binding protein and total iron-binding capacity. Thyroxin and triiodothyronine were also closely correlated and triiodothyronine was closely associated with transthyretin, transferrin, retinol, total iron-binding capacity and, as mentioned earlier to albumin, while thyroxin was correlated with none of these biochemical parameters. In addition, IgA was positively associated with retinol, transferrin, IgG and IgM (data not shown). CRP, which is a measure of infection, was negatively correlated with all of the carrier proteins except retinol-binding protein and to retinol, total iron-binding capacity, serum iron and triiodothyronine.

Anthropometry
About 55% of the children were observed to be malnourished (Table 4) with more wasting than stunting.

Table 4 Proportion of malnourished boys and girls

Sex	Normal	Wasted	Stunted	Wasted and stunted	Total[a]
M	56 (45.5%)	43 (35.0%)	14 (11.4%)	10 (8.1%)	123
F	58 (52.7%)	35 (31.8%)	9 (8.2%)	8 (7.3%)	110
M+F	114 (48.9%)	78 (33.5%)	23 (9.9%)	18 (7.7%)	233

[a] Data was unavailable for 7 children

There was no difference between the sexes while the age group most affected was that between two and four years and the mean Z-score values indicated that there was more wasting than stunting (data not shown). The weight-for-age Z-score was positively correlated with serum albumin (Table 3) and inversely associated with IgM (data not shown). Height-for-age Z-score was positively correlated with retinol and its carrier proteins transthyretin and retinol-binding protein (Table 3) while weight-for-height Z-score and the other two anthropometric parameters were all associated with thyrotropin (data not shown). No difference was observed in the anthropometric values of children with the various clinical signs of xerophthalmia.

Mortality
It was reported that 74 persons, four of whom were adults, died during the previous two years prior to the survey. Two of the adults were said to have died from tuberculosis, one from abdominal complaint and the other from malaria. Of the 70 children who died, 29 (41.4%) were males and 41 (58.6%) were females while 43 (61.4%) were below the age of 3 years and 18 (25.7%) were over the age of 6 years. Thirty seven (52.9%) were reported to have died from swelling of the body, 17 (24.3%) with ruptured or damaged eye(s), 7 (10%) from tuberculosis, 6 (8.6%) from illness with fever, diarrhea and pain, 2 (2.9%) from unknown causes and 1 (1.4%) from ulcerated mouth.

Dietary Assessment
It was not possible to conduct a proper dietary study as the people in the village insisted that they did not have regular meals and that their dietary pattern was determined largely by the availability of food aid. They were supplied monthly with the daily equivalent of 500 g of wheat flour per person, 100 g of soya-bean oil per household comprising on average 10 persons and occasionally with some butter-oil. However, it was observed that four plants, which are not normally eaten, were being consumed because of the serious food shortage. Apart from the food aid and these plants, no other food was available. The foods were the leaves of a small tree, 'merare' (*Leucaena leucocephala*); the leaves of a small plant less than 50 cm high, 'lantero' (*Lepidium sativum*); the leaves of a similar plant, 'alma' (*Amaranthus hybridus*); and the leaves of a cactus, 'qulqual' or 'tinny' (*Protulaca oleracea*) and they were found to contain per 100 g of the food 3.31 mg, 1.41 mg, 2.76 mg and 0.22 mg ß-carotene, respectively. No other nutrient analyses were done. For a period of approximately 6 weeks immediately following the rains, about 200 g of the first three plants were eaten daily after cooking as a side dish. The leaves of the cactus were available for about half of each year. Some heads of households reported that consumption of merare resulted in swelling of the body and that lantero caused hair loss in children.

Discussion

Clinical signs
The prevalence of clinical signs of vitamin A deficiency observed in this study are higher than the cut-off points set by WHO (*47*) in determining the public health significance of vitamin A deficiency. Out of the total number of children examined, nearly half had at least one sign of vitamin A deficiency (as explained in the materials and methods section, night blindness is considered as a sign). Thus of the major signs, night blindness was reported in 28.8% as compared to the WHO cut-off point of 1% (28.8x), Bitot's spots in 6.7% against 0.5% (13.3x), corneal xerosis/ulceration in 7.1% against 0.01% (710x) and corneal scars in 5.8% against 0.05% (117x).

The high proportion of severe or advanced corneal lesions might indicate that some children have developed the signs earlier than others while there were still some who were in the process of developing the more severe forms as night blindness is known to be an early sign of the deficiency state.

These proportions signify the problem as being of epidemic proportions in the area. The serum retinol level was less than 0.35 μmol/l in 30.2% of children compared with the WHO cut-off point of 5% (6-fold) again indicating the severity of the problem of vitamin A deficiency in this area. The levels of retinol-binding protein were also very low and reflected those of serum retinol.

The severity of xerophthalmia observed in this area is probably one of the most severe ever recorded. Xerophthalmia has been shown to be a problem of public health significance in Ethiopia as a whole (*46*) but the prevalence rates reported here are considerably higher: by a factor of eight for Bitot's spots and a factor of 237 for corneal xerosis/ulceration. A community survey in the south-western part of the country (*17*) showed that 22 children out of a total of 406 (5.4%) had Bitot's spots, one had corneal xerosis and another one had corneal ulceration with keratomalacia (0.05%). Another study carried out in Bale and Arssi Regions of Ethiopia (*7*) found Bitot's spots in 5.0%, corneal xerosis and ulceration with keratomalacia in 0.8% and corneal scar in 0.5% of children aged between 6 months and 6 years. Thus the present study shows how grave the situation was in the area studied when compared to results from other severe vitamin A deficient areas in the country. The hypovitaminosis A in this village could be attributed primarily to the sole dependence for such a long period of time on food aid practically devoid of vitamin A. The poor quality of food provided as aid has been reported from other refugee camps in the country (*28,29*).

The higher proportion of boys than girls with night blindness and the more severe signs of corneal xerosis and corneal ulceration is similar to the observations reported from other countries (*40*). With increasing age the proportion of males increases as it was also observed in the results from our national survey (*46*). Although the reasons for this difference are not as yet known, it might be due to the differences in the dietary intake of boys and girls, or possible hormonal influences as suggested by studies on immature pullets (*6*). The proportion of girls with corneal scars was higher than in boys while the proportions with Bitot's spots were almost identical in the two sexes but there is no ready explanation for these findings.

About 22% of those who manifested clinical symptoms were below the age of 4 years while the rest were older. This proportion is considerably less than that seen elsewhere (*5*) and an explanation for this could possibly be found in the extended period of breast-feeding characteristic of rural Ethiopian women. From our interviews, we noted that children were breast-fed up to the age of 3 years and sometimes even longer. It might well be that the consumption of breast milk by this younger age group provided sufficient fat and vitamin A to grant some relative protection against vitamin A deficiency. In reviews of the literature, it has been stated that the impact of xerophthalmia increases with age: while Bitot's spots and conjunctival xerosis are more common in pre-school age children, the more serious corneal lesions are found in older children (*40*).

Feeding habits and practices

All families living in the village were Moslems and the practice of polygamy may have contributed to the large average family size of 10.4 which is very high when compared to the national average (4.6) or the average for Hararge region (4.3) (*27*). This will no doubt increase the dependency ratio and the vulnerability of the group to nutritional problems. Food grain distributed on the basis of food-for-work or on the basis of the number of family members capable of work may not be sufficient to fulfil the nutritional requirements of all members of the household.

Another factor which may have also contributed to the parlous state of villagers could have its basis in the severe restrictions placed on women which do not allow them to meet with outsiders or to go out of the village for activities such as shopping or other social gatherings. Thus all shopping was carried out by the males who may have been less aware of the nutritional value of available foods.

The availability of (pro)vitamin A was very limited. For all intents and purposes, none was available from the food distributed as aid and practically none from other foods for most of the year. Immediately following the wet season, a limited number of foods containing ß-carotene were available but such foods could not have made a significant contribution to the vitamin A requirements.

Inter-relationships between the nutrients

Both from the clinical and biochemical assessments, it has been shown that children in the village studied were suffering from extremely severe vitamin A deficiency. This situation has made it possible to examine the inter-relationship between the various biochemical parameters in an area of severe vitamin A deficiency. This could help in the generation of hypotheses. The levels of retinol, RBP and transthyretin are all correlated with one another as would be expected as retinol forms a one-for-one complex with RBP which in turn forms a one-for-one complex with transthyretin (*32*). Such a relationship was reported earlier in a study from Nigeria (*15*). Triiodothyronine is also carried on the retinol-RBP-transthyretin complex (*32*) which could explain the correlation of triiodothyronine with retinol and transthyretin. Low values for iron parameters such as serum iron and transferrin saturation, and high values for total iron binding capacity together with correlation of these parameters with serum retinol concentration observed in these children confirm earlier reports (*4,11,20,22,24*) that anemia is associated with vitamin A deficiency. In a cross-sectional study carried out by Bloem and co-workers (*4*) in Thailand, an association was observed between serum retinol and serum iron, transferrin, transferrin saturation and ferritin. Amine and co-workers (*1*) and subsequently Mejía and associates (*21*) postulated on the basis of studies in rats that vitamin A is involved in the transport of iron to the site of hematopoiesis. This was confirmed in our laboratory (*35*) where rats fed a diet marginally deficient in vitamin A accumulated iron in the liver and had reduced femur iron concentration in the absence of marked signs of anaemia. Ferritin levels are known to be elevated in the presence of infections (*13*) and this may explain the high ferritin concentrations observed in our study where the increased immunoglobulin levels suggest much infection.

Significant correlations were observed between triiodothyronine and TIBC and transferrin which is in line with the results observed from experiments in animal models on the relationship between thyroid hormone and anemia (*2,3*) where basal thyrotropin levels were found to be depressed and plasma triiodothyronine turnover decreased in iron deficient rats. The correlation between triiodothyronine and TIBC might be indicative of an effect of iron deficiency on iodine metabolism but the iron deficiency state manifested by low levels of serum iron and transferrin saturation may be attributable to the low levels of serum retinol.

Some of the effect of vitamin A deficiency on humoral immunity may be explained by impairment of T helper-cell differentiation or function (*37,44*). Thus a decrease in immunoglobulin levels in vitamin A deficiency has been observed in some animal experiments (*37,44*) while an increase has been observed in others (*10*). In humans, particularly with severe protein-energy malnutrition, immunoglobulin levels are elevated (*19,26,30*) although it is often difficult to separate the effect of malnutrition and infection when making observations in humans. In the present study, the high levels of IgM and the very high levels of IgG may be due in part to protein-energy malnutrition but perhaps more importantly to infection thus overshadowing any effect of vitamin A deficiency.

Relationship of anthropometric variables
As would be expected, serum albumin was related to weight-for-age but there was no indication that the low levels of albumin were associated with oedema as has been reported in other studies (*45*). However, because of the extremely high death rate, children with edema may not be represented in the population studied because they have died. Heads of households and elders of the village did report that the health situation in the previous two years was far more serious than it had ever been before.

Morbidity and mortality
Based on information from the previous two years, the annual rate of mortality for the village as a whole was 32 per thousand of population. Assuming that all the deaths in children related to damage of eyes could be attributed to vitamin A deficiency, the cause-specific mortality rate was 7.4 per thousand per annum. Increased mortality has been found to be associated with xerophthalmia and with protein-energy malnutrition (*18,23,38*). Sommer *et al.* (*38*) estimated that mortality in Indonesian children from xerophthalmia in the absence of protein-energy malnutrition was 1-3% while in the presence of protein-energy malnutrition, the rate increased to 15-25% and similar results were found by McLaren *et al.* in Jordan (*18*) and by Menon & Vijayaraghavan (*23*) in India. The role of vitamin A deficiency in mortality has been confirmed in a number of recent studies in which children have been given small regular doses (*31*) or massive doses at 4-6 months intervals (*39,43*).

Most of the children reported to have died from swelling of the body (52.9% of all deaths) might have died from protein-energy malnutrition, particularly kwashiorkor, or from the toxic effect of the consumption of merare as reported by some of the parents. It is difficult to determine the relative role of merare, protein-energy malnutrition and vitamin A deficiency on mortality.

As far as morbidity is concerned, from the clinical records of the health institutions in the area and from our own observations, there were many cases of tuberculosis in the village, particularly of the nodular type. Malaria was also endemic. The well established synergistic action of hypovitaminosis A with infection might have played an important role in the high morbidity observed (*34,42*).

As mentioned earlier, neither vitamin A nor ß-carotene was available in the food distributed as aid which was the main source of food for the people. The agriculturally poor arid land in the area and the low purchasing power of the inhabitants exacerbated the situation. Thus it is important that in such food aid programmes, vitamin A capsules should be distributed as recommended by the International Vitamin A Consultative Group (*14*). The surveillance programme in drought affected areas and refugee camps, which at present is based on anthropometric measurements only, should be extended to assess vitamin A status possibly by estimating the prevalence of night blindness which can be carried out readily by the local people.

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CHAPTER 6

Inter-relationship between vitamin A, iodine and iron status in school children in Shoa Region, Central Ethiopia*

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Summary

A total of 14,740 school children in seven provinces of Shoa Administrative Region in Central Ethiopia were surveyed for the prevalence of goitre, xerophthalmia and anaemia. Haemoglobin and haematocrit were assessed in 966 children in one province while an in-depth study was conducted on 344 children in the same province and two others. Goitre, xerophthalmia (Bitot's spots) and clinical anaemia were observed in 34.2%, 0.91% and 18.6% respectively of the children. Most biochemical parameters were within the normal range while those of haemoglobin, mean corpuscular haemoglobin concentration (MCHC) and urinary iodine excretion were lower and mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and immunoglobulins G and M were higher. Haemoglobin was strongly correlated with retinol, ferritin, MCHC, MCH, haematocrit and red blood cell count while retinol formed a triad with transthyretin and retinol-binding protein which were all correlated with one another. Total and free thyroxin and total and free triiodothyronine were positively correlated as were the concentrations of the total and free hormones. Thyrotropin was negatively correlated with total and free thyroxin and positively correlated with free triiodothyronine. Thyroxin and triiodothyronine in both free and combined forms were all correlated with thyroxin-binding globulin which in turn was negatively correlated with the triad retinol, retinol-binding protein and transthyretin. The triad was also negatively correlated with C-reactive protein. Urinary iodine excretion was positively associated with total thyroxin and negatively associated with thyrotropin. The anaemia found was not nutritional in origin but due to the effect of infestation with intestinal parasites and malaria.

Introduction

The three most important nutritional problems in developing countries are those due to deficiency of vitamin A, iodine and iron. Every year as a result of vitamin A deficiency, a quarter of a million children go blind and another quarter of a million have their eye-sight impaired and at least 100,000 of those children die within a few weeks (*19*).

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Even more children are possibly affected because there is strong evidence that vitamin A deficiency increases morbidity from respiratory and gastrointestinal diseases and overall mortality (*2*). From iodine deficiency, an estimated 800 million people in the world are at risk with 190 million suffering from goitre, 3 million from overt cretinism and millions more from some degree of intellectual deficit (*19*). Anaemia is prevalent in many parts of the world particularly in developing countries with infants, young children and pregnant women being most vulnerable because of their increased physiological requirements not only for iron but also for folic acid (*9*). In areas where intestinal parasitic infestations and malaria prevail, the problem is exacerbated resulting in decreased work performance, higher morbidity and mortality during pregnancy, increased risk of infection, subnormal mental performance and behavioral changes (*29*).

As in most developing countries, Ethiopia harbours all three nutritional problems (*23,54,55*). The present survey was carried out with the aim of selecting children for a series of in-depth studies aimed at examining the interrelationships between the three nutritional conditions and the data presented are from the baseline survey of these studies. Since it was necessary to be in relative proximity to laboratories of the Ethiopian Nutrition Institute in Addis Ababa, the study areas were concentrated in the Administrative Region of Shoa in central Ethiopia.

Materials and methods

Study sites and subjects

Schools, chosen at random, located along the main roads between Addis Ababa and the district and provincial towns of Shoa Administrative Region were surveyed. The baseline survey comprised two phases in which a total of 14,740 school children (8779 males and 5961 females) from 44 schools in 7 provinces were clinically assessed in the first phase while a more comprehensive study involving 344 boys with also measurement of biochemical and anthropometric parameters was carried out in the second phase. In one of the provinces (Chebona-Gurage), haemoglobin and haematocrit measurements were carried out on the 966 school boys with pale tongues and buccal membranes indicating anaemia of the total 3725 boys seen during the first phase of the survey. For each grade in every school, a list of names with the age of each child was prepared by the school director. Informed consent in writing was obtained from Party, Health and Education Offices at Regional and Provincial level as well as from the school directors. Schools with a high prevalence of goitre and anaemia were selected for two in-depth studies based on the results of the baseline survey.

Physical examination

The physical examination comprised the following: examination of the eyes for signs of xerophthalmia which were classified as recommended by WHO (*61*) excluding conjunctival xerosis because of the lack of specificity of this symptom with respect to vitamin A deficiency; palpation of the thyroid gland for the presence of goitre which was graded according to the method recommended by Delange *et al.* (*8*); and assessment of anaemia on the basis of paleness in buccal membranes and tongue.

Biochemical tests and analytical methods
All analyses were carried out in duplicate. Blood was collected by venous puncture with anticoagulant using the Vacutainer system (Venoject; Terumo, Belgium). After transfer to the field laboratory, haemoglobin was determined according to the cyanmethaemoglobin method of van Kampen & Zijlstra (*51*) and haematocrit was determined using the microhaematocrit centrifuge. In the second phase, red blood cells (RBC) were counted by two senior technicians with many years of experience from Atat Hospital. Mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were estimated from haemoglobin, haematocrit, and RBC values.

Also in the second phase, an additional 15 ml of blood was collected using the Vacutainer system without anticoagulant and serum was separated and stored in the dark at -20^{0}C until analysis. The following analyses were carried out on the serum collected: serum retinol was analysed as described in our earlier paper (*56*); retinol-binding protein (RBP), transthyretin (TTR), transferrin, immunoglobulin A, G and M (IgA, IgG and IgM) and C-reactive protein were analyzed by immunonephelometry using reagents and equipment supplied by Behringwerke, Germany as described by Fink *et al.* (*15*). Albumin was measured using the bromocresol green method of Doumas *et al.* (*11*). Free and total triiodothyronine (FT3 and TT3), free and total thyroxin (FT4 and TT4), thyrotropin (TSH) and ferritin were measured by radioimmunoassay using kits supplied by Amersham International UK; and thyroxin-binding globulin (TBG), using the enzyme-linked immunosorbent assay (ELISA) method with kits supplied by Boehringer Mannheim, Germany. The TT4/TBG quotient, defined as 10 times TT4 divided by TBG both in nmol/l, was used to classify subjects as defined by Boehringer Mannheim as follows: hypothyroid, <3.4; borderline, 3.4 - 3.9; euthyroid, 3.9 - 6.5; borderline, 6.5 -7.7; and hyperthyroid, >7.7. Total iron-binding capacity (TIBC) and serum iron were measured as described by Schade *et al.* (*46*).

Casual urine samples were collected and urinary iodine excretion was determined using the Sandell-Kolthoff reaction (*45*). Specimens of food and drinking water were collected from some of these areas for the analysis of their iodine content as described above while in some specimens of drinking water, microbiological tests were also carried out.

Statistics
Chi square and Mann-Whitney for pair testing and Kruskal-Wallis for multiple parameter testing were used to compare significance of differences as the data were not normally distributed. For examining correlations, data were checked for normal distribution and those with skewness values outside the range of -1 to +1 were regarded as skewed and the data were transformed to natural logarithms prior to correlation analysis.

Results

Clinical

Goitre: The mean total prevalence for males and females of gross goitre in all schools was 32.7% (Table 1). In the seven provinces, the prevalence ranged from 16.4% in Selale to 49.1% in Merhabete.

Table 1 Prevalence of goitre, xerophthalmia and anaemia in seven provinces of Shoa Region, Ethiopia

Province	Sex	Number examined	Prevalence (%)		
			Goitre	Xerophthalmia (Bitot's spots)	Anaemia
Chebona-Gurage	M	3705	928 (25.0)	14 (0.4)‡	960 (25.9)
	F	1457	582 (39.9)‡	1 (0.1)	288 (19.8)
	M+F[a]	5162	1510 (29.3)	15 (0.3)	1248 (24.2)
Merhabete	M	704	276 (39.2)	15 (2.1)	226 (32.1)
	F	629	379 (60.3)‡	9 (1.4)	183 (29.1)
	M+F	1333	655 (49.1)	24 (1.8)	409 (30.7)
Selale	M	493	61 (12.4)	16 (3.2)	153 (31.0)
	F	374	81 (21.7)	4 (1.1)	86 (23.0)
	M+F	867	142 (16.4)	20 (2.3)	239 (27.6)
Kembatana-Hadya	M	1063	296 (27.8)	4 (0.4)	275 (25.9)
	F	773	395 (51.1)‡	2 (0.3)	168 (21.7)
	M+F	1836	691 (37.6)	6 (0.3)	443 (24.1)
Teguletna-Bulga	M	698	116 (16.6)	5 (0.7)	2 (0.3)
	F	676	195 (28.8)‡	3 (0.4)	6 (0.9)
	M+F	1374	311 (22.6)	8 (0.6)	8 (0.6)
Yifatna-Timuga	M	1878	533 (28.3)	44 (2.3)	217 (11.6)
	F	1885	799 (42.4)‡	16 (0.8)	165 (8.8)
	M+F	3763	1332 (35.4)	60 (1.6)	382 (10.2)
Menzena-Gishe	M	238	87 (36.6)	0 (0.0)	5 (2.1)
	F	167	87 (52.1)	1 (0.6)	6 (3.6)
	M+F	405	174 (43.0)	1 (0.2)	11 (2.7)
Total	M	8779	2297 (26.2)	98 (1.1)‡	1838 (20.9)‡
	F	5961	2518 (42.2)‡	36 (0.6)	902 (15.1)
	M+F	14740	4815 (32.7)	134 (0.9)	2740 (18.6)

[a] The prevalence for the sexes combined, expressed as a percentage have not been corrected for the unequal number of males and females in the sample studied. Prevalence was significantly higher than in the opposite sex: ‡, $P<0.001$.

The prevalence in females (42.2%) was significantly higher ($P<0.001$) than in males (26.2%) and the higher prevalence in females was found when all schools were taken individually or aggregated by province but the difference at the school and province level did not always reach significance. The male to female ratio declined with age for grade IB but not grade IA goitre (Table 2). Only 267 (1.81%) children were seen with grade II and 8 (0.05%) with grade III goitres. The mean prevalence for visible goitre for males and females was 0.9 and 3.3% respectively.

Xerophthalmia: As shown in Table 1, the average of mean prevalence values for males and females of Bitot's spots was 0.91% which is higher than the cut-off point (0.5%) regarded by WHO as indicating a problem of public health significance. The prevalence rate was higher in boys than in girls in all provinces ($P<0.01$) and there was a tendency for the prevalence to increase with age (Table 2) in boys but not in girls. Prevalence was highest in Selale and Yifatna-Timuga (2.3%) and lowest in Menzena-Gishe (0.2%). In the group as a whole, 1.4% of the children had corneal scars, affecting less than one third of the corneal surface of the eye. Corneal scars were attributed to measles in 41.1%, "mitch" (an Amharic word used to describe a vague and ill-defined febrile illness) in 34.7%, trauma in 13.9%, non-specific eye illness in 6.9%, chickenpox in 1.5% and was unknown in 1.9% of the children. More males (71.3%) had corneal scars than females (28.7%).

Anaemia: Clinical anaemia was observed in 18.6% of the children examined (Table 1) and the prevalence was higher in boys (20.9%) than in girls (15.1%). This difference was observed in the age groups 6 - 10 years and 11 - 14 years but not those aged 15 - 18 years (Table 2).

Clinical chemistry data

In children examined in Chebona-Gurage in the first phase of the study, the median haemoglobin concentration and haematocrit value were 7.63 mmol/l (25^{th} and 75^{th} percentiles: 7.14 and 8.19 mmol/l respectively; n=966) and 40% (38 and 41%; n=966) respectively. The median concentrations of the biochemical parameters measured in the selected population of the second phase of the baseline survey are shown in Table 3. Since the population is selected for studies of anaemia and iodine deficiency disorders, it is not possible to calculate prevalence rates of deficiency from this data set. However, there were 5 (1.5%) children with concentrations below 0.35 µmol/l of retinol and of retinol binding protein indicative of vitamin A deficiency (*61*). The proportion of children with haemoglobin levels below 7.45 mmol/l indicative of anaemia was 65.4% while haematocrit was less than 35% in 21.2%, ferritin was less than 10 µg/l in 1.2%, serum iron was was less than 10.74 µmol/l in 28.8% and red blood cell count was less than 4.12 million/mm^3 in 44.8% of the children. Using the multiple criteria of haemoglobin, haematocrit and serum iron values as suggested by INACG (*30*), 48.4% of the children were below the cut-off points of the three parameters. The MCV and MCH median values were within the upper range while 24.4% and 11.3% of the children had values of MCV and MCH respectively which were above the normal cut-off points. Immunoglobulins A, G and M were higher than the upper limit of the normal range in 8.1%, 23.8% and 24.1% of children respectively.

