Field guide to the detection and control of xerophthalmia

A. SOMMER

World Health Organization

The World Health Organization is a specialized agency of the United Nations with primary responsibility for international health matters and public health. Through this organization, which was created in 1948, the health professions of some 150 countries exchange their knowledge and experience with the aim of achieving the highest possible level of health throughout the world.

By means of direct technical cooperation with its Member States, and by stimulating such cooperation among them, WHO promotes the development of comprehensive health services, the prevention and control of diseases, the improvement of environment conditions, the development of health manpower, the coordination and development of biomedical and health services research, and the planning and implementation of health programmes.

These broad fields of endeavour encompass a wide variety of activites, such as developing systems of primary health care that reach the whole population of Member countries ; promoting the health of mothers and children ; combating malnutrition ; eradicating smallpox throughout the world ; controlling malaria and other communicable diseases including tuberculosis and leprosy ; promoting mass immunization campaigns against a number of preventable diseases ; improving mental health ; providing safe water supplies ; and training health personnel of all categories.

Progress towards better health throughout the world also demands international cooperation in such matters as establishing international standards for biological substances, pesticides and pharmaceuticals ; recommending international nonproprietary names for drugs ; administering the International Health Regulations ; revising the international classification of diseases and causes of death ; and collecting and disseminating health statistical information.

Further information on many aspects of WHO's work is presented in the Organization's publications.

FIELD GUIDE TO THE DETECTION AND CONTROL OF XEROPHTHALMIA

ALFRED SOMMER

Principal Investigator
Helen Keller International
Indonesian Nutritional Blindness Prevention Project

Visiting Professor of Ophthalmology
University of Padjadjaran
Bandung, Indonesia

WORLD HEALTH ORGANIZATION
GENEVA
1978

The publication of this guide was made possible through a grant to Helen Keller International, 22 West 17th Street, New York 10011, from the United States Agency for International Development (USAID).

ISBN 92 4 154 127 X

PRINTED IN SWITZERLAND

CONTENTS

PREFACE

XEROPHTHALMIA *remains an important cause of childhood blindness in developing countries, accounting for 20 000–100 000 new cases annually. Recognizing the gravity of the situation, the Twenty-Fifth World Health Assembly in 1972 urged an intensification of activities to prevent needless loss of sight, identifying xerophthalmia as one of the three most important causes of preventable blindness in the world today. Various agencies and governments have since expressed the need for a simple, practical field guide for clinicians, nurses, and public health officials involved in the diagnosis, treatment, and prevention of this appalling disease. This manual attempts to fill that need.*

Much of the material is drawn from recent meetings and discussions which have already resulted in two useful publications: Vitamin A Deficiency and Xerophthalmia,[1] *a comprehensive discussion of the problem, and* Guidelines for the Eradication of Vitamin A Deficiency and Xerophthalmia,[2] *a detailed description of assessment, prevention, and evaluation procedures.*

[1] WHO Technical Report Series, No. 590, 1976 (*Vitamin A deficiency and xerophthalmia.* Report of a joint WHO/USAID meeting).

[2] INTERNATIONAL VITAMIN A CONSULTATIVE GROUP (IVACG). *Guidelines for the eradication of vitamin A deficiency and xerophthalmia*, New York, The Nutrition Foundation, 1975.

INTRODUCTION

XEROPHTHALMIA has been recognized for thousands of years, and the ancient Egyptians appropriately prescribed liver as a cure. As recently as the late nineteenth and early twentieth centuries numerous cases still occurred among malnourished individuals in such widely scattered points of the globe as Brazil, China, England, Japan, and Russia.

Today the precise size and geographical distribution of the xerophthalmia problem are unknown. In recent years, the disease has been reported mainly from the rice-eating areas of South Asia, but it also occurs in Africa, Latin America, the Caribbean, and the Eastern Mediterranean.

Modern ideas about the disease date from Bloch's observations [1] that children raised in Danish orphanages on diets deficient in milk and milk products developed severe generalized malnutrition and xerophthalmia, while children raised in otherwise identical fashion, but fed dairy products, did not. He reasoned that dairy products contained a fat-soluble element essential to normal growth and ocular health and correctly equated it with vitamin A.

