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Nutritional Blindness

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Abstract
It is a tragic fact that in large areas of the world today despite the continuing advances in medical science many thousands of people, the majority young children, are going blind every year as a result of malnutrition. As will become apparent as this subject unfolds, we know enough about the ways in which deficiency of vitamin A and vitamins of the B complex destroy vision to be in a position to prevent much of the needless suffering. It will also be shown that there are important areas in this field where we are still ignorant, especially of the long term effects of malnutrition acting very early in life on certain parts of the eye.

Due not only to lack of time but also to the dearth of reliable data and information upon which to base an appraisal I shall not deal with certain aspects of this subject. For example, we do not yet know whether or not malnutrition plays any part in the disease process of trachoma or in the development of pterygium. We are also ignorant of the importance of an underlying deficiency of nutrients in making the conjunctiva and cornea more susceptible to infectious processes.

Leaving such speculations strictly aside my purpose is to summarize present knowledge of certain nutritional eye conditions and also perhaps to enlarge the horizon of your thinking by introducing you to some fresh problems and new concepts.

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NUTRITIONAL BLINDNESS

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It is a tragic fact that in large areas of the world today despite the continuing advances in medical science many thousands of people, the majority young children, are going blind every year as a result of malnutrition. As will become apparent as this subject unfolds, we know enough about the ways in which deficiency of vitamin A and vitamins of the B complex destroy vision to be in a position to prevent much of the needless suffering. It will also be shown that there are important areas in this field where we are still ignorant, especially of the long term effects of malnutrition acting very early in life on certain parts of the eye.

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1 *VITAMIN A*

Undoubtedly deficiency of Vitamin A with its outstanding spectrum of eye signs ranging from night blindness and xerosis conjunctivae to xerophthalmia and keratomalacia merits pride of place in our consideration. I have no hesitation in saying that in terms of numbers affected and damage done this is still the Number One vitamin deficiency disease in the world.

(a) *Extent.* Although occurring all over Europe and North America until about the beginning of this century, it has been in the highly populous technically underdeveloped countries of the world that it has taken its heaviest toll. The records of one eye hospital in Indonesia over the past 15 years show no less than 10,000 cases of xerophthalmia. Throughout the whole of Asia, Latin America and in certain parts of Africa Vitamin A deficiency is a continuing problem.

(b) *Effects.* Blindness, frequently total, occurs mainly in very young children and more frequently in boys than in girls. The true nature of the condition is frequently not recognised by the doctor and even if recognised sight has often already been destroyed when the patient is first seen. This is all

the more tragic because of the excellent preventive and early curative effects of good sources of Vitamin A or carotene. As the most severely affected are children those that survive constitute a problem for the community over many years.

A second important effect of Vitamin A deficiency is the threat it presents to life itself. In the laboratory many young deficient animals die before they ever develop xerophthalmia. Although, with the remedy to hand, we cannot study this point in man there seems no reason to doubt from the severity of the general condition of these children that many untreated cases do not survive. Thus Vitamin A deficiency is one of the few, and easily the most important, of the diseases that kill as well as blind. I have previously described the anterior segment changes which occur in Vitamin A deficiency.[1] Fig. 1 shows what I call "xerophthalmia" being the same as "xerosis conjunctivae et corneae." The bulbar conjunctivae of this 18 month old Gogo baby of Central Tanganyika were markedly dry and wrinkled and the corneae were hazy, the stroma infiltrated but there was no loss of integrity of the cornea. In Fig 2 we see commencing keratomalacia in a baby of the same age from the same area, where the cornea is heavily vascularized and as a whole is beginning to undergo liquefaction or colliquative necrosis characteristic of this condition. In certain parts of the world[2] keratomalacia is a frequent accompaniment of protein malnutrition or Kwashiorkor, and Fig. 3 shows this in a two year old boy in Guatemala.