Table 2 Prevalence of goitre, xerophthalmia and anaemia by sex and age in school children

Clinical signs	Number examined		Male (age in years)				Female (age in years)			
	M	F	6-10	11-14	15-18	18+	6-10	11-14	15-18	18+
Goitre grade										
0	6482	3443	3111 (78.7)	2788* (68.5)	538 (76.3)	45 (86.5)	1501 (64.1)	1691* (53.1)	243 (57.0)	8 (72.7)
IA	1588	1330	642 (16.2)	843 (20.7)	98 (13.9)	5 (9.6)	497 (21.2)	751 (23.6)	81 (19.0)	1 (9.1)
IB	631	991	187 (4.7)	387 (9.5)	55 (7.8)	2 (3.8)	302 (12.9)	608 (19.1)	80 (18.8)	1 (9.1)
II	77	190	14 (0.4)	49 (1.2)	14 (2.0)	0 (0.0)	42 (1.8)	127 (4.0)	21 (4.9)	0 (0.0)
III	1	7	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.2)	1 (0.2)	1 (9.1)
Xerophthalmia										
Absent	8537	5867	3866 (97.8)	3944 (97.0)	675 (95.7)	52 (100.0	2320 (99.1)	3121 (98.1)	415 (97.4)	11 (100)
Bitot's spots	98	36	38 (1.0)	49 (1.2)	11 (1.6)	0 (0.0)	11 (0.5)	21 (0.7)	4 (0.9)	0 (0.0)
Corneal scar	144	58	50* (1.3)	75 (1.8)	19 (2.7)	0 (0.0)	11* (0.5)	40 (1.3)	7 (1.6)	0 (0.0)
Anaemia										
Absent	6941	5059	3215 (81.3)	3156 (77.6)	518 (73.5)	52 (100.0	2000 (85.4)	2734 (85.9)	315 (73.9)	10 (90.9)
Present	1838	902	739 (18.7)	912 (22.4)	187 (26.5)	0 (0.0)	342 (14.6)	448 (14.1)	111 (26.1)	1 (9.1)
Total	8779	5961	3954	4068	705	52	2342	3182	426	11

Comparison between children of the same age group (Chi square): *, $P<0.05$.

Table 3 Median values of biochemical variables

Biochemical variables	Number examined	Median (25th & 75th percentiles)	Normal range (Source)[a]
Serum albumin (μmol/l)	344	558 (522-601)	507-797 (1)
Transthyretin (μmol/l)	344	3.72 (3.22-4.19)	1.82-7.27 (2)
Retinol-binding protein (μmol/l)	344	0.93 (0.71-1.16)	(3)
Transferrin (g/l)	334	2.56 (2.28-2.88)	2.95 (2.0-4.0) (2)
Retinol (μmol/l)	344	1.00 (0.77-1.22)	<0.35 deficient 0.35-0.69 low 0.70-1.05 adequate >1.05 normal (4)
Total iron-binding capacity (μmol/l)	265	51.1 (45.7-55.6)	> 70.44 (5)
Ferritin (μg/l)	264	44.5 (27.0-64.2)	> 10 (5)
Serum iron (μmol/l)	265	11.87 (9.59-14.59)	10.74 (5)
Transferrin saturation (%)	265	23.4 (18.4-28.9)	> 16 (5)
Haemoglobin (mmol/l)	344	7.14 (6.67-7.85)	> 7.45 (5)
Haematocrit (%)	344	38.0 (35.3-41.0)	> 35 (5)
Red blood cell count (million/mm^3)	162	3.52 (3.18-3.75)	4.12-5.57 (6)
Mean corpuscular volume (fl)	162	103 (96-113)	83.5-103.1 (6)
Mean corpuscular haemoglobulin (pg)	162	32.4 (30.3-35.7)	28.3-35.7 (6)
Mean corpuscular haemoglobulin concentration (mmol/l)	162	30.3 (28.9-33.6)	19.9-22.9 (6)
Free triiodothyronine (pmol/l)	174	7.55 (6.47-8.32)	3.30-8.20 (7)
Free thyroxin (pmol/ l)	173	11.58 (8.85-14.00)	9.36-25.00 (7)

Table 3 (continued) Median values of biochemical variables

Total triiodothyronine (nmol/l)	342	2.21 (1.92-2.56)	0.80-2.69 (7)
Total thyroxin (nmol/l)	342	103 (87-118)	61.8-164.7 (7)
Thyrotropin (μIU/ml)	343	2.95 (1.99-4.10)	1.00-5.50 (7)
Thyroxin-binding globulin (nmol/l)	231	236 (195-276)	168-324 (8)
Urinary iodine excretion (μg/g creatinine)	229	6.60 (1.27-19.91)	>50 (9)
Immunoglobulin A (g/l)	334	2.05 (1.62-2.65)	0.74-3.25 (2)
Immunoglobulin G (g/l)	334	19.8 (17.5-22.0)	7.3-15.1 (2)
Immunoglobulin M (g/l)	334	2.31 (1.80-2.82)	0.68-1.50 (2)
C-reactive protein (mg/l)	334	0.00 (0.00-1.01)	<0.005 (2)

[a] Source: 1, ref. *32*; 2, Behringwerke AG, Marburg, Germany; 3, see values for retinol; 4, ref. *28*; 5, ref. *30*; 6, ref. *20*; 7, Amersham International, UK; 8, Boehringer Mannheim, Germany; 9, ref. *21*.

Values for TT4/TBG quotient, TT3, TT4 and TSH were above normal limits in 6.0%, 28.2%, 3.6% and 5.4% of the children respectively, suggestive of hyperthyroidism (Boehringer Mannheim, Germany & Amersham International, UK). Hypothyroidism was observed in 8.6%, 1.8% and 14.4% of the children based on the TT4/TBG quotient, TT4 and TSH levels respectively.

The median concentrations of protein, vitamin A and iron parameters by study sites grouped by altitude and major staple foods consumed are compared in Table 4. Serum albumin, transferrin, total iron-binding capacity, ferritin, haematocrit and C-reactive protein were significantly higher and retinol-binding protein, retinol, serum iron, transferrin saturation, haemoglobin and immunoglobulin M were significantly lower in the lowland cereal staple areas (Kobo and Robi) than in the lowland ensete consuming areas (Chebona-Gurage). Transthyretin, retinol-binding protein, retinol, haemoglobin, haematocrit, immunoglobulins A and M, and CRP were significantly higher in the highland ensete staple areas (Kembatana-Hadya) than in the lowland cereal staple areas while serum albumin, transthyretin, retinol-binding protein, transferrin, haemoglobin, haematocrit, IgA and CRP were also significantly higher in the highland than the lowland ensete staple areas.

Table 4 Distribution of values of biochemical parameters by staple food and high and lowland areas

	Median values (25th & 75th percentiles)			P values		
	Lowland cereal area[1]	Lowland ensete area[2]	Highland ensete area[3]			
	n=103	n=162	n=79	1 & 2	1 & 3	2 & 3
Serum albumin (μmol/l)	587 (558-616)	540 (507-572)	587 (536-609)	0.000	0.519	0.000
Transthyretin (μmol/l)	3.60 (3.16-3.93)	3.63 (3.14-4.06)	4.18 (3.56-4.71)	0.430	0.000	0.000
Retinol-binding protein (μmol/l)	0.76 (0.58-0.93)	0.96 (0.78-1.20)	1.12 (0.81-1.31)	0.000	0.000	0.006
Transferrin (g/l)	2.61 (2.43-2.97)	2.50 (2.22-2.74)	2.69 (2.40-2.95)	0.000	0.892	0.002
Retinol (μmol/l)	0.79 (0.61-0.91)	1.10 (0.92-1.30)	1.15 (0.86-1.31)	0.000	0.000	0.644
Total iron-binding capacity (μmol/l)	53.0 (47.6-56.3)	49.7 (44.5-54.7)	n.a.	0.003	n.a.	n.a.
Ferritin (μg/l)	58.4 (34.9-68.9)	36.0 (23.5-53.3)	n.a.	0.000	n.a.	n.a.
Serum iron (μmol/l)	10.9 (8.5-13.4)	12.5 (10.2-14.9)	n.a.	0.002	n.a.	n.a.
Transferrin saturation (%)	21.4 (15.3-25.5)	24.8 (19.6-31.9)	n.a.	0.000	n.a.	n.a.
Haemoglobin (mmol/l)	6.83 (6.36-7.45)	6.98 (6.63-7.24)	8.38 (8.04-8.72)	0.965	0.000	0.000
Haematocrit (%)	38.5 (35.0-42.0)	36.5 (34.5-37.8)	42.5 (40.5-44.0)	0.000	0.000	0.000
Immunoglobulin A (g/l)	2.03 (1.55-2.63)	1.89 (1.57-2.34)	2.66 (1.91-3.18)	0.218	0.000	0.000
Immunoglobulin G (g/l)	20.2 (17.4-22.3)	19.6 (17.6-22.5)	19.6 (17.4-21.1)	0.455	0.215	0.522
Immunoglobulin M (g/l)	2.01 (1.61-2.58)	2.45 (1.87-3.01)	2.39 (1.94-2.81)	0.000	0.008	0.422
C-reactive protein (mg/l)	0.84 (0.00-2.81)	0.00 (0.00-0.79)	0.00 (0.00-0.00)	0.000	0.000	0.014
Weight-for-age Z-score	-1.43 (-1.88&-1.02)	-1.75 (-2.16&-1.35)	0.15 (-0.23&0.75)	0.000	0.000	0.000
Height-for-age Z-score	-1.26 (-1.97&-0.73)	-1.56 (-2.29&-0.98)	1.03 (0.35&2.04)	0.016	0.000	0.000
Weight-for-height Z-score	-0.81 (-1.32&-0.28)	-0.93 (-1.38&-0.57)	-0.79 (-1.40&-0.34)	0.113	0.955	0.153

n.a. = not analyzed.

Table 5 Median values of biochemical and anthropometric parameters by goitre grade

Biochemical parameters	Goitre grade			
	0	IA	IB	II
Serum albumin (µmol/l)	536 (n=112, 507-565)$^{\ddagger a,b}$	550 (n=42, 507-579)$^{\dagger c,\ddagger d}$	579 (n=141, 536-608)$^{\ddagger a,\dagger c,e}$	608 (n=49, 565-623)$^{\ddagger b,d,e}$
Transthyretin (µmol/l)	3.67 (n=112, 3.11-4.12)	3.70 (n=42, 3.16-4.12)	3.72 (n=141, 3.27-4.25)	3.78 (n=49, 3.15-4.25)
Retinol-binding protein (µmol/l)	0.97 (n=112, 0.80-1.21)^{*a,b}	0.97 (n=42, 0.77-1.29)^{*c}	0.85 (n=141, 0.68-1.13)^{*a}	0.89 (n=49, 0.64-1.06)^{*b,c}
Transferrin (g/l)	2.53 (n=111, 2.24-2.75)	2.45 (n=42, 2.21-2.74)^{*a,b}	2.62 (n=134, 2.36-2.96)^{*a}	2.64 (n=47, 2.45-2.94)^{*b}
Retinol (µmol/l)	1.12 (n=112, 0.93-1.31)$^{\ddagger a,b}$	1.11 (n=42, 0.95-1.28)$^{\ddagger c,d}$	0.87 (n=141, 0.70-1.15)$^{\ddagger a,c}$	0.89 (n=49, 0.66-1.14)$^{\ddagger b,d}$
Total iron-binding capacity (µmol/l)	50.9 (n=112, 45.3-54.9)	47.8 (n=40, 43.0-52.9)$^{\dagger a,b}$	52.3 (n=79, 47.0-56.6)$^{\dagger a}$	53.6 (n=34, 46.5-55.9)$^{\dagger b}$
Ferritin (µg/l)	35.8 (n=112, 22.5-51.8)$^{\ddagger a}$	34.0 (n=40, 25.0-58.6)$^{\dagger b}$	57.8 (n=78, 41.2-68.8)$^{\ddagger a,\dagger b}$	48.5 (n=34, 23.6-66.6)
Serum iron (µmol/l)	12.70 (n=112, 9.87-14.82)^{*a,b}	12.72 (n=40, 10.49-15.58)^{*c,d}	11.14 (n=79, 9.22-13.70)^{*a,c}	11.10 (n=34, 6.57-13.47)^{*b,d}
Transferrin saturation (%)	25.0 (n=112, 21.8-26.9)^{*a,b}	26.6 (n=40, 24.3-29.5)$^{\dagger c,d}$	21.3 (n=79, 19.6-24.2)$^{*a,\dagger c}$	20.8 (n=34, 14.0-24.2)$^{*b,\dagger d}$
Haemoglobin (mmol/l)	6.98 (n=112, 6.61-7.28)$^{\ddagger a,b}$	7.00 (n=42, 6.64-7.27)$^{\ddagger c,\dagger d}$	7.73 (n=141, 6.83-8.38)$^{\ddagger a,c}$	7.45 (n=49, 6.52-8.30)$^{\ddagger b,\dagger d}$
Haematocrit (%)	36.5 (n=112, 34.2-37.5)$^{\ddagger a,b}$	36.4 (n=42, 34.2-37.5)$^{\ddagger c,d}$	40.0 (n=141, 38.0-43.5)$^{\ddagger a,c}$	40.0 (n=49, 37.5-43.0)$^{\ddagger b,d}$

Table 5 (continued) Median values of biochemical and anthropometric parameters by goitre grade

Total triiodothyronine (nmol/l)	2.16 (n=110, 1.80-2.38)	2.21 (n=42, 1.91-2.45)	2.12 (n=141, 1.87-2.45)^{*a}	2.27 (n=49, 2.06-2.54)^{*a}
Total thyroxin (nmol/l)	110.7 (n=110, 95.2-126.1)$^{*a,\ddagger b,c}$	101.7 (n=42, 92.7-114.5)^{*a}	96.5 (n=141, 81.1-113.3)$^{\ddagger b}$	94.0 (n=49, 77.2- 110.7)$^{\ddagger c}$
Thyrotropin (μIU/ml)	2.70 (n=111, 1.60-3.90)$^{\dagger a}$	2.18 (n=42, 1.40-3.21)$^{\ddagger b,c}$	3.05 (n=141, 2.15-4.20)$^{\ddagger b}$	3.70 (n=49, 2.38-4.58)$^{\dagger a,\ddagger c}$
Thyroxin-binding globulin (nmol/l)	n.a.	254 (n=41, 233-294)^{*a,b}	228 (n=141, 186-275)^{*a}	235 (n=49, 203-268)^{*b}
Urinary iodine excretion (μg/g creatinine)	n.a.	5.28 (n=40, 1.08-18.43)	9.34 (n=140, 1.36-21.89)	3.84 (n=49, 1.12-11.92)
Immunoglobulin A (g/l)	1.97 (n=111, 1.56-2.32)$^{\ddagger a}$	2.01 (n=42, 1.53-2.40)^{*b}	2.35 (n=134, 1.71-2.96)$^{\ddagger a,*b,c}$	2.01 (n=47, 1.47-2.66)^{*c}
Immunoglobulin G (g/l)	19.7 (n=111, 17.6-22.8)	19.0 (n=42, 16.3-21.8)	20.3 (n=134, 17.8-22.0)^{*a}	19.2 (n=47, 16.4-20.5)^{*a}
Immunoglobulin M (g/l)	2.53 (n=111, 1.84-3.00)$^{\dagger a}$	2.42 (n=42, 2.05-3.01)^{*b}	2.22 (n=134, 1.82-2.74)	2.00 (n=47, 1.60-2.69)$^{\dagger a,*b}$
C-reactive protein (mg/l)	0.0 (n=111, 0.0-0.95)^{*a}	0.0 (n=42, 0.0-0.62)$^{\dagger b}$	0.0 (n=134, 0.0-0.97)	0.12 (n=47, 0.0-1.72)$^{*a,\dagger b}$

Values expressed as medians with number examined, and 25th and 75th percentiles in parenthesis and those sharing the same letter in a row are significantly different: *, $P<0.05$, †, $P<0.01$ and ‡, $P<0.001$. n.a. = data not available.

Stool examination on 344 children showed that 22.0% did not have parasites while 31.6% had hookworm, 13.1% ascaris, 7.8% amoeba cyst, 4.9% strongyloides, 0.9% schistosoma, 11.3% double parasites, and the rest (8.4%) other parasites. Malaria was reported in the areas where the prevalence of anaemia was high.

The biochemical parameters expressed in terms of goitre grade are shown in Table 5. Compared with those with no goitre or grade IA goitre, children with grade IB and II goitres were significantly heavier and taller (data not shown), had lower serum retinol, retinol-binding protein, iron, transferrin saturation, thyroxin, thyroxin-binding globulin and immunoglobulin M values; and higher serum ferritin, total iron-binding capacity, blood haemoglobin and haematocrit, and thyrotropin values. For thyroxin, the values for all grades of goitre were significantly different from one another. Thyrotropin concentrations were significantly ($P < 0.001$) inversely correlated with thyroxin/thyroxin-binding globulin quotient. However, no significant correlation was observed between triiodothyronine and thyroxin/thyroxin-binding globulin quotient (data not shown).

The correlations obtained between the various biochemical parameters were used to develop the models shown in Figures 1 and 2. In Figure 1, haemoglobin has been taken as the central parameter. On the one hand, it was significantly correlated with putative determinants of haemoglobin concentration: namely, retinol and ferritin. The triad retinol, retinol-binding protein and transthyretin were significantly correlated with one another while transthyretin, a marker for short-term malnutrition was correlated with albumin, a marker for long-term malnutrition. In addition, the triad was also negatively correlated with C-reactive protein indicated in Figure 1 by the relationship with retinol. Ferritin was correlated with transferrin saturation which in turn was correlated with serum iron. On the other hand, haemoglobin was significantly positively associated with parameters dependent on haemoglobin concentrations namely, haematocrit, MCHC, MCH and red blood cell count.

Haemoglobin was negatively correlated with free triiodothyronine, free and total thyroxin, and thyroxin-binding globulin while it was positively correlated with thyrotropin (data not shown). Haematocrit was also positively correlated with albumin (data not shown). Within the population as a whole, weight-for-age and height-for-age, which are measures of wasting and stunting respectively, were closely and positively associated with albumin, transthyretin, retinol-binding protein, haemoglobin, haematocrit, transferrin and TIBC. However, when the ensete-eating areas (Kembatana-Hadya and Chebona-Gurage) and the teff-eating areas (Kobo and Robi) were taken apart, these relationships for weight-for-age and height-for-age no longer held in the cereal staple areas (except for retinol-binding protein with weight-for-age) while there were stronger correlations in the ensete-staple areas (data not shown).

In Figure 2, correlations between thyroid hormones are considered. Total and free thyroxin and total and free triiodothyronine were positively correlated as were the concentrations of the total hormones and the free hormones. Thyrotropin was negatively correlated with total and free thyroxin and positively correlated with free triiodothyronine.

Thyroxin and triiodothyronine in both free and combined forms were all correlated with thyroxin-binding globulin which in turn was negatively correlated with the triad of retinol, retinol-binding protein and transthyretin. Albumin was also positively associated with free triiodothyronine (data not shown). In the population as a whole, weight-for-age and height-for-age were negatively and strongly associated with free triiodothyronine (-0.28 and -0.29 respectively) free thyroxin (-0.28 and -0.29 respectively), total thyroxin (-0.22 and -0.20 respectively) and thyroxin-binding globulin (-0.44 and -0.43 respectively). These relationships did not hold in the cereal staple area and only with respect to total thyroxin and thyroxin-binding globulin in the ensete staple area. Urinary iodine excretion was positively associated with total thyroxin (0.20) and negatively associated with thyrotropin (-0.19) in the total population and the cereal staple area but not in the ensete staple area.

The relative dose response test conducted on 80 children showed that 4 children (5.0%) had values above 14% while the median value was 0.00 (25^{th} and 75^{th} percentiles -8.25 and 5.20 respectively) indicating that the majority of the children had sufficient liver vitamin A stores.

Food and water analysis
The iodine content of the foods analyzed varied from none in the maize and ensete samples to a mean of nearly 400 ng/g in the kale samples while the iodine content in drinking water was low in all samples analyzed (Table 6).

Microbiological assay
Fourteen samples of drinking water from the goitrous areas were analyzed for bacterial contamination. All specimens showed growth of coliform of differing intensity (Table 7). Out of these specimens, six showed contamination with *Escherichia coli* and there is an indication that the high prevalence of goitre was related to the presence of *E. coli* in drinking water as the prevalence rate of goitre in Zuti was significantly lower ($P<0.001$) than in the other areas where the *E. coli* count was higher (Table 7).

Discussion

The schools selected for the screening study were not chosen on a systematic random selection basis. They were chosen by virtue of their location along the main roads in Shoa Administrative Region. The prevalence of gross goitre in these schools was not very different from that of school children at the national level with the exception of visible goitre (*55*). Thus the prevalence rates of gross and visible goitre were 34.2% and 2.1% respectively in the present study, as compared to 30.2% and 5.0% respectively at the national level. The sex and age distributions were similar to those reported from the national study (*55*) and from studies in other countries (*12,33*).

The median TT3 and TSH values of our study children were higher and those of TT4 lower than the values reported for Ethiopian university and nursing students (*52*). In iodine-deficient areas, TT3 thyrotoxicosis due to high TT3 was reported (*1,24*) but in our study where the goitre rate was high, deviation from the suggested reference value was not sufficient to classify the children as hyperthyroid.

Table 6 Iodine content of food items and drinking water from study areas

	Local name	Collection site	Number of samples	Iodine content (ng/g)	
Type of food				Mean	Range
Ensete *(Ensete ventricosum)*					
-root	Amitcho	Mino & Hobicheka[a]	2	42.7	0.00-85.4
-pulp (sap)	Bulla	Mino & Hobicheka	1	88.5	88.5
-pulp (solid matter)	Kocho	Mino & Hobicheka	5	74.3	45.8-85.3
Kale *(Brassica carinata)* (boiled)	Gommen	Mino & Hobicheka	6	381.5	188.0-598.4
Maize *(Zea mays)* (roasted)	Bequolo quolo	Mino & Hobicheka	4	70.6	0.0-163.2
Maize (boiled)	Bequolo nefro	Mino & Hobicheka	2	132.5	54.4-210.5
Maize (bread)	Bequolo kita	Mino & Hobicheka	2	42.5	0.0-85.0
Sorghum *(Sorghum vulgare)* (whole grain)	Mashila	Kobo & Robi[b]	2	26.2	23.7-28.6
Sweet potato *(Ipomoea batatas)* (fresh)	Sequar dinich	Mino & Hobicheka	1	145.4	145.4
Teff *(Eragrostis teff)* (whole grain)	Teff	Kobo & Robi	2	163.4	145.2-181.5
Wheat *(Triticum vulgare)* (roasted)	Sinde quolo	Mino & Hobicheka	3	23.7	9.2-39.7
Wheat-maize (roasted)	quolo	Mino & Hobicheka	1	79.3	79.3
Type of water source					
Spring		Hobicheka	2	3.7	2.5-5.0
Spring		Mino	3	7.7	2.5-12.5
Spring		Kobo	2	9.2	6.0-12.5
Well		Kobo	1	5.0	5.0
River		Robi	1	2.0	2.0
Pipe		Robi	1	1.7	1.7
Pipe		Zuti[b]	1	6.4	6.4

[a] Kembatana-Hadya
[b] Yifatna-Timuga

Table 7 Bacteriological tests by study site and type of source of drinking water

Province Site	Type of source[a]	Coliform count (per dl)	*E. coli* count (per dl)	Goitre prevalence (%)
Kembatana-Hadya				
Hobicheka	Spring (4)[b]	$3.0x10^2$-$3.4x10^3$	$5.0x10^2$ (3)[c]	80.6
Mino	Spring (4)	$2.0x10^2$-$7.9x10^3$	$2.0x10^2$ (3)	86.8
Yifatna-Timuga				
Kobo	Spring (2)	$1.4x10^3$-$5.4x10^4$	$7.0x10^2$-$1.4x10^3$ (2)	79.9
Kobo	Well (1)	$1.7x10^3$	0	79.9
Robi	River (1)	$9.2x10^4$	$9.2x10^4$	37.8
Robi	Pipe (1)	$1.2x10^3$	0	37.8
Zuti	Pipe (1)	$0.8x10^2$	0	6.5*
Tegulena-Bulga				
Gudoberet	Spring (1)	$1.7x10^3$	$1.7x10^3$	70.0
Chebona-Gurage				
Emdibir	Pipe (1)	$0.1x10^2$	0	13.0
Gubre	River (1)	$8.4x10^3$	0	10.5

[a] Source from where most of the study subject get their drinking water.
[b] Figures in parentheses denote the number of sources from where samples were collected.
[c] Figures in parentheses denote the number of specimens which showed presence of *Escherichia coli*.
* Significantly different from the goitre rates in Kobo and Robi: $P<0.001$.

Figure 1 Model based on correlations between parameters of iron and vitamin A metabolism.

