Saudi Journal of Medicine and Public Health

https://saudijmph.com/index.php/pub

https://doi.org/10.64483/202412322

Vitamin A Deficiency: Diagnosis, Management, and Nutritional Therapy

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Abstract

Background: Vitamin A is an essential fat-soluble micronutrient critical for vision, immune function, epithelial integrity, and cellular differentiation. Deficiency remains a major global health issue, particularly in resource-limited settings, where it contributes significantly to childhood morbidity and mortality.

Aim: To review the diagnosis, management, and nutritional strategies for vitamin A deficiency (VAD), emphasizing its etiology, epidemiology, pathophysiology, and clinical implications.

Methods: This narrative review synthesizes evidence from global health guidelines, epidemiological studies, and clinical research on VAD. It explores biological mechanisms, risk factors, diagnostic approaches, and therapeutic interventions, including supplementation protocols and preventive strategies.

Results: VAD predominantly affects children under five and pregnant or lactating women in developing countries, with prevalence rates reaching 30% in children and up to 76% in lactating mothers. Clinical manifestations range from night blindness to xerophthalmia and keratomalacia, often accompanied by increased infection risk. Serum retinol <20 µg/dL is a key diagnostic marker, though interpretation requires clinical context. WHO-recommended supplementation regimens significantly reduce morbidity and mortality, while food fortification and biofortification offer sustainable prevention. In high-income countries, VAD occurs mainly in malabsorptive states, liver disease, bariatric surgery, and prematurity.

Conclusion: Timely diagnosis and supplementation are essential to prevent irreversible blindness and systemic complications. Integrated strategies combining supplementation, fortification, and education remain critical for global VAD control.

Keywords: Vitamin A deficiency, xerophthalmia, supplementation, malabsorption, public health, biofortification

Introduction

Vitamin A is a lipid-soluble micronutrient of fundamental biological importance, with indispensable roles in cellular differentiation and growth, intermediary metabolism, immune competence, visual function, and reproduction.[1][2] In human physiology, vitamin A operates not merely as a dietary component but as a regulatory molecule that supports the maintenance of epithelial integrity, modulates gene expression through retinoid signaling, and contributes to systemic resilience against infection. When body stores are inadequate, the disruption of these tightly coordinated processes becomes clinically meaningful. Consequently, vitamin A deficiency (VAD) remains one of the most consequential micronutrient disorders worldwide, particularly in settings characterized by poverty, food insecurity, and constrained health systems. The burden of VAD is most pronounced among young children, in whom deficiency is associated with substantial morbidity and increased risk of mortality. In this context, inadequate dietary intake or impaired intestinal absorption represents more than a nutritional shortfall; it constitutes a major threat to normal development and survival through the compromise of essential physiological functions. From a nutritional standpoint, vitamin A is obtained through a range of dietary sources that differ in bioavailability and typical

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Receive Date: 10 December 2024, Revise Date: 30 December 2024, Accept Date: 31 December 2024

patterns of consumption. Naturally occurring vitamin, A can be derived from animal-based foods such as liver and fish, as well as from milk products, whereas plant-based sources include dark leafy greens and orange-pigmented vegetables.[3] These foods provide vitamin A in forms that enter human metabolism through distinct pathways, yet converge on the shared outcome of maintaining adequate retinoid status. However, access to and regular consumption of these foods is unevenly distributed across populations. Where diets are monotonous and primarily cereal-based, and where animal products and carotenoid-rich produce are limited by affordability, seasonality, or cultural dietary practices, the likelihood of deficiency rises appreciably. In such environments, VAD often becomes entrenched as an endemic condition, sustained by both limited nutrient intake and broader social determinants that restrict dietary diversity [1][2][3].

The biological handling of vitamin A involves a sequence of digestive, absorptive, and storage processes that reflect its fat-soluble nature. Following ingestion, vitamin A is absorbed predominantly in the duodenum after it undergoes hydrolysis mediated by pancreatic and intestinal enzymes, a step that facilitates liberation of absorbable forms from the food matrix.[4] Absorption is further dependent on emulsification with dietary lipids and bile acids, underscoring that adequate fat intake and normal biliary and pancreatic function are integral to efficient uptake.[4] Once absorbed, vitamin A is transported and preferentially stored in the liver, primarily within hepatic stellate cells, which serve as the principal reservoir for maintaining systemic availability during periods of low intake.[5] Although hepatic storage dominates, appreciable quantities can also be sequestered in extrahepatic sites, notably adipose tissue and the pancreas, indicating that vitamin A distribution extends beyond the liver and may be influenced by overall body composition and metabolic status.[6] These storage compartments provide a buffering capacity, yet they are finite; when intake or absorption is chronically insufficient, reserves decline progressively until physiological requirements can no longer be met. Nutrient recommendations provide an essential framework for evaluating adequacy at both individual and population levels. The Institute of Medicine has established recommended dietary allowances (RDA) for vitamin A that reflect the needs of healthy adults, specifying 700 micrograms per day for women and 900 micrograms per day for men.[7][8] Requirements differ across life stages, with children, pregnant women, and lactating women having distinct recommended intakes of 300 to 900 micrograms per day, 770 micrograms per day, and 1300 micrograms per day, respectively.[7][8] These values reflect differences in growth demands, maternal-fetal nutrient transfer, and nutrient losses or utilization during lactation. Of particular clinical relevance, the minimum intake estimated to prevent symptomatic VAD in children aged one to five years is approximately 200 micrograms per day, a threshold that highlights how relatively modest shortfalls can still precipitate overt deficiency when dietary quality is persistently poor. Taken together, these benchmarks emphasize that vitamin A sufficiency is not a static attribute but a dynamic balance between intake, absorption, storage capacity, and physiological demand.