Besides being a public health problem of the first magnitude Vitamin A deficiency also poses a number of problems of great interest and importance and requiring more research. These may be mentioned here without any attempt being made to elaborate on these subjects.

1. The function of Vitamin A at the cellular level, outside the retina is still not known. Recent work of Wald, who has contributed so much to our knowledge of the biochemical basis of vision, and his associates[3] may have provided the key to unlock this door. From detailed studies of the development of Vitamin A deficiency in the rat they have postulated that, as in the retina so also elsewhere, Vitamin A may be necessary to act as a stabiliser of protein.

2. Undoubtedly Vitamin A is linked with protein in many aspects of its metabolism and the part which protein deficiency may play in affecting the development and severity of xerophthalmia is still not clear, although probably a minor one.[4]

Many points about the epidemiology of Vitamin A deficiency are still far from clear. For instance it was found that there was a high incidence of keratomalacia in Orijas as compared with Khonds in a series of cases treated in India despite the fact that Khonds much more frequently attended the hospital. Dietary inquiry and other data failed to provide an explanation but differing tribal customs concerning the resumption of sexual intercourse after parturition did. A social anthropologist would find a very fruitful field here in which to work.

4. There is no reliable means of detecting Vitamin A deficiency in any but its most devastating late stages in the most susceptible age group, the young child of 6 months—3-4 years. Plasma Vitamin A levels are not of value for early detection and dark adaptation studies require co-operation. The development of such a test would be invaluable in field studies and public health work.

5. That the presence of Bitot's spots indicates Vitamin A deficiency has been copied from textbook to textbook until it has become axiomatic. However there have always been those who found no response of these lesions to even prolonged Vitamin A therapy and more recently it has been shown[5] that

they are not always accompanied by impaired dark adaptation nor are the serum Vitamin A levels lower than in controls. Vitamin A deficiency would seem to be only one, of perhaps a number, of possible causes.

6. Reversible structural changes have, from time to time, been reported in the human fundus in Vitamin A deficiency[6, 7, 8] and it has been suggested, without any real evidence that some of the choroido-retinal changes in onchocerciasis may in part be due to lack of Vitamin A.

2. *THE VITAMIN B COMPLEX*

I propose to deal briefly with three main eye conditions in this section. They are (1) the retrobubar neuritis resulting in nutritional amblyopia; (2) corneal epithelial dystrophy, and (3) corneal neovascularization.

(1) *Nutritional amblyopia*

This condition has been known and described for nearly 100 years but we are today very little nearer to an understanding of its nature. This is not surprising in view of the fact that the literature on the subject consists largely of reviews of the present literature and descriptions of clinical signs and and dietary response of a few more cases. Most Japanese authors have associated amblyopia with beriberi and there are numerous accounts of pellagra in which it is included in the symptomatology. Thousands of cases occurred in the Far East prisoner of war camps, during World War II. Certain parts of the West Indies, [9, 10] West Africa [11, 12] and part of Japan [13] are endemic foci of the condition at the present time although it is probable that it occurs in many other areas but lack of specialized facilities may prevent its recognition.

Clinical features. Young adults are usually affected although there is one report of an outbreak in children.[14] Almost invariably the amblyopia is but part of a widespread neuropathy. The ocular findings consist of impairment of central vision and the presence of roughly symmetrical central, para-central or centro-cecal scotomata larger for red than for white test objects with intact peripheral fields. Commonly there is slight pallor of the temporal portion of the discs. In the few cases examined histologically[15] the degeneration of myelinated fibers was restricted to the zone of the papillomacular bundle. Thus clinically and pathologically nutritional amblyopia appears to be identical with tobacco-alcohol amblyopia[16] and distinct from those of proven toxic origin in such as methyl alcohol and quinine. Although there is general agreement that a deficiency of Vitamin B complex is involved some favor thiamine[17] others riboflavin[18] and others more recently Vitamin B_{12}[19] in the treatment of these identical conditions. In East Africa the writer[20] has had dramatic improvement in three cases previously refractory to thiamine and riboflavin therapy in response to Vitamin B_{12}.