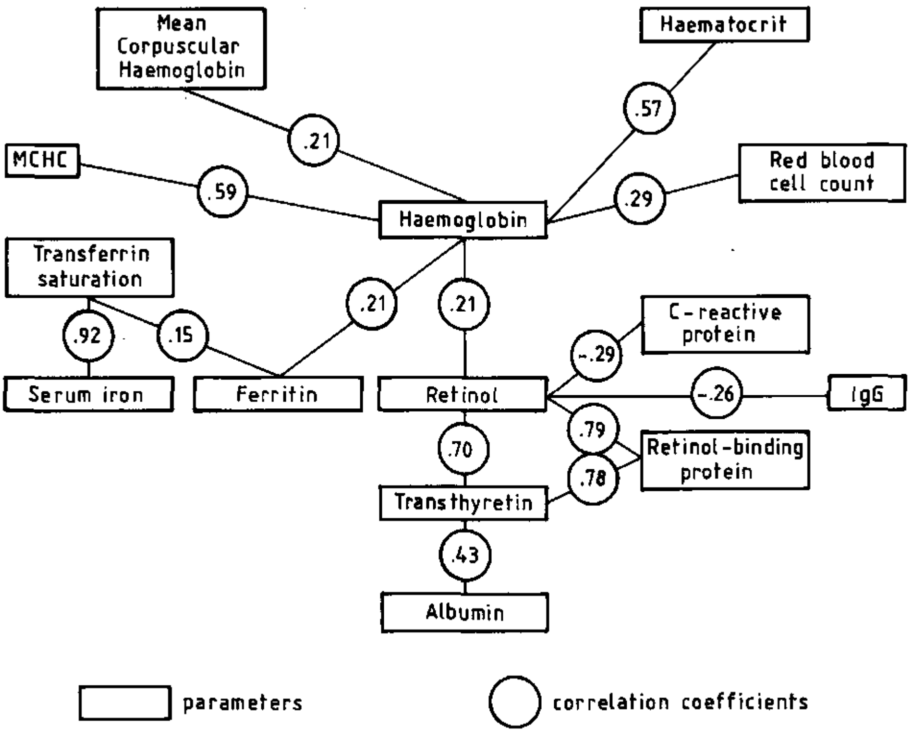
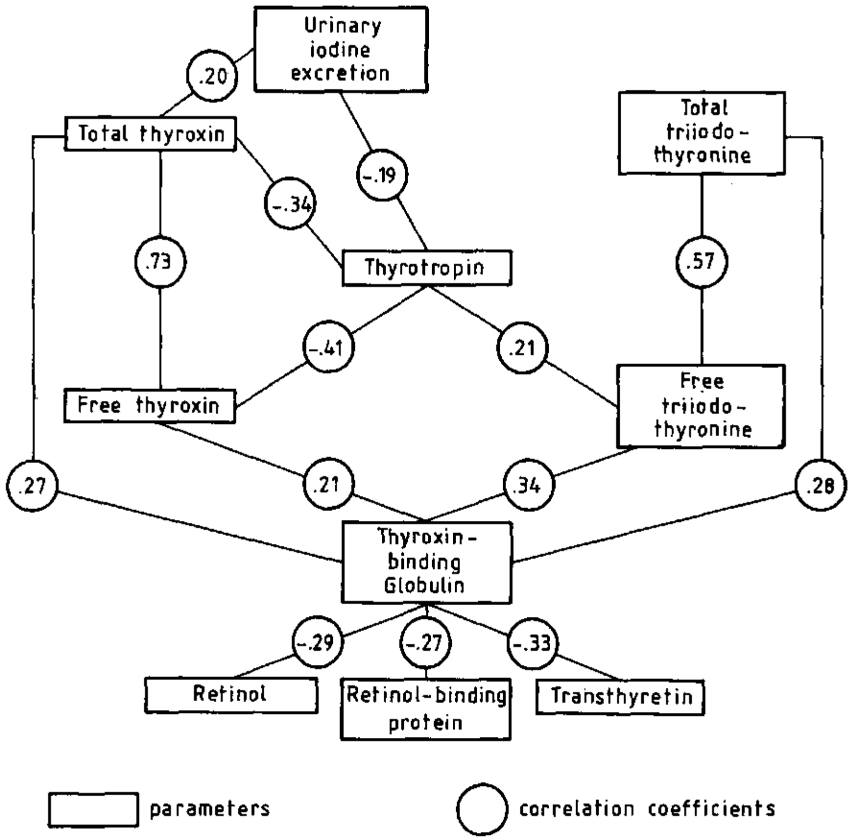


Figure 2 Model based on correlations between parameters of iodine and vitamin A metabolism.



There were large differences in the iodine content of foods and drinking water which may explain some of the variation in goitre rate between different areas. For example, the prevalence of gross goitre in Robi and Zuti schools was 37.8% and 6.5% respectively which is reflected in the lower concentration of iodine in the drinking water in Robi than in Zuti. However, other factors also must play a role because not all differences can be so explained. For example, the concentration of iodine in the drinking water consumed in Kobo and Zuti are very similar and the inhabitants of both villages buy their food from the same market in Robi while the prevalence of gross goitre in the two villages are quite different with the rate in Kobo being an order of magnitude higher than that in Zuti. This difference could be explained by the much higher contamination of drinking water with *E. coli* in Kobo especially in the spring which was the main source of water until a pump was installed on the well less than 4 months prior to the present survey. A role for *E. coli* as an important goitrogenic factor has been postulated on the basis of reports from other places (*17*).

In the present study, the prevalence of Bitot's spots was 0.9%. This indicates that the problem is of public health importance as the prevalence is above the 0.5% cut-off point set by WHO (*61*). The higher prevalence in males than in females is also similar to the findings of the national survey. Results of the national prevalence study on xerophthalmia (*54*) also showed that there were no cases of Bitot's spots or corneal lesions in the ensete staple zone as compared to 1.1% and 0.1%, respectively, in the cropping and 1.6% and 0.0% respectively in pastoral zones. Similarly, the prevalence was lower in the ensete staple areas of Kembatana-Hadya and Chebona-Gurage than in the cereal staple areas. The lower prevalence of Bitot's spots and the higher levels of serum retinol, transthyretin and retinol-binding protein in the ensete area can be attributed to the high consumption of green leafy vegetables, particularly kale, and cheese which are consumed along with ensete (*42,59*). The vitamin A store in liver as evidenced from the relative dose response was satisfactory except for four children. In these four children (two from the cereal and two from the ensete areas), the serum retinol values were less than 0.35 µmol/l confirming the biological validity of the relative dose response test (*48*).

More males had corneal scars than females and the causes for the scars were similar to those reported by children in the schools for the blind (*57*). Thus measles and mitch were the most commonly reported causes and possibly most of the mitch cases could be attributed to measles (*57*) which is known to be an important factor contributing to blindness in children especially associated with vitamin A deficiency (*16,40*). This might also indicate that vitamin A is a problem in early childhood but less common in older children as also observed in the national survey (*54*).

On the basis of clinical assessment, the prevalence of nutritional anaemia appeared to be high but clinical diagnosis of anaemia is very subjective. In the first phase of the assessment, all children with indications of paleness were registered for inclusion in the second phase. In the first phase, 18.6% of the children examined were diagnosed as clinically anaemic while in children selected from this group 65.4% had haemoglobin values less than 7.45 mmol/l which is the cut-off point set by WHO (*60*); 48.4% were classed as anaemic based on multiple criteria and 21.2% had haematocrit values less than 35%. Thus, assuming that all subjects with anaemia showed clinical signs, the overall prevalence of anaemia would be about 10%.

Iron status was poorer in the lowland ensete areas (Chebona-Gurage) than in the highland areas even though kale was consumed in both areas. The poorer iron status was probably not nutritional but due to hookworm infection as observed from the stool examinations, and to malaria. The iron parameters, especially the serum iron and transferrin saturation levels, in the lowland ensete staple area were not very low when compared to the cereal staple areas despite the fact that the children in Chebona-Gurage were selected for being anaemic. This may be due to the malaria epidemic which was reported in the cereal staple area in the six months prior to the commencement of the present study. A contribution of malaria to anaemia in the lowland areas is suggested by the higher values for MCV and MCH indicative of megaloblastic anaemia arising from malaria-induced deficiency of folic acid although we have no data on serum levels of folic acid or of vitamin B_{12}. Others have also concluded that non-nutritional factors may be responsible for the anaemia seen in parts of the country (*18,23,27*). In the cereal staple areas, teff (*Eragrostis teff*) is consumed and apart from the relatively high iron content of the grain itself, the teff as consumed contains much iron derived from contamination with soil during threshing (*4,37*). In the ensete staple areas, kale would provide substantial iron in the diet.

The close correlations observed between the various biochemical and anthropometric parameters in the population as a whole are sometimes artificial. Thus in the correlations presented in Figures 1 and 2, only those significant for the population as a whole and for the cereal and ensete areas separately have been reported and used for the basis of developing hypotheses. The artifact arises from the differences between the areas. The ensete area, in comparison with the cereal area, is characterized by a low intake of protein and perhaps of energy because of the particularly low protein density and relatively low energy density of ensete (*42*) and, as mentioned above, a high intake of (pro)vitamin A.

In Figure 1, roles for serum retinol concentration and thus (pro)vitamin A intake as determinants of blood haemoglobin concentration and thus perhaps haemoglobin synthesis are supported. It is interesting to note that the strength of the relationship between serum retinol and blood haemoglobin is as strong as the relationship between serum ferritin and blood haemoglobin and stronger than the relationship between serum ferritin and transferrin saturation since ferritin levels provide an indication of iron stores. A similar relationship between serum retinol and blood haemoglobin was found by several authors (*6,22,35,36,38*). More recently, such a relationship was also observed in a cross-sectional study on the iron status of pregnant women in West Java, Indonesia (*50*). Studies in Asia have also shown a relationship of serum vitamin A concentration with haematocrit (*5,50*) but this was not seen in the present study even though haemoglobin concentration was correlated with haematocrit, red blood cell count, mean corpuscular haemoglobin concentration and mean corpuscular haemoglobin. This may be because some of the anaemia is macrocytic indicating malaria-induced deficiency of folic acid and/or vitamin B_{12}. There are several possible sites where vitamin A may exert its action: absorption of iron from the gut, transport in serum, uptake and release of iron in the liver, uptake of iron by the bone marrow which is the site of haemoglobin synthesis; and in haemoglobin synthesis itself. Absorption of iron seems to be in fact increased in vitamin A deficiency (*47*).

As far as iron transport is concerned, we found no relationship between vitamin A and transferrin concentrations in the present study or in our study of pregnant women in Indonesia (*50*) but we did in the study of children in an area of severe vitamin A deficiency in the Hararge Region of Ethiopia (*56*) while others have found a negative correlation (*5*). In the study in Hararge where there were particularly low levels of serum retinol and in the present study, there was a strong negative relationship between serum levels of retinol and of C-reactive protein as would be expected from the well-known function of vitamin A as the anti-infection vitamin.

In the present study in which immunoglobulin levels were measured, retinol and IgG levels were also negatively related to one another indicating one of the mechanisms in which vitamin A is involved in the immune response (*53*). Uptake of iron by the liver does not seem to be affected as it is known that vitamin A deficiency results in hepatic iron accumulation (*47,49*) although it may well be that release of iron from the liver is affected. Uptake of iron by the haematopoietic tissues could possibly be inhibited by vitamin A deficiency since we have found that iron accumulation in femur is lowered in vitamin A deficient rats (*47*) but it may well be that haematopoiesis itself is directly affected as Douer and Koeffler (*10*) have shown that retinoic acid enhances the growth of human erythroid progenitor cells. Thus the most likely role for vitamin A in the aetiology of anaemia is in haematopoietic tissue while the role of vitamin A in iron transport needs to be examined under conditions where the effect of infection can be eliminated or at least controlled. Such conditions are most likely to be met in studies using animal models.

The association between retinol, retinol-binding protein and transthyretin has been found in our earlier study in Hararge (*56*) and in Nigeria (*31*) and is explained by the formation of a one-for-one-for-one complex of retinol with the carrier proteins (*43*).

In Figure 2, several relationships highlight the mechanisms by which the body compensates for low iodine intake. As would be expected, total thyroxin is positively correlated with urinary iodine excretion. The relationships of thyrotropin with urinary iodine excretion, total and free thyroxin (all negative), and with free triiodothyronine (positive) is in line with the compensatory mechanism by which thyrotropin stimulates thyroxin 5'-deiodinase activity resulting in the conversion of less active thyroxin to more active triiodothyronine (*13*) when the availability of iodine for the synthesis of thyroid hormone is limited. This mechanism was reported to be responsible for the absence of sub-clinical hypothyroidism observed in goitrous areas in India and New Guinea (*34,41*).

In humans, more than 99% of the circulating thyroxin and triiodothyronine is bound to serum proteins with more than 90% being bound to thyroxin-binding globulin. This would explain the positive relationship of thyroxin-binding globulin with the total (and free) fractions of both hormones. Since less than ten percent of the bound thyroid hormones is associated with transthyretin, albumin and other serum proteins (*44*), it is not surprising that there is no relationship between the concentration of the thyroid hormones with transthyretin and albumin.

The negative association between thyroxin-binding globulin and the triad of retinol / retinol-binding globulin / transthyretin shown in Figure 2 would explain the shift in binding of T4 from transthyretin to thyroxin-binding globulin when rats are made vitamin A-deficient (*39*). However since 90% of thyroid hormones are normally carried on thyroxin-binding globulin, it would not lend support to the hypothesis that vitamin A plays a role in the development of goitre. Such a hypothesis, addressed in a later paper (*58*), has been developed on the basis of interrelationships observed between vitamin A nutriture and occurrence of goitre on the Island of Krk in Yugoslavia (*25*) and in Senegal (*26*). The low urinary iodine excretion also indicates that the goitre problem in the surveyed areas is due primarily to iodine deficiency rather than to other factors although, as mentioned above, bacterial contamination of water may also play a significant role. As would be expected, increased thyroid size is associated with increased levels of thyrotropin and TT3 and decreased TT4 levels. This reflects the compensatory mechanisms by which the thyroid gland attempts to increase active hormone production in the face of iodine shortage. One mechanism is to increase the number of thyrotropic cells while the other is to increase the rate of conversion of TT4 to TT3. The negative association of serum retinol with goitre grade raises again the possibility that retinol plays a role in the physiology of the thyroid.

Significant increase in haemoglobin, haematocrit, ferritin and TIBC concentrations and decrease in serum iron and transferrin saturation levels was observed with increasing size of the thyroid gland. It has been shown in studies in the rat that iron deficiency lowers circulating levels of TT4 and TT3 significantly (*3*). The authors attributed this to altered hypothalamic-pituitary-thyroid control which could also influence the size of the thyroid. In humans, when there is thyroid dysfunction, it results in decreased production of circulating red blood cells as an adaptive response to tissue oxygen need and reduction in tissue oxygen consumption and tissue hypoxia. The tissue hypoxia which normally triggers erythropoietin production regulates erythropoiesis which decreases iron turnover because of its reduction (*7,14*).

This and earlier studies clearly indicate that iodine deficiency disorders, as manifested by goitre, and vitamin A deficiency are the two major nutritional deficiency problems of public health significance in Ethiopia. Unlike in many developing countries, nutritional anaemia is not a problem of major concern to the country. This paper also shows that the effects of the deficiencies of the various nutrients cannot be considered in isolation because they are very much interrelated.

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CHAPTER 7

The lack of effect of vitamin A supplementation on the treatment of goitre with iodized oil capsules*

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Summary

Studies conducted earlier have shown that deficiencies of vitamin A and of iodine are two major nutritional problems in Ethiopia. To assess the interrelationships between vitamin A and iodine metabolism, studies were carried out in one village and 8 schools in central Ethiopia. In these studies, goitre prevalence was found to be 63.3% in Kobo village while it was 93.4%, 81.1% and 29.3% in the school in Kobo village, Kematana-Hadya Province and Gubre school respectively. Signs of cretinism were observed in 14 cases (0.7% of total population) in Kobo village. The proportion of subjects with reduced goitre size was significantly higher in those who had IB goitre and those who received iodine and iodine plus vitamin A than in those who received vitamin A alone (in Kobo village) or placebo for vitamin A (in the schools in Kembatana-Hadya).

In a study where biochemical parameters were also measured, over 76% of the goitrous children were euthyroid, 8% were hypothyroid and 16% were hyperthyroid on the basis of total thyroxin/thyroxin binding-globulin quotient. The urinary iodine excretion was less than 25 µg/g creatinine in about 80% of the children signifying that the goitre problem was due to iodine deficiency. Serum retinol levels and relative dose response tests showed that almost all children had adequate vitamin A status. Concentrations of thyroxin and that of urinary iodine excretion increased significantly ($P<0.001$) while those of total triiodothyronine and thyrotropin decreased significantly ($P<0.01$ and $P<0.001$ respectively) 4 and 7/8 weeks post-treatment. The increase in retinol and retinol-binding protein was significantly higher at weeks 4 and 7/8 in children supplemented with vitamin A than those not supplemented and no other differences in biochemical parameters were observed between the two treatment groups.

**Submitted for publication*

Introduction

In many developing countries, iodine deficiency has a deleterious effect on the mental and physical development of the population (*9*). The success of iodine prophylaxis has left no doubt that iodine deprivation plays a central role in the aetiology and pathogenesis of the iodine deficiency disorders referred to as IDD (*8*). However, persistence of endemicity after appropriate iodine supplementation suggests that other aetiologic factors may be involved (*5,7,13*).

Studies on humans and experimental animals have shown that vitamin A deficiency may contribute to goitre (*5,10,13,15,20*). The adverse effects of low retinol levels on thyroid function could possibly be mediated by an early depression of thyroglobulin-glycoprotein synthesis resulting from a reduced rate of retinol-dependent incorporation of mannose (*15*). In addition to these postulated effects, low retinol levels are known to depress hepatic release of transthyretin and retinol-binding protein which together with retinol form a complex on which thyroxin is transported (*17,21*).

In order to investigate further the role of vitamin A in IDD, intervention studies were carried out in parts of Ethiopia, where vitamin A deficiency and IDD have been found to be endemic (*28,29*). The aim of the present research was to study the effect of combatting goitre by administering not only iodised oil but also vitamin A.

Materials and methods

There are three major components of the work described in this paper: a survey of goitre prevalence; an extensive study to assess the effect of vitamin A on the clinical response of goitre treated with iodized oil capsules; and an intensive study to examine the effect of this treatment regime on clinical and biochemical parameters of iodine, vitamin A and protein-energy status. The prevalence study on goitre was carried out in Kobo village and 8 schools. The data collected supplements that reported earlier (*29*). The extensive study was conducted on inhabitants of Kobo village, school children in the same village and in five schools in Kematana-Hadya Province. The schools at Kobo and Robi in Yifatna-Timuga province, Mino and Hobicheka in Kembatana-Hadya province, and Gubre in Chebona-Gurage province were selected for the intensive study.

Description of study sites

Kobo village: The village is situated 235 km north of Addis Ababa near the main road leading to Dessie at an altitude of 1250 m. It is one of the new villages created under the villagization programme of the previous government. Inhabitants were moved down from smaller villages and hamlets on the mountain slopes to the present site at the foot of the mountains. The village had 2074 inhabitants (1017 males and 1057 females) with 1009 or 49% of the population aged below 15 years. Most of the heads of the 409 households were farmers. The main staple foods were the cereals teff (*Eragrostis teff*) and sorghum while the consumption of animal products was low.

Fruits and vegetables were produced but most were sold for cash. In good rainy seasons, there can be two harvests a year. The village had one primary school which was attended by 32% of the children aged between 5 and 15 years.

Kembatana-Hadya Province: The study sites are situated about 250 km south of Addis Ababa. The villages, with their altitude in parentheses were: Serara (2700 m), Hobicheka (2250 m), Mino (1860 m), Hadero (1550 m) and Shinshicho (1450 m). Shinshicho and Hadero are small market towns while the other villages are scattered and dispersed. Shinshicho has a health centre, piped-water supply and electricity supply which operates in the evenings. The main staple in the area (*32*) is ensete (*Ensete ventricosum*) with much kale being consumed in the form of a side dish or stew. In the lowland areas of Hadero and Shinshicho, fruits and vegetables were produced in abundance, consumed by inhabitants and sold in nearby districts and provinces. They also produced coffee and ginger which provided the main source of cash.

Chebona-Gurage Province: Gubre is a small market village about 180 km southwest of Addis Ababa. The inhabitants live in scattered houses around Gubre. It is a lowland area (below 1800-2000 m) and ensete is the main staple food while kale and cheese are also consumed along with the ensete (*22,23*). The main means of income of the families in this area is from employment of the males in self-run businesses and in government or private organizations in Addis Ababa and other urban areas. Limited income is obtained from cash crops grown in conjunction with subsistence crops by the wives and children who remain in the area.

Goitre survey
Between November 1988 and September 1989, a total of 213, 1425 and 941 school children in Kobo, Kembatana-Hadya (Mino, Hobicheka, Serara, Shinshicho and Hadero) and Gubre schools respectively were examined for the prevalence of goitre. The thyroid gland was examined and graded as described earlier (*29*). The presence or absence of nodules was noted. During the same period, every household in Kobo village was registered and 1213 (58.5%) of the 2074 inhabitants were examined for goitre. Presence of clinical features of cretinism was checked to find out whether cretinism was endemic or not according to definitions given by Querido *et al.* (*24*). A questionnaire was completed for each household on socioeconomic background, whether women were pregnant or not, major health problems and past history of stillbirths and abortions.

Extensive study
Kobo village: Based on the results of the goitre survey conducted in the village, 676 goitrous, non-pregnant subjects who showed willingness to participate in the study were divided into three groups matched for gender, age (three categories: 0-12 years, 13-20 years and 21-45 years) and grade of goitre. The first group received iodine, the second vitamin A and the third both iodine and vitamin A. People above 45 years of age were excluded because of an increased risk of hyperthyroidism (*3,27*). All pregnant women (n=35) were excluded from the study and received only iodine and not vitamin A because of the risks involved (*16*).

Oral doses of iodine were given as two capsules of iodized oil, each containing 200 mg iodine (Laboratoire Guerbet, France) and of vitamin A as one capsule, containing 200,000 IU of retinyl palmitate in oil (equivalent to 60 mg retinol; Task Force "Sight & Life", Basel, Switzerland). Children below one year of age received only one iodine capsule and half of the contents of one vitamin A capsule. All subjects who could be contacted were examined again two, four and fourteen months following treatment.

Kobo school: Children with goitre were divided randomly into two groups and received either 400 mg iodine only (n=106) or iodine with 200,000 IU vitamin A (n=107). Goitre grades were assessed two, four and six months after treatment.

Kembatana-Hadya schools: Goitrous children in the five schools were divided randomly into four treatment groups which received iodine plus placebo for vitamin A (n=263), iodine plus vitamin A (n=282), vitamin A (n=315) or a placebo for vitamin A (n=293). The dose of iodine and vitamin A were similar to those described above. Assessment was carried out 12 months after treatment.

Follow-up: During the follow-up assessments, which were done without referring to the previous records, it was possible to re-examine a high proportion of the subjects. Thus in the village study in Kobo, 619 (91.6%) of the initial subjects were re-examined after 2 months, 600 (88.8%) after 4 months, and 545 (80.6%) after 14 months. In the case of school children in Kobo, 197 (92.5%), 198 (93.0%) and 197 (92.5%) were followed up at 2, 4 and 6 months after treatment respectively while in Kembatana-Hadya, 1019 (88.4%) were followed up 12 months after treatment.

Intensive study

Conduct of study: The study was carried out on boys aged between 8 and 12 years enroled at the following schools: Kobo, 20 boys; Robi, 84 boys; Mino, 48 boys; Hobicheka, 52 boys; and Gubre, 54 boys. Boys were chosen rather than girls to avoid changes associated with the onset of menstruation. Of the boys initially included, 16 were withdrawn from the study because they were absent on more than one occasion during the follow-up period. Physical examinations, in which signs of goitre, xerophthalmia and anaemia were recorded, were carried out on each boy at baseline. The examination was repeated four and eight weeks later without referring to the previous records. All the children were dewormed at the beginning and eight weeks after the initial treatment for goitre.

Clinical chemistry: The procedures for drawing blood; separating, transporting and storing serum; and carrying out the analyses are described elsewhere (*30*). The first sampling of blood was carried out one week prior to treatment (wk -1); the second on the day of treatment immediately prior to treatment (wk 0); while the third, fourth and fifth samples were taken at wk 4, wk 7, and wk 8 respectively. The mean of results at wk -1 and wk 0 and of wk 7 and wk 8 were calculated to minimise errors due to random variation. The relative dose response test was conducted on 80 children who were supplemented with vitamin A at wk 0 and at wk 8.

Anthropometry: Weights of children to the nearest 0.1 kg were recorded every week. Measurement of height to the nearest centimetre and biceps, triceps, subscapular and suprailiac skin fold thicknesses to the nearest 1 mm using a Harpenden caliper were made at wk 0, 4 and 8. Procedures for classifying children based on weight and height measurements have been described earlier (*28*).