By the 1930s, histopathological observations by Wolbach and others [2] had demonstrated that the primary role of vitamin A was the maintenance of normal epithelial integrity. The exact mechanism involved is, however, still obscure.

[1] BLOCH, C. E. *J. Hyg.*, **19**: 283 (1921); *Am. J. Dis. Child.*, **27**: 139 (1924); *Am. J. Dis. Child.*, **28**: 659 (1924).

[2] WOLBACH, S. B. & HOWE, P. R. *J. exp. Med.*, **47**: 753 (1925); *Arch. Pathol. Lab. Med.*, **5**: 239 (1928).

VITAMIN A METABOLISM

VITAMIN A, or retinol, is a fat-soluble substance found in liver, particularly fish liver, and in poultry, meat, and dairy products. Carotenes—potential precursors present in green leafy vegetables, red palm oil, yellow fruits, and the like—can be converted to retinol in the wall of the gut. The relative biological values of these various substances were formerly expressed in international units (IU) of vitamin A activity,[1] 1 IU being equivalent to 0.3 μg of retinol, 0.55 μg of retinol palmitate, 0.6 μg of β-carotene, and 1.2 μg of other provitamin A carotenoids. Not only are carotenes biologically less active than retinol, but their dietary sources are less efficiently processed and absorbed from the gut. One must therefore ingest six times as much β-carotene (by weight) as retinol for a similar degree of effect.

Some 50–90 % of ingested retinol is absorbed in the small intestine and transported, in association with chylomicra, to the liver where it is stored primarily as retinol palmitate. When needed, it is released into the bloodstream in combination with retinol-binding protein (RBP), a specific carrier protein elaborated by the liver. The retinol is then removed from the serum and utilized by epithelial cells throughout the body. The diagram overleaf gives a simplified schematic outline of these metabolic pathways.

The liver stores form an important buffer for variations in vitamin A and β-carotene intake. When vitamin A intake surpasses 300–1200 μg/day of retinol, or its equivalent, the excess is stored and liver reserves are increased. When vitamin A intake is less than this amount, liver stores are drained to maintain serum retinol (vitamin A) at a normal level (above 200 μg/l or 0.7 μmol/l). When intake remains low for prolonged periods of time the liver stores become depleted, serum retinol levels drop, epithelial function is impaired, and xerophthalmia appears. The duration of inadequate intake required for this to occur depends upon the amount of vitamin A (or precursor) ingested, the extent of pre-existing liver stores, and the rate at which vitamin A is being utilized by the body.

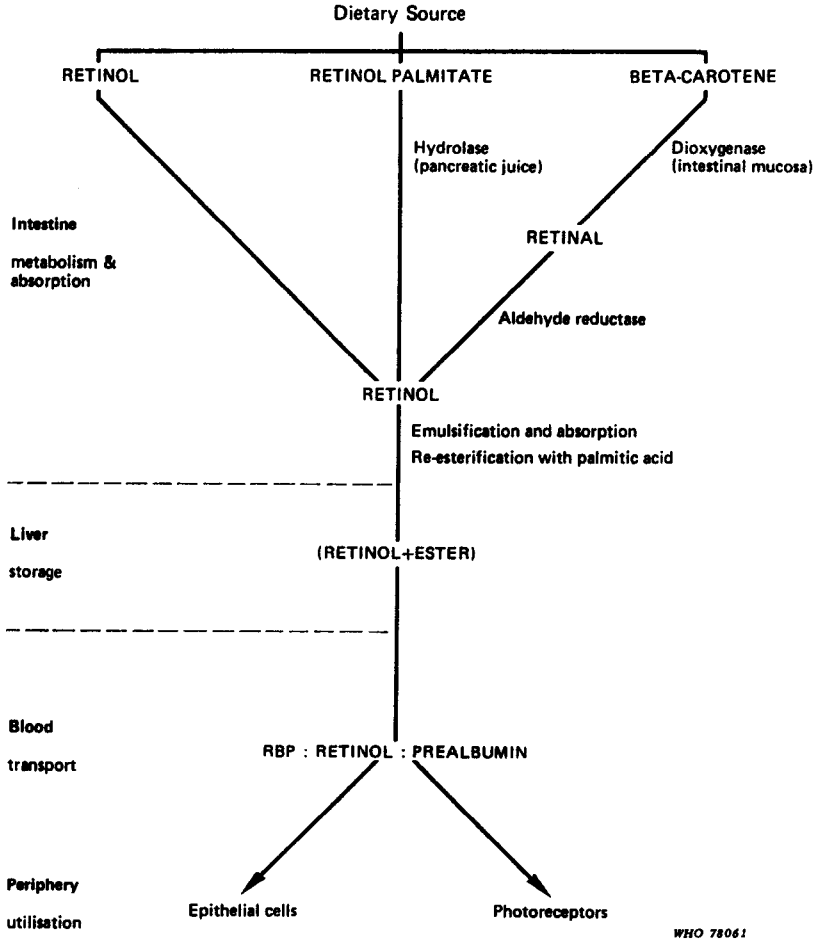
A child with borderline, marginal intake to begin with will have very limited stores. Any sudden drop in intake, either from a change in diet