It may reasonably be predicted that nutritional amblyopia will become of increasing importance and show a large apparent, if not actual, increase as more and more people demand a higher degree of visual acuity for reading and for precision work in industry.

(2) *Corneal Epithelial Dystrophy*

This name was first given to a form of punctate keratitis by Metivier[9] in Trinidad frequently complicating a generalized Vitamin B complex deficiency state. Without knowledge of this report similar changes were found in many prisoners of war in the Far East and it was suggested that they were identical. Nanagos[21] in the Philippines also claimed good response with B-complex therapy. However many accounts of nutritional amblyopia made no reference

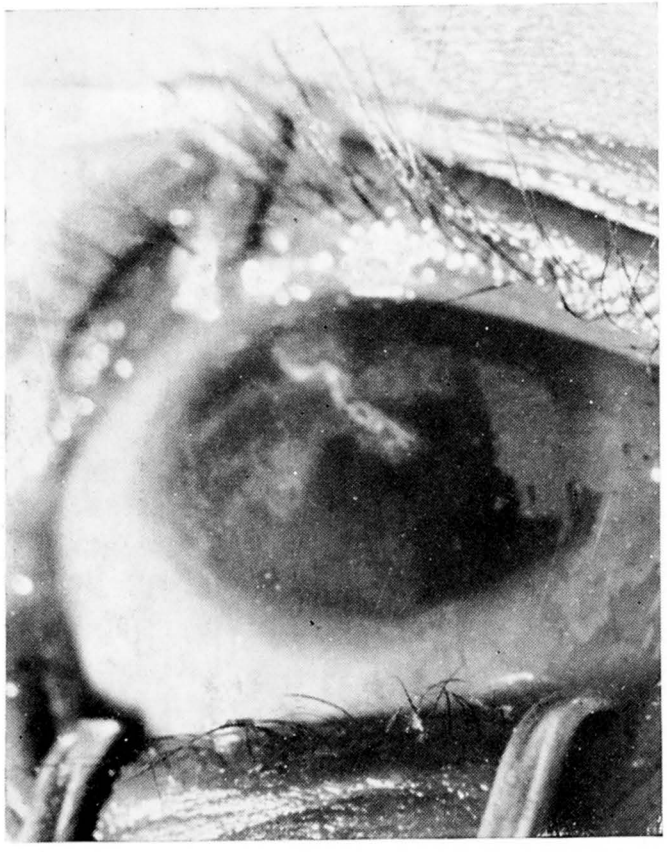

Fig. 1. "*Xerosis Cunjunctivae et Corneae.*" The eye of a young Gogo baby.