Statistics

As the data were not normally distributed, significance of differences was tested using the Mann-Whitney test for pairs and Kruskal-Wallis test for multiple comparisons. Prior to correlation analysis, data were checked for skewness. When outside the range of -1 to +1, they were regarded as skewed and were transformed to natural logarithms.

Results

Goitre survey

Kobo: The prevalence of goitre among the study population in Kobo village was 63.3% (Table 1). Visible goitre (grade II and III) was found among 31.0% of the population. Nodular glands were observed in 1.5% of the grades II and III goitres. The prevalence of goitre was more than 30% in all age groups and in both sexes except for men over 20 years of age where the proportion was 18.9%. The prevalence rate in females was significantly higher than that in males ($P<0.001$) except in children below the age of 10 years. Of the 387 women of childbearing age (15-45 years), 35 (9%) were pregnant. No significant differences in the size of the thyroid gland between pregnant and non-pregnant women were observed, although all pregnant women had grade IB goitre or above including 25.7% with grade III (data not shown). Of the women of child-bearing age, a total of 17 (4.4%) reported a history of stillbirth and 146 (37.7%) reported abortions. Signs of cretinism were observed in 14 cases (0.7% of the total population) who exhibited deaf mutism, deafness alone, mutism alone, squint, neuromotor abnormalities, impaired growth, spasticity and mental retardation. All of these signs were found together in one case.

Kobo school: The prevalence rate of total goitre was 93.4% with 38.7% visible goitre (Table 1). There were no differences between the sexes but the prevalence of visible goitre increased with age ($P<0.001$).

Kembatana-Hadya schools: Total goitre rate among school children was 81.1% and that of visible goitre 25.5% (Table 1). The prevalence was significantly higher in girls than in boys in under 10-year olds ($P<0.05$); those aged 11-15 years ($P<0.05$); and between the age of 16 and 20 years ($P<0.01$).

Gubre school: Total goitre rate in Gubre was 29.3% and that of visible goitre was 0.5% (data not shown).

Table 1 Prevalence of goitre in Kobo village, Kobo school and Kembata schools.

Location	Goitre grade	Prevalence, percent												
		Males				Females				Total				
	Age	≤10	11-15	16-20	>20	≤10	11-15	16-20	>20	≤10	11-15	16-20	>20	Total
Kobo village	0	37.5	14.9	21.9	80.1	35.3	2.8	7.4	19.7	36.3	7.7	15.3	46.6	36.7
	IA	10.1	8.5	15.6	8.1	6.3	2.9	0.0	5.3	8.1	5.1	8.5	6.5	7.2
	IB	40.3	44.7	25.0	4.5	37.3	32.9	11.1	11.6	38.7	37.6	18.6	8.5	25.1
	II	12.1	29.8	34.4	5.4	21.1	55.7	74.1	54.6	16.9	45.3	52.5	33.1	28.1
	III	0.0	2.1	3.1	0.9	0.0	5.7	7.4	8.8	0.0	4.3	5.1	5.3	2.9
	Total goitre	62.5	85.1	78.1	18.9	64.7	97.2*	92.6+	80.3+	63.7	92.3	84.7	53.4	63.3
	n[a]	248	47	32	221	284	70	27	284	532	117	59	505	1213
Kobo school	0	13.2	6.6	0.0	0.0	5.2	0.0	0.0	0.0	9.1	3.9	0.0	0.0	6.6
	IA	18.9	15.0	0.0	0.0	12.3	12.2	0.0	0.0	15.5	13.9	0.0	0.0	14.6
	IB	45.3	41.7	0.0	0.0	38.6	34.1	0.0	0.0	41.8	38.6	0.0	0.0	40.1
	II	22.6	36.7	100.0	0.0	42.1	53.7	0.0	0.0	32.7	43.6	100.0	0.0	38.2
	III	0.0	0.0	0.0	0.0	1.8	0.0	0.0	0.0	0.9	0.0	0.0	0.0	0.5
	Total goitre	86.8	93.4	100.0	0.0	94.8	100.0	0.0	0.0	90.9	96.1	100.0	0.0	93.4
	n	53	60	1	0	57	41	0	0	110	101	1	0	212

Table 1 (continued) Prevalence of goitre in Kobo village, Kobo school and Kembata schools.

Kembata schools	0	25.1	25.3	50.0	50.0	7.2	7.5	3.1	0.0	18.5	17.5	26.7	50.0	18.9
	IA	30.3	32.2	19.7	0.0	18.9	18.1	16.9	0.0	26.1	26.1	18.3	0.0	25.3
	IB	30.3	24.8	21.2	0.0	37.8	31.0	41.5	0.0	33.1	27.5	31.3	0.0	30.3
	II	14.3	17.4	9.1	50.0	35.3	43.4	38.5	0.0	22.0	28.7	23.7	50.0	25.3
	III	0.0	0.3	0.0	0.0	0.8	0.0	0.0	0.0	0.3	0.2	0.0	0.0	.2
	Total goitre	74.9	74.7	50.0	50.0	92.8*	92.5*	96.9+	0.0	81.5	82.5	73.3	50.0	81.1
	n	406	367	66	2	238	281	65	0	644	648	131	2	1425

[a] Number of subjects examined.
Significance of difference using the Mann-Whitney test from males of the same age: *, $P<0.05$; +, $P<0.001$.

Extensive study

Kobo village: The number of subjects in whom the size of the thyroid gland changed throughout the study are shown in Table 2. After two months, 22.9% of cases showed a decrease in the size of the thyroid gland while 15.4% showed an increase irrespective of the treatment type and the initial grade of goitre (Table 2). The proportion with smaller goitre increased to 45.5% after four months and to 66.8% after 16 months. There were no differences between the treatment groups except that after four months, the proportion of subjects with reduced goitre size after receiving iodine alone or iodine with vitamin A was higher than those who received vitamin A alone (for grade IB, $P<0.001$ and for grade II goitre, $P<0.05$; data not shown). There were also no differences in the response between pregnant and non-pregnant women.

Kobo school: No difference was observed between those treated with iodine alone and those supplemented with vitamin A.

Kembatana-Hadya schools: One year after treatment, grade IB goitre decreased significantly ($P<0.05$) in those who received vitamin A with iodine than those who received vitamin A alone (data not shown). Trends towards a decrease in size were observed in those with grades IB and II goitre who were treated with iodine alone than those treated with placebo ($P=0.087$). Similar trends were also observed in those who had grade II goitre and treated with iodine alone than those treated with vitamin A alone ($P=0.076$).

Intensive study

Description of study population: The mean age of the vitamin A supplemented children was 9.6 ± 1.0 years while that of the unsupplemented group was 9.5 ± 1.0 years. As shown in Table 3, the distribution of age between the two groups was very similar. The majority of the children (60.8%) had goitre of grade IB at the start while 21.1% had visible (grade II) goitre and there were no differences between the two groups in the study (Table 3).

Initially, in both the vitamin A-supplemented and unsupplemented groups, less than 20% of the children were severely malnourished (< -2 SD weight-for-age or height-for-age) while 5.1% of the supplemented and 7.6% of the unsupplemented showed wasting, and 17.9% and 21.1% respectively showed stunting (Table 3).

On asking children whether they were night blind or not, four children (two from each group) said they were and in three of the children, this was confirmed by parents. On physical examination of the vitamin A supplemented group, one child had Bitot's spots and another a corneal scar while from the unsupplemented group, two had Bitot's spots and another two corneal scars (data not shown).

Ascaris and hookworm were the most common parasites observed (Table 4). There was no significant difference in the distribution of parasites between the vitamin A-supplemented and unsupplemented groups.

Table 2 Effect of treatment with iodine and vitamin A on grade of goitre.

Location	Treatment	Number examined initially	Number of subjects showing variation in goitre size								
			2 months after			4 months after			16 months after		
			Decrease	Same	Increase	Decrease	Same	Increase	Decrease	Same	Increase
Kobo village	Iodine	249	60	135	34	109	104	8	147	60	6
	Iodine +vitamin A	220	47	129	26	106	79	8	119	56	3
	Vitamin A	207	35	118	35	58	109	19	98	50	6
	Total	676	142	382	95	273	292	35	364	166	15
			2 months after			4 months after			6 months after		
Kobo school	Iodine	106	11	19	65	9	13	74	14	24	57
	Iodine +vitamin A	107	24	68	9	9	25	68	17	29	56
	Total	213	21	43	133	18	38	142	31	53	113
Kembata schools									12 months after		
	Iodine	263							88	66	77
	Iodine +vitamin A	282							89	68	89
	Vitamin A	315							83	70	129
	Placebo	293							80	67	113
	Total	1153							340	271	408

Table 3 Characteristics of children in the intensive study

	Vitamin-A supplemented (n=123)		Unsupplemented (n=109)	
Age (yr)	n	%	n	%
8	18	14.6	17	15.6
9	39	31.7	36	33.0
10	50	40.7	42	38.5
11	11	8.9	11	10.1
12	5	4.1	3	2.8
Goitre grade				
IA	23	18.7	19	17.4
IB	71	57.7	70	64.2
II	29	23.6	20	18.4
Total	123	100.0	109	100.0
Anthropometry				
Weight-for-age Z-score				
< -2 SD	19	15.5	19	17.4
-2 SD to < -1 SD	45	36.6	46	42.2
-1 SD to median	33	26.8	39	35.8
Above median	26	21.1	5	4.6
Total	123	100.0	109	100.0
Height-for-age Z-score				
< -2 SD	22	17.9	23	21.1
-2 SD to < -1 SD	35	28.5	22	20.2
-1 SD to median	26	21.1	47	43.1
Above median	40	32.5	17	15.6
Total	123	100.0	109	100.0
Weight-for-height Z-score[a]				
< -2 SD	6	5.1	8	7.6
-2 SD to < -1 SD	37	31.6	39	37.2
-1 SD to median	57	48.7	58	55.2
Above median	17	14.6	0	0.0
Total	117	100.0	105	

[a] Six and four children, from the supplemented and unsupplemented respectively, were above 145 cm in height which is the upper limit for which the standards for weight-for-height are valid.

Table 4 Distribution of intestinal parasites by vitamin A supplemented and unsupplemented groups and different periods

Parasites	Vitamin A supplemented				Unsupplemented			
	Initial		Week 8		Initial		Week 8	
	n	%	n	%	n	%	n	%
Ascaris lumbricoides	22	17.9	5	4.1	19	17.4	1	0.9
Strongyloides sterocolaris	4	3.3	5	4.1	6	5.5	1	0.9
Ankylostoma duodenale	31	25.2	15	12.2	18	16.5	10	9.2
Giardia lamblia	0	0.0	4	3.3	1	0.9	3	2.8
Hymenolepis nana	0	0.0	4	3.3	3	2.8	7	6.4
Endamoeba histolytica (trophozoite)	0	0.0	2	1.6	2	1.8	6	5.5
Schistosoma mansoni	3	2.4	1	0.8	0	0.0	1	0.9
Two parasites	16	13.0	7	5.7	13	11.9	3	2.8
Three parasites	2	1.6	0	0.0	0	0.0	1	0.9
Four parasites	2	1.6	3	2.4	1	0.9	1	0.9
Negative	43	35.0	77	62.6	46	42.2	75	68.8
Total	123	100.0	123	100.0	109	100.0	109	100.0

The median values of the biochemical parameters at baseline are shown in Table 5 and were compared to the normal values in our earlier paper (*30*). The urinary iodine excretion was less than 25 μg/g creatinine in about 80% of all children in both groups. Initially, total triiodothyronine, thyroxin and thyrotropin concentrations were less than the suggested lower limits (Amersham International, UK) of 0.80 nmol/l, 61.8 nmol/l and 1.00 μIU/ml respectively in 0 (0.0%), 17 (7.3%) and 5 (2.24%) children respectively in all children with no differences between the groups. Those who were above the suggested upper limits of 2.69 nmol/l, 164.7 nmol/l and 5.50 μIU/ml respectively were 37 (15.9%), 0 (0.0%) and 28 (12.1%) respectively. Using the total thyroxin/thyroxin-binding globulin quotient (Boehringer Mannheim, Germany), 177 children (76.3%) were euthyroid while 19 (8.2%) were hypothyroid and 36 children (15.5%) were hyperthyroid initially and there were no differences between the groups. The serum retinol level was below 0.35 μmol/l in three children initially.

The relative dose response (RDR) ranged from -41.18% to 28.57% in the 73 children examined initially with a median of 0.00% (25th and 75th percentiles of-8.25% and 5.20% respectively). Four children (5.5%) had values of RDR greater than 14% which was used as cut-off point in previous human experiments (*6,26*).

From the information collected on the situation of environmental sanitation of the households from which the study children were drawn, more than half of the children (60.3%) obtained their drinking water from springs and rivers not protected from contamination while 28.5% obtained water from piped sources and 11.2% got it from protected wells (data not shown). About one third (29.7%) of the households used pit latrines for excreta disposal while the remainder had no latrine (data not shown).

Effect of intervention: Urinary iodine excretion increased significantly ($P<0.001$) 8 weeks after treatment in both the vitamin A supplemented and unsupplemented children (Table 5). Thus the proportion of children in whom iodine excretion was less than 25 μg/g creatinine was almost halved to 45.3%. Total thyroxin increased significantly ($P<0.001$) while total triiodothyronine and thyrotropin concentrations decreased significantly ($P<0.001$) at 4 and 8 weeks post-treatment. In the vitamin A-supplemented group, the increase in retinol concentration was higher at both week 4 ($P<0.05$) and week 8 ($P<0.01$) compared with the group not supplemented with vitamin A and this was also reflected in the increase in the concentration of retinol-binding protein at week 8 ($P<0.01$) and the number of children in whom the retinol level remained less than 0.35 μmol/l which was reduced from four to two after 8 weeks. At the end of the two-month follow-up period, the median RDR was 2.60% (25th and 75th percentiles; -4.26% and 8.79% respectively) in the 73 children on whom it was measured: 9 children (12.3%) had an RDR of more than 14% compared with 3 at the beginning which was not to be expected.

Correlations between the various biochemical parameters at baseline have been reported earlier (*30*) for a population of which the present group of subjects were a part. There were no basic differences in the correlations between the data at baseline and at 4 and 8 weeks post-treatment. This was true when all study sites were considered together or separately. However, the coefficients of correlation increased consistently after 4 and 8 weeks for the associations of retinol with TTR, RBP and albumin while that of thyroxin-binding globulin decreased.

Vitamin A supplementation had no effect on the anthropometric measurements made (Table 5) except that the increase in suprailiac skinfolds thickness and median weight-for-age Z-score difference between week 0 and week 8 was significantly higher ($P<0.05$) in the vitamin A supplemented children than in the controls supplemented only with iodine.

Four weeks after treatment, 29.3% of the vitamin A supplemented and 26.6% of the unsupplemented children showed a decrease in the grade of goitre while 7.3% and 3.7% respectively showed an increase in grade (Table 6). Eight weeks after treatment, these proportions were 39.8% and 31.2% for those who showed decreases and 3.3% and 2.8% for those who showed increases respectively. No significant difference was observed in the clinical response between those treated with iodine only or those supplemented with iodine plus vitamin A (data not shown).

After 8 weeks, the Bitot's observed initially did not resolve while the number of children reporting night blindness increased to 3 and 6 for the supplemented and unsupplemented groups respectively. After deworming, the prevalence of the parasites, particularly that of ascaris and hookworm decreased but was not eradicated and some of the parasites increased in prevalence or appeared for the first time (Table 4). The proportion of children at week 8 in whom no parasites were found in stools was similar in the vitamin A-supplemented and unsupplemented groups. The prevalence of morbidity from cough, fever and diarrhoea was about 25% at baseline and 8% after 8 weeks but there was no difference between the groups.

Thyroxin-binding globulin was significantly increased ($P<0.02$) in the vitamin A-supplemented children at week 4 but not at week 8 while there was no effect in the group not supplemented with vitamin A. The proportion of children with a low thyroxin/thyroxin-binding globulin quotient (*30*) indicative of hypothyroidism declined by about 80% at week 4 and 8. The number of children with a high quotient indicative of hyperthyroidism ($n=36$) declined to 29 after four weeks and increased to 46 at week 8.

Table 5 Median values with 25th and 75th percentiles of biochemical parameters by vitamin-A supplementation and period after treatment

Biochemical and anthropometric parameters	Vitamin-A supplemented						Unsupplemented					
	n	t_0	t_1	t_2	t_1-t_0	t_2-t_0	n	t_0	t_1	t_2	t_1-t_0	t_2-t_0
Serum albumin (µmol/l)	123	580 536&609	565 518&594	565 543&594	-14.5 -43.5&14.5	-7.2 -36.2&14.5	109	572 543&609	565 522&594	558 525&594	-7.2 -36.2&16.3	-14.5 -43.5&10.9
Transthyretin (µmol/l)	123	3.72 3.26&4.27	3.70 3.19&4.32	3.68 3.11&4.17	0.01 -0.32&0.50	-0.04 -0.42&0.27	109	3.73 3.21&4.19	3.65 3.11&4.22	3.51 3.03&4.03	0.01 -0.34&0.40	-0.14 -0.49&0.14
Retinol-binding protein (µmol/l)	123	0.88 0.67&1.20	0.89 0.69&1.22	0.91 0.70&1.21	0.05 -0.12&0.21	0.04** -0.09&0.18	109	0.87 0.67&1.11	0.89 0.63&1.11	0.88 0.59&1.07	0.01 -0.14&0.16	-0.04 -0.18&0.14
Retinol (µmol/l)	123	0.96 0.75&1.21	1.01 0.83&1.26	1.01 0.82&1.26	0.09* -0.04 &0.25	0.07** -0.05&0.19	109	0.91 0.66&1.15	0.94 0.66&1.20	0.91 0.65&1.15	0.02 -0.11&0.14	-0.03 -0.10&0.10
Free triiodothyronine (pmol/l)	91	7.70 6.47&8.63	6.47 5.24&7.40	6.86 5.55&8.01	-1.85 -3.04&-0.62	-0.92 -2.62&1.08	86	7.47 6.47&8.17	6.32 5.39&7.78	6.63 5.39&7.72	-1.54 -2.31&-.035	-0.92 -2.31&0.62
Free thyroxin (pmol/l)	90	11.6 8.38&14.2	14.2 12.6&16.7	13.4 12.0&16.1	1.03 -0.87&3.52	2.57 -0.58&4.76	86	11.6 9.01&13.5	14.9 12.2&16.7	13.4 11.6&15.3	1.03 -0.45&3.99	1.03 -0.42&4.94
Total triiodothyronine (nmol/l)	123	2.21 1.93&2.54	2.00‡ 1.55&2.38	2.02§ 1.76&2.27	-0.18 -.67&0.21	-0.20 -0.40&0.04	109	2.17 1.98&2.43	2.03 1.46&2.41	2.02‡ 1.73&2.33	-0.23 -0.81&0.18	-0.15 -0.44&0.04
Total thyroxin (nmol/l)	123	96.1 82.4&111.3	110.0§ 96.5&124.8	114.5§ 99.7&123.2	11.8 0.48&25.7	13.5 1.29&29.6	109	100.1 83.0&113.9	110.0§ 99.1&123.9	114.5§ 99.7&128.4	10.9 -0.16&25.9	12.9 -0.64&32.2
Thyrotropin (µIU/ml)	123	2.80 2.14&3.90	1.40§ 1.00&2.18	1.53§ 1.15&2.20	-1.15 -1.91&-0.5	-1.1 -2.0&-0.4	109	3.10 2.05&4.63	1.50§ 1.00&2.10	1.80§ 1.28&2.44	-1.48 -2.7&-0.4	-1.20 -2.4&-0.18
Thyroxin-binding globulin (nmol/l)	122	238 191&280	254† 215&293	252 212&240	15.3 -23.5&60.2	9.8 -27.9&49.2	109	236 195&276	254 208&289	249 211&289	15.3 -29.5&49.2	13.1 -25.2&51.4
Urinary iodine excretion (µg/g creatinine)	122	5.90 1.18&17.9	n.a.	29.1§ 12.0&54.0	n.a.	15.6 5.0&39.0	105	6.9 1.55&20.7	n.a.	28.6§ 14.2&55.8	n.a.	17.0 3.19&37.0
Weight-for-age Z-score	123	-1.04 -1.73&-0.13	-0.96 -1.58&-0.09	-0.90 -1.54&-0.07	0.11 0.00&0.19	0.13* 0.03&0.21	109	-1.24 -1.83&-0.19	-1.14 -1.71&-0.18	-1.11 -1.78&-0.20	0.06 -0.02&0.16	0.10 -0.01&0.16

Table 5 Median values with 25th and 75th percentiles of biochemical parameters by vitamin-A supplementation and period after treatment **(continued)**

Height-for-age Z-score	123	-0.91 -1.81&0.65	-0.90 -1.70&0.68	-0.79 -1.64&0.82	0.00 0.00&0.09	0.08 0.00&0.17	109	-0.78 -1.69&0.35	-0.74 -1.69&0.27	-0.65 -1.52&0.59	0.00 0.00&0.09	0.08 0.00&0.17
Weight-for-height Z-score	123	-0.75 -1.31&-0.36	-0.63 -1.14&-0.19	-0.68 -1.16&-0.17	0.12 -0.05&0.31	0.12 -0.08&0.32	109	-0.91 -1.40&-0.36	-0.77 -1.32&-0.37	-0.87 -1.24&-0.40	0.05 -0.07&0.27	0.04 -0.20&0.26
Biceps skinfold thickness (SFT) (mm)	123	3.00 2.60&3.40	2.80 2.60&3.40	2.80 2.60&3.20	0.00 -0.20&0.20	-0.20 -0.40&0.20	109	3.00 2.40&3.40	3.00 2.60&3.20	2.80 2.40&3.20	0.00 -0.20&0.20	0.00 -0.40&0.20
Triceps SFT (mm)	123	5.20 4.20&5.80	5.40 4.40&6.00	5.20 4.40&5.96	0.00 -0.20&0.40	0.00 -0.20&0.20	109	5.00 4.30&5.80	5.20 4.20&5.80	5.20 4.40&5.80	0.20 -0.20&0.45	0.00 -0.40&0.55
Subscapular SFT (mm)	123	4.00 3.60&4.40	4.00 3.60&4.40	4.20 3.80&4.40	0.00 -0.20&0.20	0.20 -0.20&0.40	109	4.00 3.60&4.20	4.00 3.60&4.20	4.00 3.60&4.40	0.00 -0.20&0.20	0.00 -0.20&0.40
Suprailiac SFT (mm)	123	4.40 3.80&4.80	4.40 3.60&5.20	4.20 3.80&4.80	0.20 -0.20&0.60	0.00* -0.40&0.40	109	4.40 3.80&5.00	4.40 3.80&5.00	4.40 3.60&4.80	0.00 -0.40&0.60	-0.20 -0.60&0.40
Mid-upper-arm circumference (cm)	123	16.5 15.5&17.2	16.5 15.5&17.3	16.5 15.5&17.3	0.00 -0.10&0.40	0.00 -0.20&0.40	109	16.4 15.5&17.0	16.5 15.5&17.0	16.5 15.5&17.0	0.00 -0.20&0.33	0.00 -0.20&0.48

n.a. = not assessed.
Significantly different from the unsupplemented group during the same post-treatment period: *, P<0.05; **, P<0.01.
Significantly different from the initial values of the same treatment group: †, P<0.05; ‡, P<0.01; §, P<0.001.

Discussion

In Kobo village, the prevalence of goitre was more than three times the national average (*29*) and more than twice the prevalence at which goitre can be regarded as a severe endemic problem requiring intervention as soon as possible (*8*). The prevalence of goitre in relation to age and sex was similar to that reported earlier from Ethiopia (*29*) and that observed elsewhere in Africa and Asia (*4,18*). Females were more affected than males and in terms of age, those between 13 and 20 years were the most affected. Pregnant women tended to have a higher frequency of large thyroid glands (goitre grade III) than non-pregnant women of child-bearing age.

The number of cretins found in the study population (0.7%) was much less than expected from the extremely high goitre prevalence. From the epidemiological prediction model for the estimation of the number of cretins in the population, based on total goitre rate (*2,9*), we would have expected a rate of 5.1%. It is true that some cretins in the village may not have been seen but we think it unlikely that this could account for the observed rate being an order of magnitude lower than expected. The stillbirth and abortion rates are expected to be high as existing reports from other countries indicate high rates in untreated hypothyroid women (*19*). Using the same epidemiological model, stillbirth and infertility/miscarriage rates are estimated to be 3.4 and 4.5 per thousand live births respectively.

As discussed in our previous paper, the main reason for iodine deficiency in this area is the low concentration of iodine in soil and drinking water although faecal contamination of drinking water may play a role (*30*). The urinary iodine excretion was less than 25 μg/g creatinine in the majority of those children in whom it was measured thus strengthening the idea that the problem of goitre was due to iodine deficiency. There was a significant increase in the urinary iodine excretion following iodine treatment but the proportion of children who excreted more than 50 μg/g of creatinine was not as high as would be expected. This could perhaps be attributed to the severity of the iodine deficiency in these children or to the effect of the intestinal parasite load on absorption of iodised oil from the gut. As would be expected, the levels of total triiodothyronine and thyrotropin declined and that of thyroxin increased following the treatment with iodine (*25*).