[1] The International units for vitamin A and provitamin A were discontinued in 1954 and 1956 respectively. However, since their use persists, particularly in the labelling of capsules and injectable preparations, all intakes and dosages mentioned in this book are expressed both in micrograms (μg) or milligrams (mg) and in the former international units.

or interference with absorption (as in gastroenteritis) or a sudden increase in metabolic demand (febrile state or growth spurt), will quickly deplete the limited reserves and may precipitate frank corneal destruction, even in eyes that had previously appeared entirely normal. Where liver stores have been very high, however, an individual may go for months without vitamin A and not suffer serious consequences.

The availability of stored vitamin A will also depend upon the child's general nutritional status. Severely malnourished, protein-deficient children synthesize RBP at a much reduced rate. Serum retinol levels will therefore be subnormal, even if liver stores are high. Finally, a diseased liver cannot store as much vitamin, or make as much RBP, as a normal one.

SCHEMA OF VITAMIN A METABOLISM



CLINICAL CLASSIFICATION AND DIAGNOSIS

VITAMIN A deficiency is a systemic disease affecting epithelial structures in a variety of organs, the eye being the most obvious and dramatic example. Keratinizing metaplasia of the respiratory and intestinal epithelia is thought to be responsible for the pulmonary and gastrointestinal symptoms found in the most severely affected children. But the classic clinical expression, present in mild to severe form, is xerophthalmia, or "dry eye".

Fig. 1 indicates the principal sites at which xerophthalmia lesions occur. With proper treatment, alterations in the retina (night blindness) and conjunctiva (xerosis and Bitot's spots) usually clear without significant sequelae. But corneal involvement (xerosis, ulcers, and keratomalacia), presented diagrammatically in Fig. 2, usually results in some degree of opacification and loss of vision, and all too often in blindness. Proper treatment, however, may still limit the extent of corneal damage, or prevent it entirely in the opposite eye if it is not yet affected.

The major xerophthalmia signs have recently been reclassified (Table 1). X1A (conjunctival xerosis) through X3B (keratomalacia) and XN (night blindness) all indicate active xerophthalmia and vitamin A deficiency requiring immediate therapy.

X1A, IB. Conjunctival xerosis and Bitot's spots

Alterations in epithelial architecture accompanying vitamin A deficiency are termed "keratinizing metaplasia". The epithelium of the

Table 1. Classification of xerophthalmia

Primary signs	
X1A	Conjunctival xerosis
X1B	Bitot's spot with conjunctival xerosis
X2	Corneal xerosis
X3A	Corneal ulceration with xerosis
X3B	Keratomalacia
Secondary signs	
XN	Night blindness
XF	Xerophthalmia fundus
XS	Corneal scar

conjunctiva is transformed from the normal columnar to the stratified squamous type, with a resultant loss of goblet cells, formation of a granular cell layer (Fig. 3), and keratinization of the surface (Fig. 4). This is the histopathological picture of conjunctival xerosis.