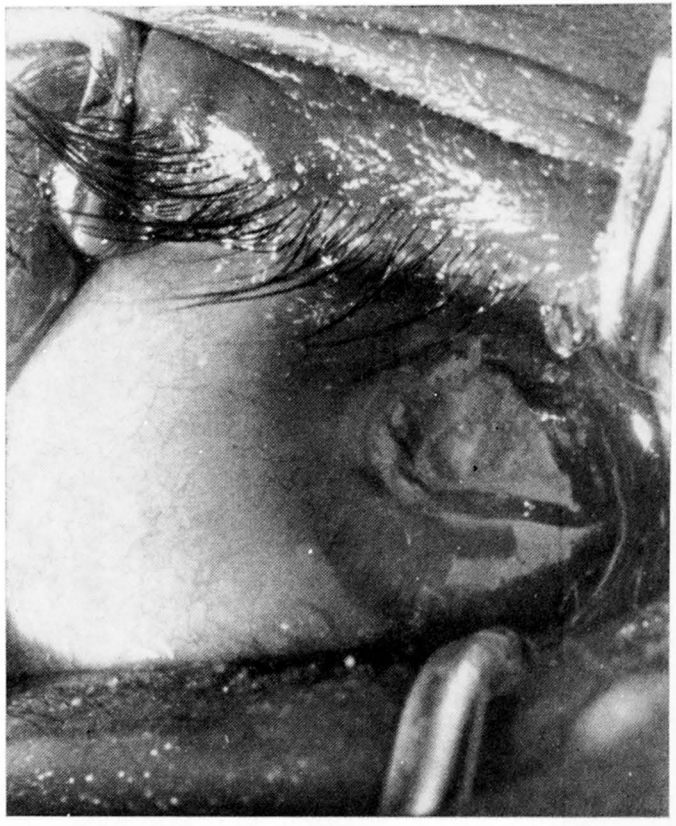

Fig. 2. "*Keratomalacia.*" The eye of a young Gogo baby showing marked corneal vascularisation and commencing colliquative necrosis of the whole cornea.

to corneal involvement. It is now known that there is a wide variety of kerato-conjunctivitides in the tropics, mostly of virus origin and in Tanganyika the writer found as many as one third of all African hospital patients admitted for other than eye diseases had active punctate keratitis or inactive scars. In the absence of better evidence for a nutritional etiology it would seem to be advisable not to regard this as a separate entity. In the writer's view the most likely explanation is that the epithelial and subepithelial changes of superficial punctate keratitis are of varied etiology and are enhanced by deficiency of B vitamins although this at present is purely speculative.

3. *Nutritional Corneal Vascularization*

Invasion of the corneal substance by capillary loops from the limbus has accompanied a variety of deficiency states in experimental animals but as far as we know is limited in man to that seen late in xerophthalmia and that attributed to ribo-flavin deficiency. The first description of ocular hyporiboflavinosis[22] occurring in pellagrous patients included inflammatory factors which suggest that there was complicating infection. There is no reason to doubt that the corneal vascularization at least responded to riboflavin. Although the muco-cutaneous lesions of riboflavin deficiency frequently accompany pellagra corneal vascularization is an unusual feature and it rarely, if ever, occurred in prisoners of war with nutritional amblyopia. Pellagra is a multiple deficiency state and the diet which caused it in the Southern United States was quite different from the pellagragenic diet in other parts of the world. In East Africa the writer has failed to find a single case of pellagra with corneal vascularization nor does it accompany angular stomatitis, perleche and magenta tongue. Several riboflavin deficiency trials in man have failed to produce corneal vascularization. In summary it would seem that, although riboflavin deficiency may in man occasionally produce corneal vascularization as in experimental animals, this is rather uncommon.

3. *Discrete Colliquative Keratopathy*

I have applied[20] this descriptive but rather cumbersome name to a fascinating condition of the cornea first described in malnourished South African Bantu children by Blumenthal.[23] As far as I know it has not been reported outside Africa. I did not see it during my 5 years in India and in other Asian and Central American countries. I have shown pictures of the disease (Fig. 6) but ophthalmologists there have not recognized it. To my mind this casts serious doubt on a purely nutritional theory of etiology and in my experience in East Africa it seems to have a distinct seasonal incidence; all my cases have occurred during the rainy season October - May. The essential process here is a quiet dissolving away of the cornea confined to a small area usually about 5 or 7 o'clock with a striking absence of accompanying symptoms or history of trauma. The rest of the cornea appears grossly normal but under the slit-lamp there is usually minimal vascularization. Iris prolapse follows corneal softening and may be asymptomatic. Some of the examples I have seen have been in children admitted to hospital for other conditions and in whom the iris prolapse has passed unnoticed by the medical staff. More than once I have heard of mothers bringing their children to the doctor and asking him to remove the " black speck " from the front of the eye i.e. the prolapsed iris, showing that frequently mothers are more observant of their children's welfare than those who attend them medically. There is no clear response to vitamin therapy or protein feeding and in this respect and by its nature discrete colliquative keratopathy is to be distinguished from keratomalacia. The

prolapse may be abscissed but is probably best left alone and healing with leucoma adherens is the inevitable end result.