The correlations between the various biochemical and anthropometric parameters at baseline have been presented in an earlier paper (*30*). Similar correlations were also observed amongst the different biochemical and anthropometric variables after supplementation with no differences between the vitamin A non-supplemented and supplemented groups. The concentration of retinol in serum was consistently negatively associated with that of thyroxin-binding globulin and positively associated with transthyretin concentration.

If vitamin A were to be an important secondary factor in the aetiology of iodine deficiency disorders, it would be expected that the correlation between the concentrations of retinol and of thyroxin-binding globulin would be positive instead of negative since about 90% of circulating thyroxin and triiodothyronine is transported by this carrier protein. The rest is transported by transthyretin and albumin. The lack of effect of vitamin A supplementation is thus consistent with this finding. Since retinol circulates as a one-for-one-for-one complex triad with retinol-binding protein and transthyretin, increase in serum retinol level is associated with a shift in thyroxin from thyroxine-binding globulin to the triad but it should be remembered that the proportion of thyroid hormones carried in this way is low.

Iodine supplementation itself had a clear effect on the decrease of the size of the thyroid gland. However, no effect of vitamin A supplementation was found in this study. In earlier studies both in animals and humans, an effect of vitamin A was described on the function of the thyroid gland (*5,10,13,15,20*). Ingenbleek and co-workers concluded that vitamin A is capable of influencing thyroid hormone status since retinol is involved in the incorporation of mannose into thyroglobulin in the thyroid gland and in the retinol/retinol-binding protein/transthyretin triad (*12,13,14,15*). However as mentioned above, thyroxin-binding globulin is more important in the transport of thyroid hormones than transthyretin. Oba & Kimura (*20*) found that replenishment of vitamin A in deficient rats resulted in restoration of the hypertrophic thyroid gland to its normal size while Frape *et al.* (*5*) found that there was an increase in the secretion of thyroxin when pigs were supplemented with vitamin A. In one study carried out in school children on the island of Krk in Croatia, Horvat *et al.* (*10*) examined the effect of vitamin A supplementation on thyroid size. Three months after supplementation with vitamin A, the number of children with goitre decreased by half raising the possibility that vitamin A deficiency has an important role in goitre. However, in a later study in which uptake of iodine by the thyroid gland was measured using radioactive iodine, Horvat *et al.* (*11*) concluded that low intake of vitamin A was not a factor on the occurrence of goitre on the island of Krk. In another study in Guatemala, Ascoll *et al.* (*1*) administered 5,000; 15,000 and 40,000 IU of vitamin A for a period 23, 17 and 13 days respectively to 78 children and did not observe any effect on hyperkeratosis or goitre. However in relation to the study of Ascoll *et al.* (*1*) and the study reported in this paper, assessment of clinical goitre might not be the optimal method to make comparisons between different treatment regimes as they are very subjective and the inter- and intra-examiner variation is high.

It may well be that vitamin A supplementation would have an effect on thyroid hormone status under conditions of severe vitamin A deficiency such as those reported from Hararge Region (*31*). However, at this stage, there is no consistent epidemiological evidence to support the hypothesis that it would be useful to incorporate vitamin A supplementation into iodine deficiency disorder control programmes.

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CHAPTER 8

The relative lack of effect of vitamin A on iron metabolism of anaemic school children in Ethiopia*

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Summary

A total of 162 anaemic boys with a mean age of 10.0±1.3 years were selected based on their low haemoglobin levels and were treated for a period of 8 weeks with 100 mg ferrous sulphate with folic acid tablets twice daily. Half of them received 200,000 IU vitamin A capsule while the rest did not. In both groups, there was a significant increase in the levels of haemoglobin, haematocrit, red blood cell count, serum iron, transferrin saturation, ferritin and mean corpuscular haemoglobin concentration and significant decrease in the levels of total iron binding capacity and transferrin at 4 and 7/8 weeks post-treatment. The increase in red blood cell count and decrease in mean corpuscular volume was significantly higher in those who were vitamin A supplemented than those not supplemented while no other differences were observed. Initially 57% of the children had hookworm infestation.

Introduction

Anaemia is one of the main diseases occurring in both developing and developed countries with pregnant women and children being the most affected (*5*). The causes of anaemia are multiple: nutritional anaemia is caused by lack of iron, vitamin B_{12} and folic acid; genetic factors such as thalassaemia, sickle cell trait and favism are primary causes of anaemia in some populations; while infections such as malaria and hookworm are important in tropical countries as they cause anaemia or exacerbate nutritional anaemia. Epidemiological, experimental and metabolic studies have revealed that vitamin A is also associated with or a causative agent in anaemia (*4,10,13,15,16,17*).

As in many other developing countries, vitamin A deficiency is a problem of public health significance in Ethiopia (*21*). Anaemia has been reported to be another nutritional problem in certain areas where the iron-rich cereal, teff, is not the staple (*26*) while it is rare in teff-eating areas (*7,11*).

**Submitted for publication*

The present study was conducted with the aim of examining the effect of vitamin A supplementation during the treatment of anaemia with iron and folic acid in school children in an African setting.

Subjects and methods

Selection of study sites and subjects

The selection of study sites and children was described in an earlier paper (*22*). Chebona-Gurage Province was selected because of the relatively high prevalence of clinical anaemia. Haemoglobin and haematocrit were assessed on 966 boys from 14 schools who were screened as being clinically anaemic and of these, 162 boys with haemoglobin level below the cut-off-point of 7.48 mmol/l (*12*) from Gubre, Jatu and Gurde schools were selected for the intervention study. Jatu and Gurde villages are very similar to Gubre which was described earlier (*22*).

Conduct of study

The procedures for drawing blood; separating, transporting and storing serum; and chemical analyses have been described elsewhere (*22*) while the design was similar to that of our study on vitamin A and iodine intervention (*23*).

Treatment regimes

The children in each of the schools were divided into two groups matched for age and haemoglobin level. Both groups received 100 mg of ferrous sulphate with folic acid (Rivopharm, Switzerland) twice daily from week 0 for eight weeks. One of the groups received vitamin A capsule of 200,000 IU (Task Force "Sight & Life", Basel, Switzerland) at week 0 in addition to the ferrous sulphate and folic acid. Deworming was carried out in all children at weeks -1 and 8 but no other treatment was given by the project staff. Blood samples were taken at week -1, 0 (prior to supplementation), 4, 7 and 8 and the results at week -1 and 0 and at week 7 and 8 were averaged.

Statistics

As the data were not normally distributed, significance of differences was tested using the Mann-Whitney and Wilcoxon signed-rank tests. Prior to correlation analysis, data were checked for skewness and, when outside the range of -1 to +1 were regarded as skewed, were transformed to natural logarithms.

Results

Description of the study population

The mean age of the vitamin A supplemented children was 10.0 ± 1.3 years while that of the unsupplemented group was 9.9 ± 1.3 years.

As shown in Table 1, the distribution of age between the two groups was very similar. Clinically, 90.5% were diagnosed as mildly anaemic while the rest (9.5%) were moderately anaemic and enlargement of the spleen or that of the liver was observed in two children each and heart murmur was present in two other children while ten children had tachycardia. Three children had corneal scars which were all due to trauma while no child reported the presence of night blindness.

Table 1 Baseline characteristics of children and their households.

	Vitamin A supplemented		Unsupplemented	
	Number	%	Number	%
Age (years)				
8	14	17.7	17	20.5
9	14	17.7	14	16.9
10	24	30.4	23	27.7
11	13	16.5	19	22.9
12	14	17.7	10	12.1
Water supply				
- River	39	49.4	54	65.1
- Spring	18[a]	22.8	11	13.3
- Well	12	15.2	10	12.0
- Pipe	10	12.7	8	9.6
Excreta disposal				
- Private pit latrine	68	86.1	70	84.3
- Communal pit latrine	3	3.8	7	8.4
- Open field	8	10.1	6	7.2
Total	79	100.0	83	100.0

[a] Includes one family who also obtained water from river.

Initially, 95 children (58.6%) had normal nutritional status (above -2 SD weight-for-age and -2 SD weight for height) while 54 (33.3%) were stunted, 9 (5.6%) were wasted and 4 children (2.5%) were wasted and stunted (data not shown).

The prevalence of hookworm was 57% in both the vitamin A-supplemented and unsupplemented groups while about 20% were not infested (Table 2). There was no significant difference in the distribution of parasites between the vitamin A-supplemented and unsupplemented groups.

Table 2 Proportion of children infested with intestinal parasites

Intestinal parasites	Vitamin A supplemented Week -1 %	Vitamin A supplemented Week 8 %	Unsupplemented Week -1 %	Unsupplemented Week 8 %
- Hookworm (*Ankylostoma duodenale* - & *Necator americanus*)	57.0	15.2	56.6	22.9
- Strongyloides (*Strogyloides sterocolaris*)	7.6	7.6	3.6	3.6
- Amoeba (cyst) (*Entamoeba histolytica*)	3.8	3.8	6.0	3.6
- Ascaris (*Ascaris lumbricoides*)	2.5	1.3	3.6	2.4
- Taenia (*Taenia saginata*)	0.0	0.0	2.4	0.0
- Giardia (*Giardia lamblia*)	0.0	2.5	1.2	3.6
- Two parasites	8.9	3.8	6.0	3.6
- Three parasites	1.3	0.0	0.0	0.0
- Four parasites	1.3	0.0	0.0	0.0
- None	17.7	64.6	20.5	59.0
Total (number)	79	79	83	83

At baseline as described earlier (*22*), values of biochemical parameters were very similar in the two groups. The haemoglobin level was less than 7.48 mmol/l in all the children and red blood cell count was less than 4.12 million/ mm^3 in 95.1% while total iron-binding capacity was below 70 μmol/l in all children and transferrin was less than 2.95 g/l in 86.4% of children and only three children showed ferritin level of less than 10 μg/l (data not shown). Mean corpuscular haemoglobin concentration was higher than 22.9 mmol/l in all children.

The median values of anthropometric, immunoglobulin and C-reactive protein parameters at baseline by vitamin A supplementation are shown in Table 3. The concentrations of immunoglobulins IgG and IgM, were above the upper limits of the normal range (15.1 g/l and 1.50 g/l respectively) in 139 (85.8%) and 146 (90.1%) children respectively (data not shown). The serum level of C-reactive protein was also higher than normal in 55 (34.0%) children.

Table 3 Median values (with 25[th] and 75[th] percentiles) of anthropometric parameters and serum immunglobulin concentrations at baseline

	Vitamin A supplemented n=79	Unsupplemented n=83
Weight (kg)	22.3 20.2&26.2	23.1 20.3&25.3
Height (cm)	126.0 120.0&132.5	127.0 120.5&132.0
Mid-upper-arm circumference (cm)	15.5 15.0&17.0	15.7 14.8&16.7
Biceps (mm)	2.6 2.2&3.0	2.4 2.2&3.0
Triceps (mm)	4.4 4.0&5.8	4.6 4.0&5.6
Subscapular (mm)	4.2 3.6&4.8	4.0 3.8&4.4
Suprailiac (mm)	4.2 3.6&4.8	4.0 3.6&5.0
Weight-for-age Z-score	-1.75 -2.20&-1.29	-1.74 -2.14&-1.35
Height-for-age Z-score	-1.53 -2.32&-1.08	-1.61 -2.28&-0.93
Weight-for-height Z-score	-0.96 -1.48&-0.50	-0.92 -1.29&-0.59
Immunoglobulin A (g/l)	1.87 1.57&2.36	1.97 1.56&2.32
Immunoglobulin G (g/l)	20.00 17.9&22.4	19.30 17.3&22.9
Immunoglobulin M (g/l)	2.58 2.06&3.01	2.34 1.72&3.01
C-reactive protein (mg/l)	0.00 0.00&0.73	0.00 0.00&0.82

Table 4 Median values (with 25th and 75th percentiles) of biochemical parameters by vitamin A supplementation and periods after treatment

Biochemical parameters	Vitamin A supplemented					Unsupplemented				
	t_0 (n=79)	t_1 (n=79)	t_2 (n=79)	t_1-t_0 (n=79)	t_2-t_0 (n=79)	t_0 (n=79)	t_1 (n=83)	t_2 (n=83)	t_1-t_0 (n=83)	t_2-t_0 (n=83)
Serum albumin (μmol/l)	536 450&572	522† 478&551	522 485&565	-14.5 -43.5&21.7	-11.6 -50.7&21.7	543 507&572	522‡ 478&562	529 500&558	-14.0 -36.2&19.9	-10.2 -36.2&14.5
Transthyretin (μmol/l)	3.66 3.19&4.26	3.67 3.21&4.26	3.76 3.27&4.07	0.15 -0.40&0.64	0.04 -0.42&0.55	3.57 3.06&3.97	3.80§ 3.37&4.42	3.66† 3.17&4.09	0.31 -0.12&0.73	0.16 -0.24&0.45
Retinol-binding protein (μmol/l)	0.99 0.84&1.21	1.00 0.91&1.25	1.02 0.86&1.23	0.07 -0.12&0.27	0.04 -0.50&0.21	0.96 0.71&1.18	1.03§ 0.88&1.28	0.95 0.80&1.16	0.14 -0.01&0.28	0.03 -0.13&0.20
Transferrin (g/l)	2.50 2.27&2.80	2.32§ 2.11&2.63	2.28§ 2.06&2.55	-0.18 -0.44&0.02	-0.26 -0.48&0.00	2.52 2.18&2.72	2.29§ 2.08&2.63	2.29§ 2.06&2.48	-0.14 -0.31&0.03	-0.20 -0.36&0.01
Retinol (μmol/l)	1.14 0.96&1.35	1.15 0.80&1.47	1.17 1.00&1.36	0.04 -0.11&0.23	0.05 -0.18&0.19	1.08 0.87&1.28	1.12‡ 0.95&1.46	1.10 0.91&1.28	0.09 -0.05&0.19	-0.01 -0.14&0.14
Total iron-binding capacity (μmol/l)	50.65 44.60&55.27	47.39§ 42.76&51.26	45.38§ 41.07&49.06	-3.31 -8.17&0.90	-5.40 -9.20&-1.00	49.58 43.74&54.21	47.44‡ 43.24&52.14	45.86§ 41.09&49.90	-2.04 -5.08&1.45	-3.81 -7.64&0.78
Ferritin (μg/l)	34.0 22.0&49.5	59.0§ 43.8&91.0	85.0§ 65.5&111.0	26.5 9.90&51.6	57.0 35.0&74.5	36.5 25.5&64.0	64.0§ 45.8&89.3	87.5§ 67.0&113.0	21.8 9.63&44.25	54.9 30.5&63.5
Serum iron (μmol/l)	12.15 10.03&14.87	14.87† 11.35&21.19	15.36† 11.67&19.00	2.82 -2.19&9.77	3.24 -1.85&7.86	12.98 10.24&14.58	15.29§ 10.87&22.39	14.36† 10.66&18.62	2.90 -0.83&10.07	2.90 -2.19&6.22
Transferrin saturation (%)	24.8 19.2&31.8	31.4§ 26.5&41.3	34.3§ 25.2&44.9	6.6 7.3&9.5	9.7 6.0&13.1	24.9 20.1&32.2	32.3§ 25.1&42.9	31.9‡ 23.7&43.6	7.3 5.0&10.7	8.4 3.7&10.8
Haemoglobin (mmol/l)	6.98 6.61&7.23	8.07§ 7.68&8.32	7.85§ 7.60&6.07	1.07 0.58&1.63	0.92 0.53&1.30	6.98 6.64&7.29	8.07§ 7.70&8.44	7.85§ 7.42&8.13	1.23 0.56&1.61	0.83 0.40&1.27
Haematocrit (%)	36.5 34.5&38.3	39.5§ 38.0&41.0	37.0 35.5&38.3	3.25 0.94&5.00	0.72 -1.50&2.50	36.5 34.5&37.5	40.0§ 37.5&40.9	36.8 35.0&38.5	3.25 1.50&4.50	0.48 -1.50&2.00
Red blood cell count (million/mm³)	3.42 3.12&3.66	3.77§ 3.43&4.13	3.60† 3.40&3.79	0.35* -0.04&0.92	0.22* -0.20&0.53	3.57 3.24&4.13	3.74‡ 3.52&4.13	3.58 3.29&3.80	0.31 -0.13&0.55	0.03 -0.29&0.36
Mean corpuscular volume (fl)	105.6 96.6&119.9	103.2 95.5&111.6	103.5 98.6&108.1	-3.73* -17.1&7.55	-8.32* -19.0&6.5	101.2 93.7&108.1	102.6 95.8&112.2	102.8 97.4&108.3	1.20 -7.85&9.91	-1.97 -7.25&8.95
Mean corpuscular haemoglobin (pg)	32.7 30.5&36.4	34.1 31.6&36.9	35.6‡ 33.6&37.4	0.90 -4.60&4.18	1.45 -1.10&5.95	32.8 30.0&35.2	34.1† 32.0&36.6	35.8§ 33.2&37.3	2.63 -2.24&6.00	2.27 0.30&6.25
Mean corpuscular haemoglobin concentration (mmol/l)	30.0 28.9&33.5	33.0§ 31.7&33.9	34.3§ 33.6&35.2	3.05 -0.63&4.48	3.37 1.05&5.15	30.4 29.1&33.7	33.2§ 32.2&34.1	34.3§ 33.4&35.6	2.58 0.00&3.98	3.27 1.50&5.10

Values significantly different from values in unsupplemented group: *, $P<0.05$.
Values significantly different from values at t_0: †, $P<0.05$; ‡, $P<0.01$ and §, $P<0.001$.

Only 10% of the families had access to piped water while the rest obtained their water from unprotected sources which were generally unsafe. About 90% of the families used latrines for excreta disposal while the remainder had no access to such facilities.

Effect of intervention:
In both the vitamin A- supplemented and unsupplemented groups who also both received iron, there were significant increases at week 4 and weeks 7/8 compared with week -1/0 in parameters associated with iron status including haemoglobin, haematocrit, red blood cell count, serum iron, transferrin saturation, ferritin, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration while there was a decrease in total iron-binding capacity and transferrin (Table 4). The increase of red blood cell count and decrease in mean corpuscular volume after week 4 and weeks 7/8 was significantly greater ($P<0.05$) in vitamin A-supplemented children than in their unsupplemented counterparts. The levels of IgA, IgG, IgM and C-reactive protein remained the same throughout the study in both groups.

Amongst the children on whom relative dose response was carried out (n=32), all children had values below 14% both at baseline and eight weeks post-treatment. Correlations were observed at baseline between retinol and albumin, transthyretin, retinol-binding protein, transferrin, serum iron, transferrin saturation, haemoglobin, haematocrit and red blood cell count as described earlier (*22*). Similar correlations were observed at 4 and 7/8 weeks except those of haemoglobin, haematocrit and red blood cell count which did not show association at weeks 7/8.

Eight weeks after deworming, the infestation rate with hookworm was reduced to about one fourth of pre-treatment levels while that for ascaris was also reduced. There was no effect on the rate of infestation from other parasites and no effect of vitamin A supplementation. At around week 4, about 5% of the children in each group had fever which, on the basis of clinical signs was attributed to malaria.

A general increase in the anthropometric measurements was observed 4 and 8 weeks post-treatment but there was no effect of vitamin A supplementation. The proportions of children with wasting, stunting or both together were similar for the two treatment groups throughout the study.

Discussion

From the present study and studies done in the past (*7,11,20*), nutritional anaemia was found to be not a problem of public health significance in Ethiopia. However, anaemia due to secondary causes, particularly malaria infection and hookworm, has been observed in the present study and in other localized studies in the past (*26*). The lack of nutritional anaemia can be attributed to the high consumption of the iron-rich cereal teff (*Eragrostis teff*).

Other staple foods in the country such as ensete (*Ensete ventricosum*), sorghum and barley are also reasonably good sources of iron (*1*). In the ensete staple areas, such as Chebona-Gurage, Kembatana-Hadya, Wolaita, Sidama, Gedio and some parts in Keffa and Gamo Gofa, the consumption of kale and cheese along with ensete contributes much to the high intake of dietary iron (*18,19,25*). Thus, data from dietary surveys in Chebona-Gurage and Kembatana-Hadya show that the daily iron intake was 142% of the daily requirement (*19,25*). Thus these findings also corroborate that anaemia in Chebona-Gurage was mainly due to intestinal parasites, particularly hookworm, which were commonly found and to malaria from which a considerable number suffered from during the course of the study. Little is known of consumption in these areas of phytate which can also contribute to poor absorption of iron from the gut (*8*). Cheese and kale consumed along with ensete are relatively rich in calcium (*1*) which can also reduce iron absorption (*9*). These negative effects could be counteracted by vitamin C also present in kale although this nutrient is liable to destruction and leaching during cooking. Consumption of other vitamin C-rich foods such as fruit are not common in these areas.

Studies conducted on humans and experimental animals have demonstrated that when there is vitamin A deficiency, there is interference with iron metabolism and results in anaemia (*2,6,13,17*). Others have also reported that supplementation of anaemic subjects with vitamin A improves the iron status (*4,14,16*).

Close associations were observed between serum retinol and serum iron, haematocrit, haemoglobin, transferrin saturation and ferritin in children in Thailand and Guatemala (*4,16*). In our study on severely vitamin A deficient children in Hararge (*24*), close correlation was observed between retinol and ferritin, serum iron and transferrin saturation. Similar relationships between retinol and some of the parameters mentioned were also observed in the present study although the association between retinol and haemoglobin, haematocrit and red blood cell count was no more present at week 8.

In the present study, the increase in red blood cell count and decrease in the mean corpuscular volume 4 and 8 weeks post-treatment periods were significantly higher in the vitamin A-supplemented children than the unsupplemented group.

While increase in red blood cell count indicates a rise in the cell mass as result of the treatment, the decrease in mean corpuscular volume might indicate the effect of the folic acid which was given along with the iron. The absence of any difference in other parameters between the vitamin A-supplemented and unsupplemented groups could perhaps be attributed to several factors. Bloem and colleagues observed the effect of supplementation of vitamin A two weeks after supplementation and this effect was not observed 4 weeks after while in our study the assessment to see the effect of vitamin A was conducted 4 and 8 weeks after supplementation. The anaemia in our study subjects was due to hookworm and malaria while in the other studies it was due to nutritional deficiencies. The children were treated daily with iron and folic acid in our study while in the study in Thailand, the children did not receive iron (*4*) while in the case of the study in Central America, iron was administered in the form of fortified salt (*15*). However the prime reason why no effect was found is probably that the vitamin A status of the children was adequate.

Under such circumstances, any additional vitamin A supplementation would have no influence on iron transport and metabolism as suggested by Amine *et al.* (*2*).

A study carried out in India (*3*) showed that two weeks after immunization with diphteria and tetanus toxoid, there was significant increase in the IgA, IgG and IgM levels but there were no differences in the iron treated and control subjects indicating that iron deficiency did not have any effect on the humoral immune response. In our present study, it was observed that the immunoglobulins IgG and IgM were high initially, for what ever reason it might be, and remained to be high after treatment with iron which is in line with the findings of Bagchi *et al.* (*3*).

Our studies on vitamin A deficiency and anaemia (*21,22,24*) have indicated that vitamin A deficiency is a problem of public health significance in certain agro-ecological zones and relief-food dependent areas while nutritional anaemia is absent particularly in the teff-staple areas of the country. Thus influence of vitamin A deficiency on the incidence of anaemia may not be an important factor in Ethiopia. So, attention should be paid to programmes on the control of malaria and combatting of hookworm and other parasites through personal hygiene and appropriate environmental sanitation.

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CHAPTER 9

General discussion

Introduction

It is estimated that 40 million preschool children are affected by vitamin A deficiency and 250,000 children become blind every year while 34 countries are reported to be affected from health problems due to vitamin A deficiency (*13*). It is also estimated that 800 million people in the world are living in iodine-deficient areas while about 200 million people have goitre and 3 million are estimated to have overt cretinism (*14*). Nutritional anaemia is estimated to be present in 11% and 47% of the population of the developed and developing countries respectively (*8*).

Ethiopia is a large country with over 50 million people comprising many ethnic groups with diversified food habits and cultural practices. It would be erroneous to claim that a sample survey can represent every sector of the population and region of the country. Systematic and stratified sample surveys conducted in major settlements such as villages, towns and cities can give an overall indication of the extent and magnitude of the problem. However, pocket areas where the situation is more severe can be missed in such surveys. The results of the nationwide prevalence study on vitamin A deficiency and the severe vitamin A deficiency problem observed in Hararge Region illustrate this point well.