Clinically, these changes are expressed as marked dryness or unwettability, the affected area appearing roughened rather than smooth and glistening. Tears, which may be plentiful, form distinct droplets, leaving the affected areas uncovered.

The entire surface of the bulbar conjunctiva may be affected. More commonly, the changes are limited to one or more patches, usually at the temporal or, less frequently, nasal limbus. The condition is almost always bilateral.

Fig. 5 and Fig. 6 depict temporal patches of conjunctival xerosis. The rest of the conjunctiva is clear and glistening, as is the cornea.

When covered by a fine foamy or cheesy material these temporal and nasal patches are known as Bitot's spots. Small to large foamy spots, some heavily pigmented, are illustrated in Fig. 7–11. The foamy material is easily wiped off, the amount present often varying from day to day. Cheese-like accretions (Fig. 12 and Fig. 13) are more tenacious, usually occurring in longer-standing disease.

Chronic vitamin A deficiency may lead to thickened plaques that persist long after the vitamin A status has returned to normal; diagnosis can only be made retrospectively, after they have failed to respond to adequate vitamin A therapy. Although they usually lack areas of true xerosis, irregular ridges and troughs may break up the light reflex and appear to be dry and non-wettable. Closer examination will usually reveal that the conjunctiva covering the narrow ridges is, in fact, "moist" and glistening.

Bitot's spots should not be confused with pinguecula or pterygium, which are more often nasal than temporal, and limited, for the most part, to adults. Pinguecula is an elevated fatty, yellowish lesion. Pterygium is fleshy and actually invades the cornea (Fig. 14).

Fig. 15 and Fig. 16 demonstrate marked, widespread conjunctival xerosis. The entire conjunctiva appears dry, roughened, and corrugated, almost skin-like. Prominent conjunctival thickening and folds are also present, but are not sufficient in themselves for diagnosis. This is an advanced lesion, frequently accompanied, as in these instances, by corneal xerosis.

X2. Corneal xerosis

Keratinizing metaplasia of the cornea is far more dangerous. Instead of being smooth, clear, and glistening, the corneal surface has a hazy, dry, roughened, often pebbly appearance, usually most marked in the

lower part. Fig. 16 and Fig. 17 illustrate early corneal haze, and Fig. 15, Fig. 18, and Fig. 19 a dry pebbly surface, demonstrated by the diffuse breakup of the light reflex. Occasionally, a tough foam-like substance may be seen tightly adhering to it (Fig. 20).

The epithelium may already be lost (erosion), but the cornea has not yet suffered permanent alteration. Prompt therapy can still restore its normal appearance.

X3A. Corneal ulceration with xerosis

Ulceration indicates destruction of the underlying stroma and results in permanent structural alteration of the cornea. When ulcers are still superficial (Fig. 21), prompt therapy may produce rapid healing with minimal residual opacification and little or no interference with vision. But deeper ulcers often perforate, resulting in iris prolapse, dense opacification (adherent leucoma), and significant reduction in visual acuity.

X3B. Keratomalacia

The most serious and least understood alteration is keratomalacia, a rapidly destructive liquefactive necrosis of the cornea, commonly resulting in perforation, extrusion of intraocular contents, and loss of the eye. Fig. 22–24 are examples of keratomalacia involving the entire cornea. In the last two, brown iris tissue is forcing its way through softened, necrotic peripheral cornea. Fig. 25 illustrates a localized area of keratomalacia, and Fig. 26, taken one month later (after treatment), shows how it has healed, leaving an adherent leucoma.

Characteristically, eyes with active corneal involvement related to vitamin A deficiency (X2, X3) are relatively "white and quiet", in sharp contrast to the red swollen lids, injected conjunctiva, and purulent discharge seen in cases of bacterial, fungal, and viral conjunctivitis and keratitis (Fig. 27). This important difference is useful in distinguishing between the two conditions. Occasionally lesions related to vitamin A deficiency become secondarily infected, in which case the accompanying malnutrition, systemic illness, and evidence of conjunctival xerosis are useful in arriving at the correct diagnosis. However, in some instances of precipitous deterioration of vitamin A status—usually brought on by measles or gastroenteritis in a child already suffering from protein-energy malnutrition—corneal involvement can precede the appearance of typical conjunctival changes.