4. *Cataract*

Several nutritional deficiencies, including riboflavin, certain amino acids and protein[24] are known to result in cataract in experimental animals. Other preliminary work[25] which, because of the exceedingly critical nature of the experimental condition, it has so far not been able to repeat suggest that prolonged protein deficiency in the mother rat may lead to congenital cataract and defects involving connective tissue and ground substance elsewhere in the eye. This work suggested that the cataractous process in the human lens might possibly be speeded up as a result of nutritional deficiency in early life.

In many countries where malnutrition is rife so-called "Senile" cataract is very common and appears to occur at a significantly earlier stage than elsewhere. Unfortunately these statements have as their basis only the experience and impressions of practitioners as no really objective study has been made. However the evidence is very considerable and is all consistent with these views. It has been shown[26] in Tanganyika that by the age of 7 years or so the large majority of African children already have minimal cuneiform water-cleft opacities in the extreme periphery of the lens. Children of the Indian community in East Africa also have these opacities but they were not found in a group of 100 European children of the same age many of whom had spent most of their life in Africa. These opacities appear to increase in number, intensity and size with age developing over the years into intumescent and mature cataract in many of those living until late middle age and old age. It is not known yet, of course, whether malnutrition is really playing any part in this process. If it is then it is probably acting very early in life. It has been possible to examine a few children known to have survived severe marasmus or kwashiorkor and they do not show grosser changes than most for their age. It may well be that the responsible factor is acting even earlier on probably in the first few months of intra-uterine life when the lens along with the rest of the eye and the nervous system is growing and differentiating more rapidly than other tissues and might be regarded to be especially susceptible to nutritional, as it is to other insults.

5. *Refraction*

From time to time the possible role of dietary deficiency in the aetiology of myopia and other errors of refraction has been mooted, usually wildly speculative in nature and without any real evidence. It must be admitted that the idea in itself is not in any way outlandish for it is known that the overall refraction of the eye is dependent upon the growth and development of the various parts of the eye. Nutritional deficiency occurring in the early formative months might reasonably be expected to adversely affect the growth of these tissues and also the organizing power which the retina appears to possess over this process.

In the Central Province of Tanganyika periods of severe food shortage have occurred several times during the past one hundred years and thousands of Gogo tribes people are reckoned to have died from starvation during the most recent famine in 1953-4. With the object of seeing whether the refractive state of young children who had survived this famine was adversely affected nearly one thousand children in the area were refracted and the results compared with data for African and Indian children in non-famine areas. When analysed the data for the famine area children showed very marked abnormalities in three main respects. (1) The spread of mean refraction values in the

range of the aberrations of emmetropia was much greater than normal. In the non-famine area data there were no representatives higher than +1.5 and −2.5 D whereas in the famine area data values occurred out to the limits of + and −4.0 D. (2) Beyond the limits of emmetropia and its aberrations, that is to say axial ametropia, there were 27.5 times as many representatives for the famine area data, the majority of these being high myopia. (3) When the data were analysed for the incidence of mixed astigmatism and anisometropia of a degree of 1.0 D and more it was found that these conditions were both present 5-7 times more commonly in the famine area.

Here again, in conclusion, we cannot yet say whether malnutrition really is involved or not, although it may well be. Even assuming the cause to be malnutrition there are many possibilities as to its precise nature. The importance of Vitamin A in the retina for scotopic vision is well known and it might well be important much earlier in life. Although there is a continuing xerophthalmia and keratomalacia problem in infants of that area I know of no report of such gross refractive errors from any other part of the world where this is is severe deficiency of Vitamin A. At present I would rather favour total inanition of starvation as being responsible. However, this is a good note upon which to end, calling attention to our great ignorance and the need for much more work in this important but hitherto largely neglected "no man's land."

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