The problem of vitamin A deficiency

Clinical and biochemical data from the nationwide survey (**Chapter 2**) and the survey in schools of Shoa Region (**Chapter 6**) indicated that the prevalence of vitamin A deficiency was very low in the ensete-staple areas. Dietary studies carried out previously (*33*) and referred to in **Annex 2** have shown that ensete foods are supplemented with kale and cheese which can supply pro-vitamin and vitamin A respectively. The cereal-staple areas, referred to as the cropping zone in **Chapter 2**, and the pastoral areas are those most affected as they have the highest prevalence of vitamin A deficiency. An even higher prevalence of vitamin A deficiency was found in Melkaye village which is in the cereal cropping zone in Hararge Region (**Chapter 5**). This village does have the potential to grow coffee and chat (*Khat edulis*) which would enable it to have a cash-crop economy. The prevalence of vitamin A deficiency in the area was high not only because of the crops grown but also because of the failure of rains over a six-year period which resulted in total dependence of the inhabitants on relief food supplies.

The food distributed was very poor in vitamin A. From these studies we can conclude that vitamin A deficiency is a problem of public health significance in the cropping and pastoral zones of the country and is exacerbated in the relief food-aid dependent areas. On the other hand, the ensete-staple areas are relatively non-affected.

Distribution of vitamin A capsules should not overshadow other approaches which could be used to control vitamin A deficiency. Up until now, most efforts have been directed towards the use of capsules but food-based intervention programmes are more appropriate in countries such as Ethiopia. The relative low prevalence of vitamin A deficiency in the ensete areas as the result of the consumption of kale and cheese provides an indication of the approach which could be followed in combatting the problem of vitamin A deficiency. For example in Kobo and Robi in the cropping area, the prevalence of vitamin A deficiency was not particularly high probably because of the establishment of small irrigation schemes which enable production of foods rich in pro-vitamin A.

Several studies (*7,10,11,21,22,26,30,32*) have showed that measles in children with vitamin A deficiency can lead to blindness. The study on the cause of blindness in schools for the blind (**Chapter 3**) indicates that measles was the factor predisposing to blindness in about half of the children. This proportion comprises not only those who reported measles as the predisposing factor but also perhaps most of those who regarded "mitch" as being responsible. Mitch is an Amharic term describing a febrile illness which in most cases is probably measles. Thus measles and vitamin A might be important factors in the causation of blindness in Ethiopia. There are also reports confirming that supplementation of children with vitamin A reduces complications of measles such as pneumonia and even the incidence of death (*3,18*). The proportion of children who were immunized against measles in Ethiopia was only 16% in 1987-88 (*13*). Thus efforts need to be strengthened to increase the coverage of measles vaccination within the Expanded Programme of Immunization. This together with programmes to increase the intake of (pro)vitamin A is essential if the serious consequences of the vitamin A/measles disease complex are to be attacked and ultimately eliminated.

At first sight, it seems strange that the nomadic pastoralists of Ethiopia, who are dependent on livestock for their livelihood and have a relatively high consumption of dairy products, have such high prevalence rates of vitamin A deficiency. However, as explained in **Chapter 2**, the (pro)vitamin A content of the milk is possibly low in the arid areas in which the nomadic people live. In addition, they consumed practically no fruit or vegetables of any sort. Deficiencies of other nutrients such as vitamin C and various trace elements were almost certainly also a problem in this population.

In general, low serum retinol levels are found to be associated with protein-energy malnutrition (*25*) and this has been found in the studies reported in this thesis (**Chapters 2 and 5**). This could arise from the low vitamin A and fat content of food and to impairment of vitamin A absorption as a result of the malnutrition itself or concurrent infections and parasitic infestations (*24*). Intestinal parasites were found in 85% of the children in the anaemia intervention study (**Chapter 8**).

Iodine deficiency disorders

Based on the results of the nationwide prevalence study (**Chapter 4**), it is estimated that one fifth of the total population of Ethiopia or 10 million people have goitre. Of these, nearly two million people would have visible goitre. From the total goitre rate it was estimated that there were 59,000 cretins and 176,000 cretinoids in 1990. However, no direct estimates of these conditions have been made in the country. The prevalence rate of cretinism in Kobo village (**Chapter 7**), where total goitre rate was 73.2%, was 0.7% which is lower than the 5.1% one would expect from the goitre rate and the epidemiological model developed by Clugston and colleagues (*5*). Although some cretins may have been missed, the question could be asked whether the epidemiological model is appropriate to this setting. It may well be that dietary factors such as cyanogenic glycosides, which are not consumed to any large extent in Kobo, may contribute to the high prevalence of cretinism in other places. In areas with high prevalence of goitre, about 80% of children excreted less than 25 μg/g creatinine in the urine. When the proportion is higher than 30% iodine deficiency disorders, (IDD) is regarded as being endemic in the area (*16*). Although iodine deficiency is the prime cause of IDD in Ethiopia, other factors also may play a role. In **Chapter 6**, the possible role of faecal contamination of water supplies is discussed. However, vitamin A deficiency is probably not as important as had been proposed (**Chapter 7**).

It is interesting to see the compensatory mechanisms brought into play at low intakes of iodine (**Chapter 6**). Urinary iodine excretion, a measurement of iodine intake, is positively correlated with serum total thyroxin and negatively correlated with serum thyrotropin. Serum thyrotropin is in turn negatively correlated with free thyroxine and positively correlated with free triiodothyronine. This is in line with the stimulation by thyrotropin at low iodine intakes of the deiodination of thyroxin to triiodothyronine.

Previous studies have demonstrated the deleterious effects of iodine deficiency on pregnancy outcome (*6,15,28,29*). From goitre prevalence rates found in the nationwide survey and using the epidemiological model mentioned above (*5*), it was estimated that there were 13,600 neonatal deaths, 14,800 stillbirths and 20,000 infertility/miscarriages in 1990 in the country. However, as for cretinism, no direct estimates have been made and this would be a worthwhile area of research in Ethiopia.

The majority of places where the prevalence of goitre was found to be high are mountainous and usually not accessible by roads. During earlier surveys (*23*), it was observed that some of these areas use rock salt containing low levels of iodine and high levels of impurities (*34*). It may be difficult to replace the salt being currently consumed by iodised salt because of the difficulties of getting salt to the area and the low purchasing power of the people. Thus oral administration of iodized oil will probably be the most effective method of controlling IDD in many areas of the country. Some progress is being made in controlling IDD through programmes involving salt iodination and the use of orally administered iodized oil and these programmes should be supported.

Anaemia

Some studies have been carried out in Ethiopia to establish reference haematologic values for the population (*1,27*) while other studies aimed at determining the extent of the problem of anaemia have also been conducted (**Chapter 6**). These studies have indicated that anaemia is not a serious problem of public health significance especially in parts of the country where the staple diet is teff *(Eragrostis teff)* which is rich in iron (*12,17,19,31*). However, a study conducted in Gondar Region (*35*) revealed that anaemia was observed in 40.5% of the population examined and that the proportion decreased with increasing altitude. In the lowland areas, much of the anaemia could be attributed to intestinal parasites, particularly hookworm, and to malaria which is not only a problem for lowlanders but also for highlanders who move to the lowland areas to work as migrant labourers. Other factors contributing to anaemia could be the 150 days of fasting per year observed by Coptic Christians, who comprise about half the population, and exclusive consumption of milk by many infants. It has also been reported that anaemia is the fourth most important disease leading to hospitalization and general morbidity in Gondar Region (*27*) where prevalence rates of anaemia were 23%. Although few in-depth studies based on the use of multiple parameters for assessing nutritional anaemia have been carried out (*4,20*), available evidence would suggest that nutritional anaemia may not be a problem of public health significance in Ethiopia.

Up until the present studies were conducted, no work on the prevalence of anaemia had been carried out in the ensete staple areas where the prevalence of anaemia was generally believed to be high because ensete was regarded as having a relatively low content of iron (2). However as shown in **Annex 2**, ensete provides 28% of iron intake and that the total diet provides 175% of the recommended daily intake of iron with much of the additional iron coming from kale. As discussed above, much of the anaemia can be attributed to hookworm and malaria rather than to malnutrition.

Impact of vitamin A on iodine metabolism

In the present study, the number of persons in whom goitre decreased in size was significantly higher in those who received an oral dose of iodized oil. This was true for those who had goitres of grade IB and grade II goitres initially and examined four months after treatment in the case of Kobo village and 12 months after treatment in the case of Kembata (**Chapter 7**). The administration of vitamin A had no effect on goitre size nor on parameters of iodine metabolism. As discussed in **Chapters 1 and 7**, earlier studies on experimental animals and humans produced equivocal results on the effect of vitamin A supplementation on the reduction of goitre size and on parameters of iodine metabolism. Our studies suggest that vitamin A deficiency is not involved in the aetiology of goitre. The negative correlation of the concentration in serum of retinol with that of thyroxin-binding globulin can be explained by a shift in the binding of thyroid hormones at lower levels of serum retinol from transthyretin to thyroxin binding globulin since the concentration in serum of retinol is positively related to that of transthyretin (**Chapter 6**).

Two factors should perhaps be taken into account when considering the absence of any effect of vitamin A on goitre and iodine metabolism. Firstly, the vitamin A status of the subjects studied was reasonable. Secondly, goitre size was assessed by physical examination which is very subjective as indicated by the observation that a substantial proportion of subjects showed increase in thyroid gland size even after treatment with iodine. The use of ultrasonography in the assessment of thyroid size may hopefully go some way towards solving this problem.

Impact of vitamin A on iron metabolism

In the study on the effect of vitamin A supplementation on anaemia, there was an increase in red blood cell count and decrease in the mean corpuscular volume in those children who were supplemented with vitamin A. No effect of vitamin A on other parameters was observed. This may be due to the adequate serum retinol levels in these children and because the anaemia was not nutritional but due to hookworm infestation and malaria. This lack of effect of supplementation of vitamin A on iron metabolism occurs despite the significant correlation between the concentration of serum retinol with that of haemoglobin (**Chapter 6**). As discussed in **Chapter 8**, the main reasons for the lack of effect of supplementation of vitamin A on parameters of iron metabolism, as reported from studies in Thailand and Guatemala, are that the vitamin A status of the subjects studied was reasonable and that the anaemia was not primarily nutritional but due to parasites and malaria. In addition in the present study, the effect of vitamin A was measured four and 7/8 weeks post-treatment while in the study in Thailand, positive effects were seen only after two weeks.

In previous studies on iron intake (*9*) and as reported in **Annex 2**, the intake of iron has been found to be extremely high in almost all the Regions of the country. This would suggest that the bioavailability of iron is low in the country but more research in relation to the various diets consumed needs to be done.

Ensete in the diet

The contribution of ensete to the Ethiopian diet is very substantial. However, the importance attached to the research and expansion of its utilization has been very limited in the past. Results of the studies presented in **Annexes 1 and 2** show that the yield of ensete is higher than any of the food items grown in the country except cassava. As the yields of energy and that of protein per unit area of land are remarkably high, the use of ensete should be extended in the densely populated highlands where it seems to be making a great contribution to combatting under-nutrition even in drought-prone areas.

Conclusion and recommendation

In combatting the problem of vitamin A deficiency, the most appropriate and realistic approach would be to divide the country into areas of high, medium and low risk. The high-risk areas would include those communities dependent on relief food for long periods of time; the medium risk areas those in the cropping and pastoral agroecological zones where vitamin A deficiency of public health significance has been demonstrated; while the low risk areas would comprise the cash-crop and ensete agroecological zones.

Immediate steps should be taken to ensure that food aid consists of food which can provide sufficient amounts of all nutrients including vitamin A. In addition, all children under the age of 6 years in these areas should receive high-dose vitamin A capsules at 4 to 6 month intervals. This could be done through existing health institutions and/or through village volunteers. In settlement villages, the production and consumption of vitamin A-rich vegetables and fruits should be encouraged. These measures should become standard policy of the Ministry of Health and of the Relief and Rehabilitation Commission. Although adults in relief-food dependent areas were not studied, it would seem advisable also to provide vitamin A supplements to those over the age of 6 years. For all such people, except women of reproductive age, this could involve massive dosing while pregnant women would need to receive smaller doses of vitamin A at more regular intervals. In the medium-risk areas, promotion of the growing and consumption of foods rich in (pro)vitamin A should be encouraged. In all areas, including the low risk areas, conditions which exacerbate vitamin A deficiency should be eliminated. This means improving the effectiveness of the measles vaccination campaign within the Expanded Programme of Immunization and combatting diarrhoeal diseases and intestinal parasites. In addition, vitamin A capsules should be distributed to those children under the age of 6 years with measles and other febrile illnesses, diarrhoea and severe malnutrition. Sufficient supplies of high-dose vitamin A capsules should be available through the Essential Drug Programme.

The nutrition surveillance programme does not collect data on vitamin A deficiency. Hence, the on-going nutritional surveillance programme particularly that in drought-prone areas, should collect data such as the prevalence of night blindness.

The number of schools for the blind when compared to the estimated number of blind children is very small. Thus the means to open some more schools and the expansion and improvement of the existing schools must be sought. Standardization of the schools, in terms of their health and medical services, admission, teaching, living, etc. should be considered.

Health workers in the country should be made aware of the blinding consequences of measles in the presence of marginal vitamin A deficiency, the inter-relationship between vitamin A deficiency and diseases such as respiratory tract infection and diarrhoea.

The approach outlined above for attacking the vitamin A deficiency/measles disease complex involving horticulture, distribution of vitamin A capsules and immunization particularly against measles should be adopted.

As outlined in **Chapters 4, 6 and 7**, the problem of IDD in the country is mainly due to iodine deficiency. Thus the ongoing salt iodination programme and the distribution of iodized oil capsules to areas with limited accessibility should be expanded. Surveillance on IDD and quality control of iodinated salt need to be carried out regularly. Research topics which need to be addressed include the following: the prevalence of cretinism and the mild motor and neurological disorders; the effect of intestinal parasites on the effectiveness of oral iodized oil distribution; the relationship between IDD and pregnancy outcome; the effect of supplementing mothers with iodized oil during pregnancy on the health of mother and child; and the possible role of various foods in the diet, such as sorghum, in the aetiology of IDD in Ethiopia. Distribution of iodized oil capsules to pregnant mothers in endemic goitre regions should be incorporated into the antenatal programme even though the knowledge available on this topic is limited at the present time.

Nutritional anaemia is not a serious problem in Ethiopia. Secondary anaemia due to hookworm and malaria is a problem in certain areas where these diseases are highly prevalent. Health education, improvement of environmental sanitation, effective malaria control programmes have to be considered. The cultivation of teff should not be discouraged as has been the practice over the last decade. Even though yield is low and mechanization of production and harvesting are not easy, it does offer protection against anaemia. Therefore, rigorous research to improve yield and to mechanize cultivation and harvesting should be planned and implemented.

Further nationwide surveys for assessing the extent and severity of vitamin A deficiency and of IDD should be planned as the previous surveys were carried out over ten years ago.

Ensete has proved itself to be a useful crop in the most densely populated areas of the country because of its high yield, relative drought resistance, and contribution to household food security. Its production and consumption along with protein-rich foods should be encouraged as its consumption together with kale and cheese can provide sufficient protein, (pro)vitamin A and iron. Research should be conducted on the improvement of its nutritional quality through fermentation especially to increase energy density which is particularly important for infant and child feeding. Attention should also be directed towards agricultural aspects particularly protection against pests, shortening of the maturation period, and hygienic processing, storage and preparation for consumption.

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ANNEX 1

Cultivation, harvesting and yield of ensete (Ensete ventricosum) in Ethiopia*

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Summary

In Ethiopia almost 10 million people are dependent on ensete (*Ensete ventricosum* (Welw.) Cheesman), also known as "false banana". In the Gurage area in Central Ethiopia cultivation, harvesting and yield of ensete were studied in about 60 households in six villages. It is propagated vegetatively and has a six year growing cycle in which it is transplanted three or four times. Men harvest the plants; women scrape the pseudostem in order to separate the starchy pulp from the fibre, and pulverize the corm. The pulp is fermented and stored in earthen pits. The yield of ensete food ("ko'cho") was 34 kg per plant or 9.5 tons/yr/ha. Except for cassava, the energy yield of ensete (6.1 $MJ/m^2/yr$) was higher than that from all cereals grown in Ethiopia, from Irish potato, sweet potato and from banana. The protein yield of ensete was higher (11.4 $g/m^2/yr$) than of all crops mentioned above, except banana and Irish potato but the protein density is very low (12 g/kg). Supplemented with high protein foods such as legumes, it could be a suitable crop for highland areas where drought and famine frequently occur. Ensete can withstand dry periods. Since it can be stored for years and is readily available throughout the year, cultivation of ensete can significantly improve household food security.

Introduction

Ensete ventricosum (Welw.) Cheesman (*6*), usually referred to as "ensete", provides the staple food for eight million people in the most densely populated areas of the country, especially the south-west. They are inhabited by the Gurage, Sidama, Kembata, Hadya, Wollaita and related tribes. It is the co-staple food for two million people in south-west and western Ethiopia. Altogether they comprise about one-fifth of the population (*12,23*). Because of its resemblance to the banana plant, ensete is also referred to as "false banana". It grows best at an altitude of 1600 to 3000 m and can withstand dry periods (*10,23*).

Ensete is grown in a semi-permanent cultivation system marked by a complex cycle of transplanting lasting from five to ten years (*17*). The plant is used for the production of a starchy food mainly derived from the corm and pseudostem.

**Submitted for publication*

These parts are pounded and scraped to pulp, which is fermented and stored in a pit for a period lasting from a few days up to five years. From the fermented pulp, a sour starchy food, referred to as "ko'cho", is prepared (*9*). The plant also provides fibre which is used for rope, sieves and cleaning material (*10*). Ritually prepared ensete has an important role in birth, circumcision, marriage, and death ceremonies (*16*).

As already noticed by Smeds (*19*) and Stanley (*20*), but also in the decades after them, little has been recorded about the cultivation and harvesting of ensete. Most of the scarce information now available was collected in Sidamo Region several decades ago. This paper presents the results of a study on the cultivation, harvesting and yield of ensete which was conducted recently in the Gurage area in Southern Shoa. The Gurage are heavily dependent on ensete, and they probably are the best known ensete growers (*20*). Ensete plays a central role in their culture. A subsequent paper presents information on its preparation, food value and consumption (*14*).

Methods

Study area and design

The present study was conducted in six villages within a radius of 6 km of Attat Hospital, which is located in Chebona-Gurage Province at an altitude of 1900 m, 175 km south-west of Addis Ababa. The area served by the hospital, which provides both curative and preventive services, is densely populated by the Gurage (135 persons/km^2) (*5*). The fieldwork was carried out by the first two authors, with assistance of two interpreters. Both of them were Gurage, speaking both Guragegna (the language of the Gurage) and English. About 60 households were visited and, after the aims of the study were explained, most people agreed to cooperate.

Cultivation and harvesting

All activities involved in the cultivation, harvesting and further processing of ensete were observed repeatedly until a detailed description was obtained. Each aspect was checked at several places and each inconsistency in the information obtained was clarified. Some processes could not be observed and were therefore described by the people themselves. Meetings of women's groups in two villages were attended in order to obtain additional information. Questions formulated in advance were addressed to the group as a whole and were answered by several women. Descriptions, written in italics, of plants, processes, tools and other terms are followed by their Guragegna names in parentheses.

Yield

An estimate of the annual yield of ensete was obtained by combining plot size and number of plants harvested yearly on that plot. Since most plots were rectangular, area was calculated from width and length measured by pacing. First, pace length of the two investigators was standardized. The head of the household was asked for the average, minimum and maximum number of plants harvested yearly from that plot.

The yield per plant of fermenting pulp was determined by weighing pulp from a number of plants with a Seca bathroom scale at the time that the pulp was put into an earthen pit for storage.

The yield of *light-coloured pulp* (me'chee) and of *dark coloured pulp* (tikuree'ye) was measured separately. In Guragegna both are referred to as "wu'ssa"; in Ethiopia they are generally known as "ko'cho". The yield of "a'tmet", a highly appreciated white fibreless product (generally known as "bu'lla") was also measured on four occaisions. The products are fermented further in the earthen pit, pressed by stones, squeezed, cut, mixed with water and baked prior to consumption. Processing of these different products is described under Results. Measurements using a Salter kitchen scale were carried out at different stages of processing, in order to estimate the final yield. The fluid loss during storage and as a result of squeezing before baking was estimated. If the pulp is prepared after a relatively short period of storage, the pulp is squeezed to obtain a rather dry product, similar to older pulp which does not need to be squeezed. To estimate total fluid loss, women were asked to squeeze homogenized samples of two-week old ready-for-storage pulp after which the fluid obtained was weighed. Finally the amount of water added during further preparation and that which evaporated during baking were determined by weighing before addition of water and after baking.

The yield of edible product was calculated by combining the data on the amount of harvested pulp per plant, fluid loss during storage and squeezing, and weight changes during preparation.

Results

Cultivation

The Guragegna name "ye'sete" denotes not only the mature plant at time of harvest but also all plants in general, of all ages. Figure 1 shows such a *mature plant with inflorescence* (shi'ra). In general, ensete is harvested before it starts flowering so the inflorescence is not often seen. The growing cycle, which usually lasts six years, is presented schematically in Figure 2. In Figure 3, drawings of the most typical tools which are used only for the cultivation, harvesting and processing of ensete are presented.

All plants are *transplanted* (ku'bar) three or four times. This has to be done in the period January to March because the space required for transplanting only becomes available then after the mature plants have been harvested in November to January. Thus the oldest plants are transplanted first. All the work involved in this is done by men and boys. Before the ensete is transplanted, the small adventitious roots, leaves, and outer shrunk layers of the pseudostem are removed with a large knife referred to as a "tebe'cha" (Fig 3). It has an iron cutting part and a handle made out of any hard wood available. The cutting facilitates transport and is said to stimulate growth. Then the plants are pushed over or pulled out and planted in new holes which are dug with a *two-pointed stick* (mare'sha), a *flat-edged stick* (ta'rbe) or a spade. Two adults are needed to transplant the older, heavier plants.

The first stage of growth is started by means of vegetative propagation. For this, a *four year old plant* (hee'ba) is cut 15 to 25 cm above the ground and the upper central part of the corm is removed with a woge'nya; an old broken sibi'sa with a sharp cutting edge. The sibi'sa is a tool made out of bamboo, used for processing of the pseudostem (Fig 3).

The corm is buried under 10 to 20 cm soil mixed with cows' manure. After a few weeks 50 to 150 sprouts have grown. After one year they are transplanted one meter apart, in groups of three. One year later they are planted one meter apart and individually, and after a further two years they are planted individually, 1.5 to 2 meters apart. The four stages of growth are referred to as fa'nfa, yesostee'ye, te'ket and hee'ba respectively. Intercropping of oranges (*Citrus sinensis*), coffee (*Coffea arabica*) and cha't (*Khat edulis*) is generally applied, especially in between hee'ba. Manure is applied to all plants in all stages of growth at least once a year. The length of a growth stage may be extended if plants have not grown sufficiently at the time of transplanting. For example, the smallest of the one-year old *sprouts* (fa'nfa) can first be planted in groups of six where they will stay for one year, after which they will also be planted in groups of three (te'ket). The last stage (hee'ba) may also be extended from two years to five years.

As observed in the Gurage area, ensete is grown near the house on rectangular plots divided into different sections, each accommodating plants of the same stage of growth. Each section is referred to by the name corresponding to that stage. The more vulnerable young sprouts are planted close to the house whereas mature plants can be found further away.

Harvesting and processing
Most of the ensete is harvested from November to January. All the work is carried out in the *field* (go'na) itself. The number of plants harvested by a household on one day varied from three to fifteen.

Preparation of *mature plants* (ye'sete) for further processing. With a tebe'cha (Fig 3) the men and boys remove the leaves, *dry and shrunken ends of outer layers of the pseudostem* (e'nwa) and small adventitious roots from the corm. Several *outer, rather green sheaths of the pseudostem* (urchee'ye) are removed. The plants are then pushed over and divided into the *corm with 20 to 30 cm of lowest part of the pseudostem* (wo'quta), the *inner sheaths of the pseudostem, above the wo'quta* (nechee'ya), and the *outer sheaths of the pseudostem together with the lower part of the ribs of the leaves* (guneree'ye). *The sheaths of the pseudostem* (gu'ppa) are discarded except for the *central part* (enkerkee'na). All further processing is carried out strictly by women and girls.
Preparation of working sites. A smooth surface is prepared with leaves of which the convex sides of the *ribs* (chimbee'na) are removed with a *curved knife* (woka'ra). The site where the pseudostem is processed is called yekasse're, the corm is processed at yo'qute.

Processing of the pseudostem. The concave sides of the sheaths are peeled, cut into pieces one meter long and split lengthwise. A *plank (2 m x 0.3 m)* (wa'ttar) is placed against an ensete plant at an angle of 45°. While sitting on a stone, a women uses one foot to hold a piece of a sheath of the pseudostem up against the plank. First the lower part is scraped with a sibi'sa, a sharp-edged tool made out of bamboo wood (Fig 3). The scraping yields a *pulp* (kissa'ra) that is collected underneath the plank, and *fibre* (ka'ncha) that remains on the plank. This fibre from the lower part is wound around her foot after which the remaining part of the sheath is scraped.