XS. Scars

Healed sequelae of prior corneal disease related to vitamin A deficiency include opacities or scars of varying density (nebula, macula,

leucoma) as in Fig. 26, weakening and outpouching of the remaining corneal layers (staphyloma as in Fig. 28, and descemetocele as in Fig. 29) and, where loss of intraocular contents had occurred, phthisis bulbi, a scarred shrunken globe. Such end-stage lesions are not specific for xerophthalmia and may arise from numerous other conditions, notably trauma and infection.

XN. Night blindness

Retinol is essential for the elaboration of rhodopsin ("visual purple") by the rods, the sensory receptors of the retina responsible for vision under low levels of illumination. Vitamin A deficiency can interfere with rhodopsin production, impair rod function, and result in night blindness.

Night blindness of recent onset in a preschool child is practically pathognomonic of vitamin A deficiency and is frequently accompanied by conjunctival xerosis and Bitot's spots. Other causes of night blindness are relatively rare and almost never present in this fashion. Mothers are usually quick to recognize the problem, though not its cause. The children no longer move about the house or village after dusk, but prefer to sit in a secure corner, often unable to find their food or toys. In some cultures specific terms exist to describe this condition, such as "chicken eyes".

The diagnosis is usually made from the mother's history. Objective evaluation, comparing the response of the affected child with those of his normal peers after sunset or in a darkened room, is both impractical and unnecessary in most routine clinical situations.

XF. Xerophthalmia fundus

The small white retinal lesions described in some cases of vitamin A deficiency are at present of investigational interest only (Fig. 30).

All children suspected, or at risk, of having xerophthalmia must have *both* eyes examined in open shade or with the aid of a flashlight and loupe, if available. Unfortunately, because of the pain and reflex blepharospasm accompanying corneal involvement, these children tend to keep their eyes tightly shut. When necessary, the child's head can be stabilized by a parent or attendant, while a *physician* carefully separates the lids with a sterile Desmarres retractor, lid speculum, or bent paper-clip (as seen in most of the illustrations). The leading edge of the clip should be held parallel to the lid. Once it has passed behind the lid margin it should be gently angled forward, to avoid abrading the cornea or placing undue pressure on the globe.

EPIDEMIOLOGY

XEROPHTHALMIA results from an insufficient supply of vitamin A to the eye. The cause of such a deficiency can be quite complex, and depends upon the type and amount of vitamin and provitamin (primarily β-carotene) ingested, the absorptive, transport, and storage capacities of the individual, and his metabolic needs. Seemingly unrelated disease states can dramatically alter each of these parameters and, in turn, the child's vitamin A balance. For example, gastroenteritis will change the types and amounts of food offered to the child and his appetite, while the shortened transit time will decrease absorption of what vitamin A is ingested. If he is already protein-deficient, transport and storage may be decreased and the fever will increase his metabolic needs.

The cause and contribution of each of these factors will vary from one community to another, resulting in different epidemiological patterns in respect of age, sex, season, magnitude, and relative proportion of cases with and without corneal involvement.

A general pattern, however, seems to exist. Vitamin A deficiency can occur at any age, but clinical xerophthalmia is predominantly a disease of young children. The prevalence of milder manifestations (night blindness, Bitot's spots, and conjunctival xerosis) usually increases from the age of about 2 years up to the early school years. In some areas males are more commonly affected than females. Malnutrition, if present, is usually mild. These signs may persist for months, tend to be seasonal, and usually disappear spontaneously, probably with increased availability and consumption of foods containing vitamin A (and carotene). They probably represent relatively mild, isolated vitamin A deficiency and do little lasting damage, but they identify children at increased risk of developing destructive corneal lesions.

Children suffering from forms of the disease destructive to the cornea are usually younger (often less than 1 year of age), more severely malnourished, and more deficient in vitamin A. History of a recent precipitating event (pneumonia, measles, gastroenteritis, tuberculosis, etc.) is