The wettest part of the pulp is also referred to as "yewatta'yre". *Fibre from urchee'ye* (kapsa'ssa) is not as fine and as white as ka'ncha. Both ka'ncha and kapsa'ssa are dried in the sun. Ka'ncha is used for many purposes such as making rope, mats and bags. Kapsa'ssa is used for squeezing fermented pulp of ensete. In addition, the concave layers from the lower parts of the leaf ribs are removed by hand and *the inner soft part* (zya'nzya) is torn out and cut into smaller pieces with a woka'ra.

Processing of the corm. First the outer soiled part of the corm is removed with a tebe'cha (Fig 3). Then it is pulverized with the zigzag sharp-edged end of the "zyeeba'nzyeebye" (Fig 3), made out of any type of hard wood available. *Pulp from the outer layer of the corm* (zanzee'ye) and *from the white inner part* (bure'ma) are kept separate. The *most central part of the corm* (dida'fo) is often retained intact and used as payment for the labour of women not belonging to the household.

Mixing to obtain two qualities of pulp. At the end of the day kissa'ra, bure'ma and guneree'ye are mixed resulting in a light-coloured, rather highly appreciated pulp called me'chee. Zya'nzya, zanzee'ye and urchee'ye are mixed resulting in a dark-coloured, not much appreciated pulp referred to as tikuree'ye. Only if a'tmet (a white fibreless luxury food, see further) has been produced, guneree'ye is added to tikuree'ye. Me'chee is collected at yekasse're and tikuree'ye at yo'qute. Both are put in a layer of 15-20 cm and covered with leaves.

Initial fermentation, above ground. Over a 10 to 15-day period, *all pulp* (ti'kot) is mixed twice and then piled up on the ground to allow fermentation to take place, after which it is referred to as wu'ssa.

Storage in earthen pits. Ten to fifteen days after harvesting, the pulp is placed in earthen pits for storage. A new *pit* (gua'ji) is dug or an existing pit is renovated. Tools used for cultivation are also used for this purpose. The inside of the pit is covered with ribs of leaves, with their concave sides towards the soil. The pulp is cut roughly and transported to the pit in a basket on a stretcher. In the pit pressure is applied on the wu'ssa; first by standing on it and then, after covering it with leaves, with heavy stones. Here it can be kept for a period of up to five years, during which time it is readily available throughout the year.

Production of a'tmet. A'tmet is a highly appreciated white fibreless product. In order to produce it, me'chee is put in a basket, rinsed with water and squeezed. The basket is put on the *inner bark of sheaths of the pseudostem* (a'ba), next to a *rectangular pit* (go'je) which is lined with *heated soft leaves* (yageko'ree) to make it watertight. A turbid fluid pours out through the basket and is collected in the pit. The pulp is rinsed repeatedly with that fluid. More leaves are put around the pit to collect spent pulp. A few days later, the solid particles in the fluid have precipitated. After removal of water, the *solid part* (a'tmet) is wrapped in leaves and put in the pit and then often covered with me'chee or tikuree'ye.

Sometimes the amount of ensete harvested does not supply sufficient food until the next annual harvest. Then extra plants are harvested as required. The freshly harvested corm is consumed after cooking without prior fermentation. The pseudostem is fed to cattle.

Yield

In Table 1 data on ensete yield are presented. An average household had about 1615 m^2 planted to ensete. From this area, 46 plants were harvested yearly, equivalent to a yield of 0.028 plants/m^2/yr. The yield per plant of pulp fermented for 10 to 15 days was 28 kg of ensete of higher quality (me'chee plus a'tmet when measured) and 14 kg of ensete of lower quality (tikuree'ye). Since the only weight loss was due to expression of fluid from the pulp (15, 21 and 22%), the estimated food yield was 34 kg per plant or 0.95 kg/m^2 (9.5 tons/ha) annually. A'tmet was produced in only 4 out of 23 households at the time the study was conducted, yielding on average 2.1 kg per plant (range 0.3 to 3.8 kg).

Table 1 Yield of ensete in Gurage area, Ethiopia

	n	Mean (SD)	range	
Yield of fresh fermenting pulp per plant, kg (a)	208	42 (9)	24	62
Proportional weight loss after squeezing pulp (b)	3	0.19	0.15	0.22
Proportional weight change after baking pulp (c)	14	0.00 (0.06)	-0.11	0.09
Yield of ensete food per plant, kg (d=a((1-b)(1-c))		34		
Number of plants harvested per household/yr (e)	45	46 (19)	12	110
Area used for ensete by household/m^2 (f)	45	1615 (875)	335	3665
Number of plants harvested/m^2/yr (g=e/f)	45	0.028		
Yield of ensete food, kg/yr/m^2 (d g)		0.95		

In order to evaluate the yield of food prepared from ensete, comparative data on the yields of foods prepared from other crops were calculated (Table 2). Compared to cereals, the yield of ensete in terms of weight (0.95 kg/m^2/yr) and energy, (6.1 MJ/m^2/yr) was about four times higher while the protein yield (11.4 g/m^2/yr) was about 50% higher. Also compared to other tuber crops such as Irish potato and sweet potato, ensete had a high yield. Compared to cassava, ensete had a low energy and similar protein yield, whereas compared to banana, ensete had a higher energy and lower protein yield.

Table 2 Yield of crops grown in Ethiopia, in terms of weight, energy and protein

Food[a]	Yield		
	Weight g/m²/yr	Energy, MJ (kcal)/m²/yr	Protein, g/m²/yr
Ensete *(Ensete ventricosum)*	950[1]	6.1 (1450)[2]	11.4[2]
	240[3]	2.0 (490)[4]	2.9[4]
Barley *(Hordeum vulgare)*	230[5,6]	1.6 (390)[6]	8.1[6]
Maize *(Zea mays)*	170[5,6]	1.3 (320)[6]	8.6[6]
Sorghum *(Sorgum vulgare)*	260[5,6]	1.5 (365)[6]	7.7[7]
Finger millet *(Eleusine coracana)*	170[5,6]	1.2 (290)[6]	6.5[6]
Teff *(Eragrostis teff)*	200[5,6]	1.4 (330)[6]	8.5[6]
Wheat *(Triticum vulgare)*	170[5,6]	1.3 (300)[6]	9.3[6]
Irish potato, grilled *(Solanum tuberosum)*	500[3]	1.4 (335)[8]	11.5[8]
Sweet potato, boiled *(Ipomosea batatas)*	420[3]	2.1 (510)[8]	3.4[8]
Cassava *(Manihot esculenta)*	880[9]	8.5(2070)[10]	10.4[10]
Banana *(Musa acuminata)*	1110[9]	3.8 (910)[10]	16.6[10]

[a] Ensete was prepared as ko'cho, cereals as enje'ra, cassava was cooked, banana was raw.

[1] present study; [2] ref. 14; [3] ref. 3; [4] ref. 11; [5] ref. 5; [6] ref. 7; [7] ref. 2; [8]; ref. 8; [9] ref. 1; [10] ref. 22

Discussion

Cultivation and harvesting

Few quantitative data concerning ensete are available. The area allocated per plant has been estimated to range from 4 to 20/m² *(4,18,20)*. The Gurage generally plant their ensete close together not more than 2 m apart, giving each plant 4 m². If the data in Table 1 are used and a six years cutting cycle is taken into account, the average area per plant in the studied area seems to be greater: 5.8 m². This is probably so because the area in use for the cultivation of ensete as measured by pacing might be over estimated. Sometimes minor areas, included in the total area paced, were not being used for the cultivation of ensete but for coffee, ch'at or oranges. The area calculated is an average based on all plants including smaller plants, which require less than 4 m². Another type of quantitative estimate on ensete was made by Bezuneh *(3,4)*. In one study, he estimated that a household dependent on ensete cultivates 200 to 400 plants (*3*), while in a second study the estimate given is 500 to 750 ensete plants (*4*). Considering a six-year cutting cycle and 4.5 persons per household (*13*), the second estimate would seem too high as it provides more than 20 plants per person per year.

Regarding the cultivation and harvesting of ensete, there are several brief descriptions in the literature (*3,10,15,20,21*) which are not consistent with our observations. According to Straube (*21*) two or three year old plants are used for propagation, while the Gurage in the present study used only four year old plants for this purpose. Straube also described stages of growth lasting three years, which is longer than in the present study. Bezuneh and Feleke (*3*) reported that, with an average temperature of 16 to 20 ^{0}C, there were three years between planting in the permanent field and the time of harvesting. The finding that this stage of growth usually lasted only two years can be explained by the higher average day temperature (23-25 ^{0}C) in the Gurage area. Straube (*21*) stated that, if the owners can afford it, the plants are harvested after flowering. In the Gurage area, harvesting takes place before flowering, because flowering is said to decrease the food value of the plant markedly. This decrease results from the depletion of carbohydrate stores during the flowering process. Instead of putting the non-fermented, fresh pulp in earthen pits, as is practised in Sidamo (*21*), the Gurage always ferment the freshly scraped pulp above ground first.

Yield

Ensete is grown in several regions of Ethiopia (*23*), which are the most densely populated regions of the country (*5*). This has been mentioned by earlier investigators (*4,17-21*). Thus Smeds, Shack and Stanley concluded that ensete gives a higher yield per unit of land than other crops such as seed-crops. This has never been verified. An estimate given by the Central Statistical Authority (*5*) for 1967-1968 of 2.4 tons of edible ensete per hectare (cited in *4*), suggests that the yield of ensete is only slightly higher than the yield of cereals, and even much lower than that of other common food crops such as Irish potato and sweet potato.

We calculated an annual yield (9.5 tons/ha) that was four times the yield given by the Central Statistical Authority (*5*). Because our calculations were based on weighing, pacing and counting it can be assumed that our figure is relatively reliable. Information on the number of plants harvested by each household annually was not obtained by observation but by questioning. This estimate may be the least reliable step in the calculation.

The presence of Attat Hospital may have influenced our findings and could possibly make our figures less representative for the Gurage area as a whole. A number of people in the area earn money by working in the hospital and may, therefore, have more cattle. Because of this they have extra manure available, which could increase the yield of ensete.

Be that as it may, it would still appear that annual yield per unit area, compared to that of sweet potato and to all of the cereals grown in Ethiopia, in terms of both energy and protein, is high (Table 2). From this one might conclude that the cultivation of ensete is to be recommended. However, the high yield of protein can be attributed to the high yield in terms of weight and not to a high protein density because this is only 12 g/kg. This low density is a problem because the amount of ensete which needs to be consumed daily to meet protein requirements is very high. To provide 60 g of protein 5.0 kg of ensete bread has to be consumed. However, regarding energy intake the amount of ensete to be consumed daily is much less; 1.3 kg provides 2000 kcal (*14*).

The production of the luxury food a'tmet involves further refining of freshly harvested pulp: during the process a starch-rich fraction is extracted from the fibrous me'chee pulp. The more the pulp is rinsed in this process, the less starch remains behind. Thus the nutritional value of the remaining pulp decreases and it is then no longer regarded as a high quality product. Therefore the yield of a'tmet varies greatly; in our four observations, it varied from 0.3 to 3.8 kg per plant. Yield of a'tmet does not say much about the quality of ensete plants, although *maximum possible yield* of a'tmet would be a valid measure for this purpose. However, since then the quality of the remaining pulp would be very low, it is very unusual to produce as much a'tmet as possible, especially in those households with limited production of ensete.

Figure 1 Full-grown ensete with inflorescence.

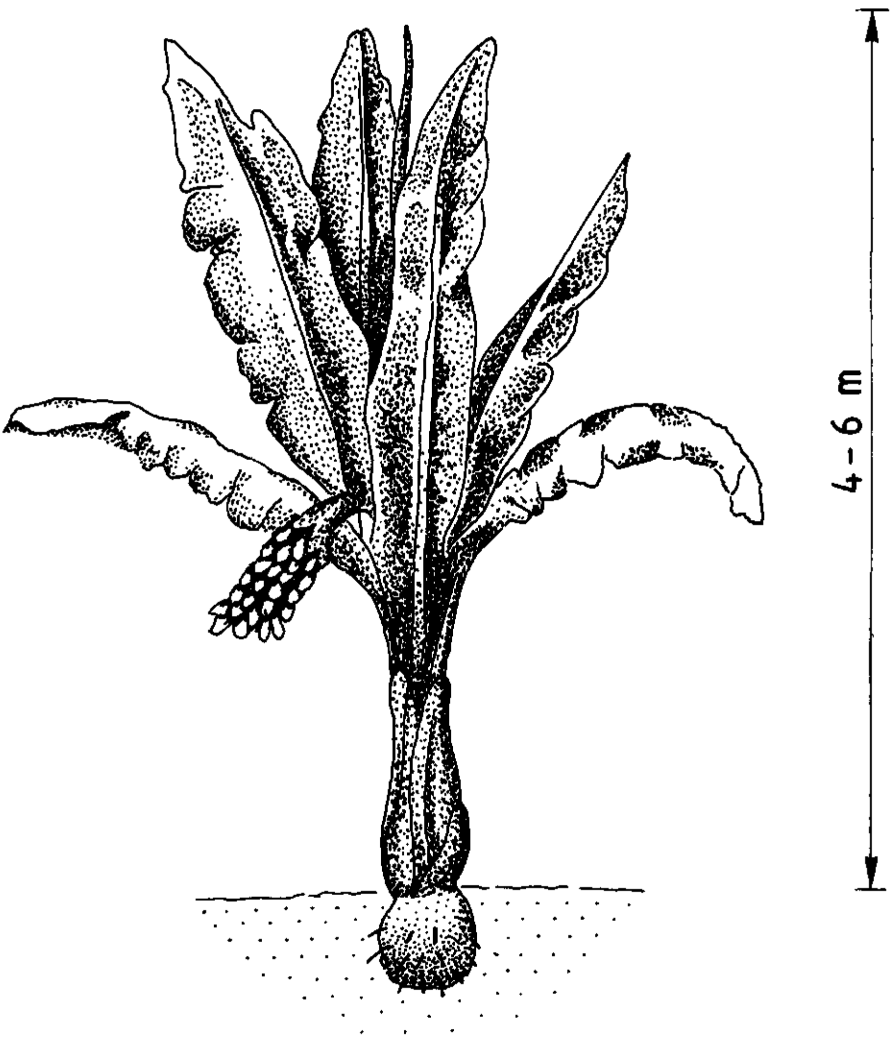


Figure 2 Stages of growth and transplantation of ensete, as practised by the Gurage in Ethiopia.

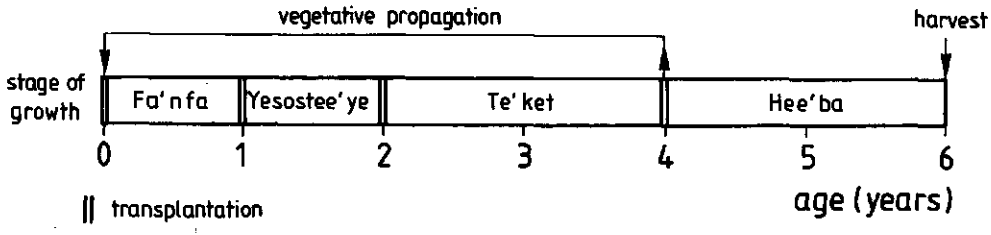
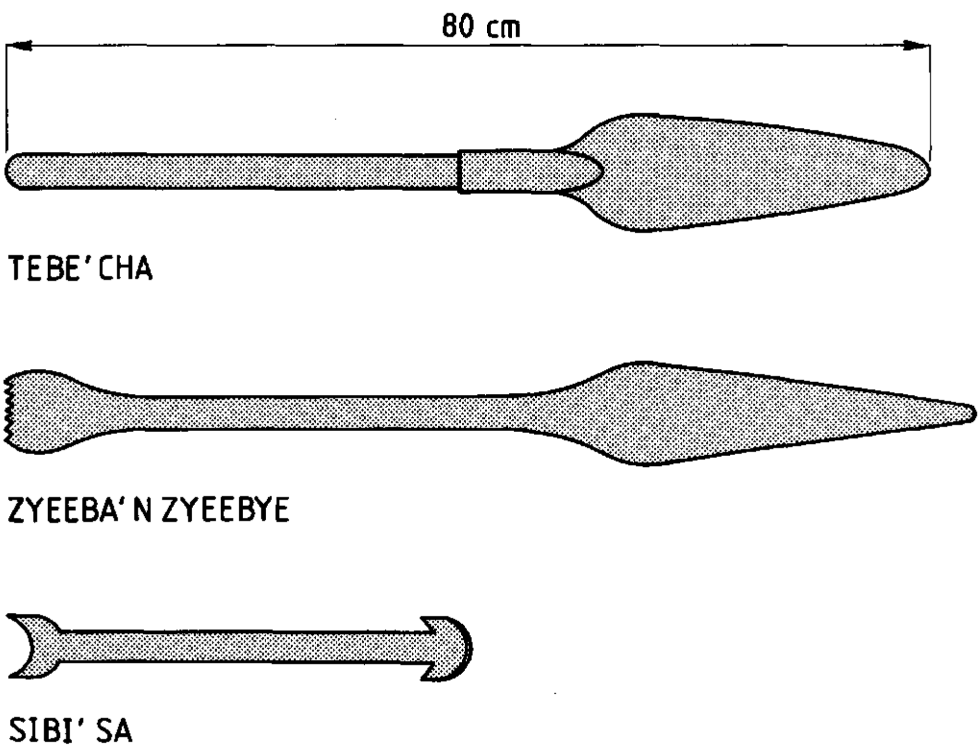


Figure 3 Tools typically used in the cultivation of ensete by the Gurage in Ethiopia.



Conclusions

Because of its high yield of energy and protein, it has been suggested that the cultivation of cassava should be promoted to improve household food security in areas in Ethiopia prone to famine. However, because of its sensitivity to low temperature it cannot be grown in the highlands. There also is the danger of cyanide intoxication after consuming inadequately processed cassava. In the highlands ensete, which can withstand dry periods (*3*) because of its water reserves (*20*), might be a feasible and effective alternative for cassava. In areas where it is already a co-staple food, the contribution of ensete to total food intake could be increased. In addition, ensete could be introduced slowly to other areas, especially in those adjacent to where it is already grown for consumption.

In view of the danger of erosion, ensete cultivation should be discouraged on slopes without adequate soil protection. Intercropping should be encouraged because it decreases the danger of erosion and also increases productivity. Ensete foods can be stored for up to several years and are readily available throughout the year, thus significantly contributing to household food security. If ample fertilizer is available, ensete is a suitable crop for cultivation in highland areas prone to drought and famine. Because of the relative low protein density, it should be consumed along with protein-rich foods such as legumes or milk products.

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ANNEX 2

Preparation, food value and consumption of ensete (Ensete ventricosum) in Ethiopia*

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Abstract

In Ethiopia almost 10 million people are dependent on ensete (*Ensete ventricosum* (Welw.) Cheesman) or 'false banana'. In the Gurage area in Central Ethiopia nutritional aspects of ensete were studied in about 60 households. The pseudostem and corm provide a starchy pulp which is fermented and can be stored for up to 5-7 years in an earthen pit. To make ensete bread (ko'cho), fermented pulp is squeezed to make it drier, chopped to shorten the fibres after which a layer of 2 cm is baked for 15 minutes. White fibreless luxury food (bu'lla) does not need squeezing or chopping. Unfermented freshly harvested corm is also eaten after boiling. All foods have a low protein content (4-22 g/kg). Bu'lla is more energy dense (8.46 MJ/kg) and contains less moisture (488 g/kg) than ko'cho (6.46 MJ/kg and 580 g/kg). Based on measurement of dietary intake in another 39 households, the mean intake of ensete of 0.55 kg per day provided 68% of total energy intake, 20% of protein, 28% of iron but no vitamin A. Energy intake from all food consumed is extremely low, being only 60% of requirements.

Introduction

Ensete ventricosum (Welw.) Cheesman (*5*) resembles the banana plant but bears no edible fruit. Hence it is referred to as 'false banana' in addition to the name 'ensete' which is generally used in Ethiopia. A number of foods are produced from its corm and pseudostem: one is ko'cho, a fermented product from the pulp of the pseudostem and corm, and another is bu'lla, a desiccated juice collected from this pulp (*2*).

Ensete is the staple food for eight million people in the most densely populated areas in south and south-western parts of Ethiopia, inhabited by the Gurage, Sidama and related tribes. It also is the co-staple food for about two million people in South-west and Western Ethiopia, altogether representing one-fifth of the population (*13,22*). From the good physical appearance of the Gurage and Sidamo people, Smeds (*20*) concluded that ensete food is deservedly highly appreciated for its health stimulating qualities. Little information on its preparation, food value and consumption is available.

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* *Submitted for publication*

Thus in the present study such information was gathered in a systematic way, in an area inhabited by the Gurage. They are probably the best known ensete growers (*21*) and are heavily dependent on ensete which plays a central role in their culture (*19*). Most information available up to now was collected several decades ago in Sidamo Region about 200 km further to the south. An earlier paper presents data on the cultivation, harvesting and yield of ensete in the same area (*15*).

Methods

The present study was carried out in six villages within a radius of 6 km from Attat Hospital located in Chebona-Gurage Province, 175 km south-west of Addis Ababa at an altitude of 1900 m. The area served by the hospital, which provides both curative and preventive services, is densely populated by the Gurage (135 persons/km^2, (*4,14*)). The fieldwork on the preparation and food value was carried out with the assistance of two Gurage interpreters. About 60 households were visited and, after the aims of the study were explained, most people agreed to cooperate.

Food preparation was observed repeatedly in different houses until detailed descriptions were obtained. Meetings of women in two villages were attended in order to verify information collected previously and to obtain additional information. Questions formulated in advance were asked to the group as a whole after which several women answered.

Samples of foods were taken and stored at -20 ^{0}C for one to three weeks. Moisture content was determined by drying 16 to 18 hours at 92 ^{0}C, the boiling point of water in Addis Ababa which is at an elevation of 2400 m. Nitrogen was determined by the Kjeldahl method using selenium and potassium sulphate as catalysts as described in the manual of the manufacturer of the equipment used (Tecator, Sweden). Protein content was calculated by multiplying nitrogen content by 6.25, while crude fibre was determined by the Weende method. Fat was determined by the Soxhlet procedure, in which dried samples were extracted with peroxide-free diethyl ether for four hours. Then carbohydrate was calculated by difference from the values for protein, fat, crude fibre and ash. Energy content was calculated by applying the Atwater factors: 17 kJ/g for protein and carbohydrates and 38 kJ/g for fat.

Forty-seven households, originating from a total of 102 households included in a study on anaemia were selected for a dietary survey, full details of which are being published elsewhere (*24*). Valid information on dietary intake could be collected in 39 households, comprising 237 persons (44 % females) with a median age of 12 years.

Their dietary intake was estimated using a three-day weighed record in which food quantities were weighed immediately prior to eating or by weighing duplicate portions, using a Salter kitchen scale. In October 1989 the survey was conducted by five local people, trained by an experienced dietician, and repeated two months later.

The MicroNAP program (version 4.21 (*17*)) was used to convert data on food intake to intake of energy and nutrients per household. Based on age and sex, the relationship with recommended individual intakes was determined (see Table 3). Adults were regarded as moderately active while average body weights of 50 kg for women and 55 kg for man were used in the calculations. Since the diet of the Gurage is very limited in animal products, iron requirement was based on that for a low bio-availability diet. For energy and all nutrients, adequacy of intake was calculated by dividing total intake of all 39 households by the total requirement of the 237 persons they comprised. Finally, the contribution of ensete to total intake of energy and nutrients was estimated by dividing intake from ensete by total intake.

Results

Food preparation

In this section descriptions, written in italics, of plants, processes, tools and other terms are followed by their Guragegna names in parentheses.

The *fermenting pulp as stored in a pit* (wu'ssa) comprises both material which is *light coloured, highly appreciated* (me'chee) and *dark coloured, not much appreciated* (tikuree'ye) (*15*). Both types of wu'ssa can be prepared as asha'shat (from me'chee or tikuree'ye), while only me'chee is used for da'puha or for wu'ssa techo'chim. The *white fibreless product* (a'tmet) can be prepared in four ways: as a'tmet, bra'brat, gu'nfo or yicho'chee. In addition, unfermented parts of the *corm* (wo'quta) can be prepared as wo'quta or kuchku'cher. **Wu'ssa** and **a'tmet** are more generally known as **ko'cho** and **bu'lla** respectively. The foods are baked at the *fireplace* (go'dred, usually located centrally in the round house) comprising a circular raised concrete belt surrounded by three or four *earthenware pots* (gonzee'ya) supporting an iron *circular concave hotplate* (meta'd).

In order to prepare **asha'shat** or **da'puha** the dough to be baked is processed as follows: The stones and covering leaves are removed from a pit in which fermenting pulp is stored. An amount allowing for one or a few meals is taken out. Pulp less then a few months of age has a rather high moisture content making it difficult to cut its fibres. Therefore it is wrapped in *ensete fibre of low quality* (kapsa'ssa) and *squeezed* (yikoku'ree). The *liquid that exudes* (bu'ya) is collected in a *pot* (tinkee'ya) and dried, resulting in a *powder* (aterku'ye). Then the pulp is kneaded on a *wooden plank* (zebo're), pressed with a *hooked wooden tool* (yichochee'que e'nche) which also protects the hand, and over a period of about 20 minutes it is chopped to break the fibre. Since the fibre slowly decays, less cutting is needed the longer the pulp has been stored. The dough is *kneaded* (yishe'shee) on a *square mat made from ensete fibre* (yetephe'pe, 0.4 m by 0.4 m) until an elastic dough is formed. Some water might be added.

To prepare **asha'shat** the dough is subsequently treated as follows: It is stretched out on the mat onto a layer of 1.5 to 2 cm and laid upside down on the hotplate. Then the mat is removed and the dough is baked on both sides for 10 to 20 minutes. In order to get a softer outer layer, the dough can be covered with ensete leaves, or some water is poured onto the hotplate. The space arising between hotplate and dough is ventilated by lifting the bread a little.

In order to bake **da'puha**, usually prepared at the occasion of religious feasts, the dough is stretched out onto a somewhat thicker layer 3 to 4 cm thick. The hotplate is covered with narrow strips of leaf ribs and with two leaves crossed, in which the dough is wrapped. Again this is covered with strips of leaf ribs, and sprinkled with water. As such it is steamed for 70 to 100 minutes and turned several times.

Wu'ssa techo'chim is a more refined food prepared from me'chee. The pulp is kneaded while water is poured on it. The liquid that pours out is filtered through thin pieces of wood covered with *fibre of lower quality* (kapsa'ssa). The larger fibrous particles remain on this filter. The filtrate is collected in a cotton bag which hangs in a clay pot, the bag serving as a second filter which removes smaller particles. The filtrate collected in the clay pot is added to bu'ya. The contents of the bag are kneaded and baked in a similar way as asha'shat. Since it contain very little fibre, the dough is baked while wrapped in ensete leaves, preventing it from falling apart.

Four preparations of the *white fibreless pulp* (**a'tmet** or as referred to more generally, **bu'lla**) were observed. It can be prepared similarly to asha'shat except for that no squeezing or cutting is needed. Since it hardly contains fibre it is always wrapped in leaves during baking, and after baking it is also referred to as **a'tmet. Bra'brat** is fresh a'tmet which is reduced to crumbs, roasted on a hotplate for five minutes and then mixed with water, butter and spices such as dried pepper (*Capsicum frutescens*). Fresh a'tmet which is reduced to crumbs, cooked in water for 10 to 15 minutes and then mixed with butter and spices is referred to as **gu'nfo**, or as **yicho'chee** if it is mixed with sugar or salt.

Pieces of *freshly harvested corm* (**wo'quta**) are cooked for 20 minutes and eaten with dried pepper, referred to as **wo'quta**. Pounding of cooked pieces of the corm (with a zyeeba'nzyeebye, see *15*) results in a porridge (**kuchku'cher**) which is eaten with spices.

Food value

All of the foods prepared from ensete in the Gurage area contained little protein (4-22 g/kg) and almost no fat (1 g/kg), so that 97 % of the energy is present as carbohydrate. The nutritional value of the four different foods in Ethiopia generally referred to as ko'cho was rather similar. Probably because it is steamed, da'puha had a slightly higher moisture content. Since wu'ssa techo'chim had been sieved it contained less fibre (14 g/kg) than the other ko'cho's. Compared to ko'cho (wu'ssa), bu'lla (a'tmet) had a lower and wo'quta a higher moisture content. Bu'lla had the lowest fibre content (4 g/kg).

Except that the carbohydrate content and therefore the energy value were lower and that the protein content was higher in the preparations described here, the nutrient values found were similar to those described by others (Table 2).

Consumption

The proportion of energy derived from protein, carbohydrate and fat from all food sources was 11%, 82% and 7% respectively. As shown in Table 3, the intake of energy is very low (60% of requirement) while the intakes of protein (107%), vitamin A (113%), iron (175) and calcium (140%) exceeded the requirements considerably. All vitamin A came from sources other than ensete, principally kale and cheese, as ensete contains no (pro)vitamin A.

Discussion

When comparing the preparations and parts of ensete plants consumed in the Gurage area with the scarce information available in the literature, several differences are seen. According to Bezuneh and Feleke (*3*), parts of the stem and corm are usually cooked fresh. We observed, as did Huffnagel (*11*) and Selinus *et al.* (*16*) that this is only done in summer when food is in short supply. Bezuneh and Feleke (*3*) also stated that the fermented pulp is mixed with spices and butter *before* baking, whereas in the Gurage area spices are added only *after* baking. Although the studies cited here were carried out about 30 years ago, they were conducted in Welkite and Wolliso which are near to the area of the present study. In studies carried out in Eastern Sidamo stretching back to 1844 (*20*), consumption of young shoots, the medulla of the inflorescence, seed contents and also the fruit itself were reported but these plant parts were not consumed by the Gurage.

The main feature of foods from ensete is their high energy value coming mainly from carbohydrate. A daily energy requirement of 8.4 MJ for an adult can be obtained from 1.3 kg of ensete but this same amount would supply only 26% of a daily protein requirement of 60 g. Since young children in particular cannot eat large quantities of food, the low protein density of ensete makes it difficult for them to obtain sufficient protein from a diet comprising only ensete. The protein content of ensete reported here is comparable to or slightly higher than that reported from other studies (Table 2). It is interesting to note the findings of Besrat *et al.* (*2*) who measured the protein content of 29 ensete cultivars and found an average of 33 g/kg which is much higher than that reported from other studies.

Bu'lla is a food that is appreciated for its fine structure and taste. It indeed contains less fibre than other ensete foods (Tables 1 and 2). Ko'cho is not so much appreciated by those not accustomed to it because of its fermented smell and taste and its fibrous structure. However, the fibre content of ko'cho is similar to that of teff enjera (11 g/kg, (*8*)). Possibly much of the fibre in teff enjera comprises rather small particles compared to that in ko'cho.

Table 1 Composition and energy content of ensete foods expressed per kg[a]

	Asha'shat		Da'puha	Wu'ssa techo'chim	A'tmet	Wo'quta
	Me'chee	Tikuree'ye				
Number of samples	6	2	1	1	1	1
Moisture, g	581	578	609	559	488	699
Energy, MJ (Kcal)	6.50 (1550)	6.38 (1530)	6.07 (1450)	7.07 (1960)	8.46 (2020)	4.65 (1110)
Protein, g	9	18	11	8	4	22
Carbohydrate, g	375	361	350	412	496	254
Fat, g	2	1	1	1	2	1
Crude fibre, g	24	30	20	14	4	13
Ash, g	9	13	9	6	6	11

[a] For descriptions of foods; see Results

Since bu'lla is said to be good for healing bone fractures, its calcium content would be expected to be high. However, as shown in Table 2, it contained only half the amount of calcium as ko'cho. Enjera from barley, maize, wheat and white sorghum do indeed contain less calcium, but enjera from teff and especially finger millet has much more (*6*).

The contribution of carbohydrate to total energy intake was found to be 82% which was similar to the value found by Stanley (*21*) in the same area. This is somewhat lower than the 90% reported by Selinus *et al.* (*16*) for Sidamo Region where the daily intake of ensete was found to be 0.80 kg compared with 0.55 kg in the present study. This difference may reflect the worsening food situation in the country as a whole due, among other reasons, to the high growth in the population which is 2.9% per year (*13*). The total intake of energy is extremely low, being only 60% of requirements. Such low energy intakes have been reported from other studies in the Region (*7*) while in Sidamo Region, energy intakes are higher (*7,16*). The low energy intake and possible adaptation to it is the topic of a number of studies presently underway. The intakes of protein, vitamin A, iron and calcium from all food sources were between 107 and 175% but foods particularly kale (*Brassica carinata*) and cheese are important for the provision of these nutrients.

Table 2 Composition of foods prepared from ensete expressed per kg

Food	Ko'cho (wu'ssa)[a]					Bu'lla (a'tmet)			
Reference	Present study[b]	ICNND (*12*)	Ågren (*1*)	ENI (*6*)	ENI (*8*)	Present study	ICNND (*12*)	Ågren (*1*)	ENI (*8*)
Moisture, g	580	563	553	617	487	488	437	484	549
Energy, MJ (Kcal)	6.46 (1550)	8.48 (2030)	7.35 (1760)	6.34 (1520)	8.40 (2010)	8.46 (2020)	9410 (2250)	8.32 (1990)	7.14 (1710)
Protein, g	12	12	8	9	6	4	3	10	2
Carbohydrate, g	370	413	427	367	490	496	554	480	444
Fat, g	2	2	1	3	1	2	1	2	1
Iron, mg	n.a.[c]	53	35	36	37	n.a.	77	24	26
Calcium, g	n.a.	1.20	1.11	0.75	0.82	n.a.	0.44	0.83	0.41
Dietary fibre, g	26	n.a.	21	11	12	4	n.a.	18	3

[a] General name with Guragegna name in parenthesis.
[b] Weighted average of "me'chee" (2/3) and "tikuree'ye" (1/3), see Table 1
[c] Not available

This could explain the low prevalence of vitamin A deficiency and nutritional anaemia found in the area (*23*). Similar results have been reported by Selinus *et al.* (*16*) for the Sidamo Region.

While evaluating the intake of iron, a specific feature of the households studied has to be considered. Since the dietary survey was conducted only in households that included an anaemic boy, the data collected may not representative of the area. This prevalence of anaemia cannot be attributed to insufficient intake of iron, which exceeded the requirements by 75%. Results from a follow-up study in the same area indicated that infection with malaria and the severe load of intestinal parasites could explain the relatively high prevalence of anaemia (*24*).

Table 3 Intake of energy and nutrients in Gurage

	Proportion of requirement, %[a]	Contribution of ensete to total intake, %
Energy	60[1]	68
Protein	107[1]	20
Carbohydrate	-	78
Fat	-	11
Vitamin A	113[2]	0
Iron	175[2]	28
Calcium	140[3]	65

[a] Proportion of requirement of households as a whole based on recommendations for individuals: [1], ref. 9; [2], ref. 10; [3], ref. 25

Estimates on the number of ensete plants consumed annually per person varying over a wide range have been reported: 3 by Wohlenberg in 1936 as cited in Smeds (*20*), 9 by Stanley (*21*), 10 by Shack (*19*), 12 by Smeds (*20*), 10 to 12 by Bezuneh and Feleke (*3*), 12 to 15 by Shack (*18*), and 15 to 20 by Huffnagel (*11*). Using data on the yield of ensete food per plant of 34 kg reported earlier (*15*) and the daily consumption of ensete reported here of 0.55 kg, it can be calculated that the number of ensete plants consumed annually is 5.9 per person or 36 per household averaging 6.1 persons. This compares with the reported number of plants harvested annually per household of 46 (*15*). This discrepancy could possible be explained by household sales. At present, each household cultivates about 0.17 ha with ensete but in order to increase energy intake to an acceptable level, this area should be increased to 0.28 ha per family assuming that the proportion of ensete to total energy intake remains the same. Other authors have considered that even larger areas are necessary even when disregarding the possible contribution to energy intake from other foods. Stanley (*21*) suggested that 0.42 ha would be sufficient for an average family while Shack (*19*) suggested that one hectare is needed to support a household of five to 10 members.

Based on the population density in the area of 135 persons/km^2 (*4*), the proportion of land under ensete cultivation is now 3.8%. The area devoted to staples will need to be increased if the low intake of energy is to be improved.

Ensete would appear to be the crop of choice for the highlands because the only other local crop which can supply the energy required is cassava which does not thrive here because of its sensitivity to low temperatures.

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SUMMARY

A nationwide study on the prevalence of xerophthalmia was carried out in 6,636 children aged 6 months to 6 years in all the Regions of Ethiopia except Eritrea and Tigrai which were excluded for security reasons. Bitot's spots were observed in 1.0% of all children with higher prevalence in the pastoral (1.6%) and cropping (1.1%) agro-ecological zones than in the cash-crop (0.4%) and ensete ('false banana', *Ensete ventricosum* (Welw.) Cheesman) (0.0%) zones. Conjunctival xerosis and Bitot's spots were twice as common in boys than in girls and this was seen in all age groups. One case of corneal xerosis and two cases of corneal scar (0.03%) were also found. Serum retinol levels were deficient (<0.35 µmol/l) in 16% and low (0.35-0.69 µmol/l) in 44% of children. Results of the present survey indicate that the problem is, according to WHO criteria, of public health significance. More stunting than wasting was observed, with peak prevalence of these signs of malnutrition being observed in the second year of life.

It is estimated that there are three quarters of a million blind persons in Ethiopia. Results of a study of the 721 pupils in the six schools for the blind showed that 70% of the blindness was due to corneal opacity or shrinkage of the eye ball. Measles was implicated as a cause of blindness in 40% of the children while a further 13% regarded "mitch" as the predisposing factor. Mitch is an Amharic term used to describe a wide range of vague illness with fever and measles possibly comprising a large proportion of these cases.

A nationwide study on 35,635 school children and 19,158 household members showed that the prevalence of gross goitre was 30.6% and 18.7% respectively while that of visible goitre was 1.6% and 3.2% respectively. Prevalence was significantly higher in females than in males and increased with age more in females than in males. Prevalence increased with increasing altitude. Based on an epidemiological model, the numbers of people suffering from various iodine deficiency disorders have been estimated.

In Melkaye village of Hararge Region, a high prevalence of symptoms of vitamin A deficiency were found in 240 children examined: night blindness, 28.7%; Bitot's spots 6.7%; corneal xerosis 0.83%; corneal ulceration/keratomalacia 6.3%; and corneal scars 5.8%. Of the children studied, 30.2% had deficient serum retinol levels (< 0.35 µmol/l) while 58.0% had low levels (0.35-0.69 µmol/l). Thus both the clinical and biochemical parameters indicate that the problem of vitamin A deficiency was probably the most severe ever reported. The reason for the very severe deficiency of vitamin A in this area was the total dependence of the inhabitants for six years on supplies of relief foods which were devoid of vitamin A. About 55% of the children were malnourished with more wasting than stunting. Seventy children were reported to have died two years prior to the survey.

In a study of 14,740 children in Shoa Region of Central Ethiopia, goitre, xerophthalmia (Bitot's spots) and clinical anaemia were observed in 34.2%, 0.91% and 18.6% respectively of the children. Based on a sample of 344 children, the median of most biochemical parameters was within the normal range except for haemoglobin, mean corpuscular haemoglobin concentration (MCHC) and urinary iodine excretion where the median was lower, and mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and immunoglobulins G and M where it was higher. Many significant correlations were observed and these were used as the basis for the formulation of hypothethes. The anaemia found was not nutritional in origin but due to the effect of infestation with intestinal parasites and malaria.

The effect of vitamin A supplementation on the treatment of goitre with iodized oil was assessed in a series of studies in Shoa Region. Iodized oil supplementation significantly reduced goitre size in those who had grade IB goitre (observable when neck extended). After 4 and 7/8 weeks post-treatment, concentrations of thyroxin and that of urinary iodine excretion increased significantly, while those of total triiodothyronine and thyrotropin decreased significantly. Vitamin A supplementation increased serum levels of retinol and retinol-binding protein at weeks 4 and 7/8 but had no effect on goitre size or parameters of iodine metabolism.

In a similar study on anaemia, supplementation with iron and folic acid significantly increased levels of haemoglobin, haematocrit, red blood cell count, serum iron, transferrin saturation, ferritin and mean corpuscular haemoglobin concentration and significantly decreased levels of total iron binding capacity and transferrin at 4 and 7/8 weeks post-treatment. Only the increase in red blood cell count and decrease in mean corpuscular volume were significantly greater in those supplemented with vitamin A than those who were not supplemented.

In the Gurage area in Central Ethiopia, cultivation, harvesting, yield and processing of ensete were studied in 60 households in six villages. Ensete was propagated vegetatively and has a six-year growing cycle in which it was transplanted three or four times. The yield of ensete food ("ko'cho") was 9.5 tons/yr/ha (6.1 $MJ/m^2/yr$). Except for cassava, the energy yield of ensete was higher than that from all other crops grown in Ethiopia while the protein yield (11.4 $g/m^2/yr$) was higher than that of all crops except banana and Irish potato although the protein density is very low (12 g/kg). The pseudostem and corm provide a starchy pulp which is fermented and can be stored for up to 5-7 years in an earthen pit. It can then be prepared for consumption in a variety of ways which have been studied in detail. The mean intake of ensete was 0.55 kg/day and provided 68% of total energy intake, 20% of protein, 28% of iron but no vitamin A. Energy intake from all food consumed was extremely low in Gurage, being only 60% of requirements.

SAMENVATTING

Een nationale studie naar de prevalentie van xerophthalmie werd uitgevoerd onder 6.636 kinderen van 6 maanden tot 6 jaar oud in alle Regio's van Ethiopië, behalve Eritrea en Tigre die werden uitgezonderd vanwege veiligheidsredenen. Bij 1.0% van de kinderen werd Bitotse vlekken waargenomen. Bitotse vlekken kwam vaker voor in de pastorale (1.6%) en voedsel-landbouw (1.1%) agro-ecologische zones dan in de commerciële landbouw (0.4%) en ensete (valse banaan, *Ensete ventriculosum* (Welw.) Cheesman) (0.0%) zones. In alle leeftijdsgroepen werd uitdroging van het slijmvlies en Bitotse vlekken tweemaal zo frequent waargenomen bij jongens dan bij meisjes. De studie trof één kind aan met uitdroging van het hoornvlies en twee kinderen met hoornvlieslittekens (0.03%). Het serum retinolgehalte was deficiënt (<0.35 µmol/l) in 16%, en laag (0.35-0.69 µmol/l) in 44% van de kinderen. De resultaten van deze studie tonen aan dat xerophthalmie volgens normen van de Wereldgezondheidsorganisatie een significant volksgezondheidsprobleem is. Eiwit-energie ondervoeding bereikte de hoogste prevalentie gedurende het 2e levensjaar: "stunting" (achterstand in lengte-groei) werd méér frequent aangetroffen dan "wasting" (uittering).

Naar schatting is drie-kwart miljoen personen in Ethiopië blind. Een studie onder de 721 leerlingen van de 6 blindenscholen in Ethiopië toonde aan dat 70% van de blindheid te wijten was aan troebeling van het hoornvlies of aan verschrompeling van de oogbol. Mazelen werd als oorzaak voor blindheid gevonden bij 40%, terwijl een additionele 13% van de kinderen "mitch" als oorzaak beschouwde. Mitch is een uitdrukking in de amharische taal voor een breed spectrum van vage aandoeningen, waaronder koorts en mazelen die mogelijk een groot deel van deze gevallen verklaren.

Een landelijke studie onder 35.635 schoolkinderen en 19.158 leden van huishoudens leverde schattingen op voor de (totale) krop-prevalentie van respectievelijk 30,6% en 18,7%, en voor de zichtbare krop-prevalentie van respectievelijk 1,6% en 3,2%. De prevalentie was significant hoger en nam met de leeftijd sterker toe bij vrouwen dan bij mannen. De prevalentie nam tevens toe op grotere hoogte. Met behulp van een epidemiologisch rekenmodel werden schattingen verkregen van de aantallen personen in Ethiopië die aan de verscheidene jodiumgebreksziekten lijden.

Bij een onderzoek onder 240 kinderen in het dorp Melkaye van Hararge Regio werd een hoge prevalentie van vitamine A gebreksziekten waargenomen: nachtblindheid 28,7%; Bitotse vlekken 6,7%; hoornvliesuitdroging 0,83%; hoornvliesverweking of keratomalacie 6,3%, en hoornvlieslittekens 5,8%. Van de kinderen in deze studie had 30,2% deficiënte (<0.35 µmol/l) en 58,0% lage (0.35-0.69 µmol/l) serum retinolgehaltes. Zowel de klinische als de biochemische bevindingen geven derhalve aan dat het vitamine A gebrek in dit dorp waarschijnlijk de ernstigste deficiëntie is die ooit werd gerapporteerd. Oorzaak voor de ernstige vitamine A deficiëntie in dit gebied was de totale afhankelijkheid door de inwoners gedurende zes jaar van hulpvoedsels waarin vitamine A ontbrak.

Ongeveer 55% van de kinderen waren ondervoed; wasting kwam méér frequent voor dan stunting. Er werd gerapporteerd dat 70 kinderen waren gestorven in de 2 jaar voorafgaande aan de studie.

Bij een studie onder 14.740 kinderen in de Shoa Regio van Centraal Ethiopië werden krop, xerophthalmie (Bitotse vlekken) en klinische anemie waargenomen bij respectievelijk 34,2%, 0,91% en 18,6% van de kinderen. De mediane waarden van biochemische bepalingen bij een steekproef van 344 kinderen lagen voornamelijk in het normale gebied. Echter, lage mediane waarden werden waargenomen voor het hemoglobinegehalte van het bloed, de gemiddelde hemoglobineconcentratie per bloedcel en de jodiumuitscheiding in de urine. De serumconcentraties van immunoglobuline G en M vertoonden hoge mediane waarden. Veel correlaties waren statistisch significant en dit leidde tot formulering van hypothesen. De anemie in dit gebied had geen voedingsoorzaak maar was toe te schrijven aan een combinatie van infectie met darmparasieten en malaria.

In een serie studies in de Shoa Regio werd de invloed van een vitamine A supplement bestudeerd op de behandeling van krop met jodiumhoudende olie. Suppletie met jodium leidde tot een significante afname van de kropgrootte in proefpersonen met een kropgrootte IB (zichtbaar met een uitgestrekte nek). Op de tijdstippen van 4 en 7 à 8 weken na behandeling waren de thyroxinegehaltes in serum en de jodiumuitscheiding in urine significant toegenomen, terwijl de serumconcentraties aan trijodothyronine en thyrotropine (TSH) significant waren gereduceerd. De verstrekking van vitamine A verhoogde de serumgehaltes van retinol en retinolbindend eiwit op de tijdstippen van week 4 en 7 à 8, maar er werd géén effect waargenomen op de kropgrootte of op indicatoren van het jodiummetabolisme.

In een vergelijkbaar onderzoek naar de invloed van vitamine A supplementatie op de behandeling van anemie had een dosering met ijzer en foliumzuur een significante toename tot gevolg in de bloedwaarden voor hemoglobine, hematokriet, aantal rode bloedcellen, serum ijzer, transferrineverzadiging, ferritine en gemiddelde hemoglobineconcentratie per bloedcel terwijl de niveaus van totale ijzerbindingscapaciteit en transferrine na 4 en 7 à 8 weken significant gedaald waren. Alleen de stijging in het aantal rode bloedcellen en de daling in het gemiddeld bloedcelvolume waren significant groter in de proefpersonen die vitamine A hadden ontvangen.

In het Gurage gebied van centraal Ethiopië werden de verbouw, oogst, opbrengst en bewerking van ensete bestudeerd bij 60 huishoudens uit 6 dorpen. Ensete wordt vegetatief vermeerderd. Het heeft een groeicyclus van 6 jaar en wordt tijdens deze periode 3 tot 4 keer overgeplant. De opbrengst (in de vorm van "ko'cho", een plat brood) was 9,5 ton/ha/jr (6,1 $MJ/m^2/jr$). Met uitzondering van cassave is de energieopbrengst van ensete hoger dan die van enig ander voedselgewas in Ethiopië terwijl de eiwitobrengst (11,4 $g/m^2/jr$) hoger is dan van enig ander gewas behalve bananen en aardappelen, ondanks de erg lage eiwitdichtheid (12 g/kg).

De zetmeelrijke pulp uit de pseudo-stam en het rizoom wordt gefermenteerd en dit kan in de aarde worden bewaard voor een periode van 5 tot 7 jaar. Daarna kan ensete worden bereid voor consumptie op verschillende manieren die in detail werden bestudeerd. De gemiddelde enseteconsumptie was 0,55 kg/dag hetgeen overeenkwam met met 68% van de energie-, 20% van de eiwit- en 28% van de ijzeropname. Ensete bevat geen vitamine A. Met een opname van slechts 60% van de aanbevolen hoeveelheden was de totale energieconsumptie zéér laag in Gurage.

CURRICULUM VITAE

Zewdie Wolde-Gebriel was born on 31 August 1945 in Debre Sina, Shoa Region, Ethiopia and attended elementary school in Debre Sina and high school in Debre Berhan. He joined Gondar Public Health College in 1963 and graduated as Health Officer in June 1967. After serving the Ministry of Health as Health Officer-in-Charge in Were-Illu and Dabat health centres in the period 1967-70, he joined the Debarek Nutrition Project (1970-72) and served as Health Officer-in-Charge of clinical services and clinical research.

Zewdie studied nutrition (1972-73) at Queen Elizabeth College, University of London and after obtaining his MSc degree, was employed by the Ethiopian Nutrition Institute where he served as Field Team Leader (1973-75), Head of Medical Department (1975-79) and Director (1979-87). From October 1987 until April 1992, he carried out the work described in this thesis with the field work being carried out in Ethiopia and the preparatory and final phases being undertaken in the Department of Human Nutrition of Wageningen Agricultural University.