Assessment of vitamin A status commonly relies on biochemical indicators, among which serum retinol concentration is widely used as a practical marker of nutritional adequacy. Serum retinol levels, while subject to modulation by infection and inflammation, provide a meaningful approximation of vitamin A status at the population level and can support clinical interpretation when considered within an appropriate context. Deficiency is conventionally defined as a serum retinol concentration below 20 micrograms per deciliter.[8] At more severe degrees of depletion, functional consequences become increasingly apparent, particularly in tissues with high retinoid dependence. Ocular manifestations represent a classic and clinically significant domain of deficiency-related pathology, and vitamin A deficiency-associated eye symptoms have been shown to emerge at serum retinol concentrations below 10 micrograms per deciliter.[8] This threshold underscores the relationship between diminishing biochemical reserves and the onset of clinically observable impairment, especially in vision-related tissues where vitamin A is central to phototransduction and epithelial maintenance. Dietary vitamin A exists in two principal categories that differ in chemical form and biological activity: carotenoids derived from fruits and vegetables and retinoids derived from animal products. Carotenoids serve as provitamin A compounds, with beta-carotene being the most prevalent and nutritionally significant, whereas retinoids represent the preformed, active forms of vitamin A, including retinol and retinyl esters. The distinction has important implications for nutritional planning because absorption efficiency and conversion to active vitamin A differ substantially between these forms. Retinoids generally demonstrate high absorption efficiency, estimated at approximately 75% to 100%, reflecting their direct usability by the body.[9][10] In contrast, carotenoid absorption is far more variable and depends on factors such as the food matrix, preparation methods, fat content of the meal, and the specific carotenoid consumed.[9][10] Consequently, populations relying primarily on plant-based provitamin A sources may remain vulnerable to inadequate vitamin A status if dietary patterns do not support optimal absorption and conversion [9][10].

To facilitate dietary assessment across diverse foods, conversion factors are used to estimate the retinol activity equivalent of provitamin A carotenoids. The Centers for Disease Control and

Prevention has employed an estimated conversion ratio of 12 to 1 for beta-carotene to retinol absorption within mixed diets containing fruits and vegetables, reflecting the reduced efficiency of conversion relative to preformed vitamin A.[7] While such estimates provide a useful standard for population-level evaluation, they also implicitly highlight a structural vulnerability: even when plant foods are present, substantially greater quantities may be required to achieve the same biological effect as smaller amounts of animal-derived retinoids. This challenge is magnified in regions where diets are dominated by staple grains and where consumption of meat, dairy products, or carotenoid-rich vegetables is infrequent. In many developing countries, limited access to animal-source foods and inconsistent availability of nutrient-dense produce constrain the capacity of households to meet daily requirements, thereby sustaining conditions under which VAD persists. Within these dietary and socioeconomic constraints, vitamin A deficiency becomes not only a biomedical issue but also a reflection of broader inequities in food systems, health resources, and living conditions [7][9].

Etiology

Vitamin A deficiency arises from a convergence of dietary inadequacy, impaired absorption, altered transport, and heightened physiological requirements, with the dominant causal pathways differing substantially between resource-limited environments and high-income settings. Globally, the most prevalent drivers of vitamin A deficiency are embedded in conditions of poverty where low dietary diversity, limited access to nutrient-dense foods, and recurrent infectious disease exposures interact to eroding micronutrient status over time. In such contexts, vitamin A depletion is rarely an isolated nutritional event; instead, it often reflects a broader pattern of undernutrition compounded by sustained inflammatory and enteric burdens that undermine the body's ability to absorb and conserve essential nutrients. In resource-poor regions, the most common etiology of vitamin A deficiency is therefore insufficient intake, frequently complicated by chronic inflammation resulting from recurrent gastrointestinal infections.[11] These infections not only reduce appetite and oral intake but also disrupt intestinal epithelial integrity and absorptive function, creating a self-reinforcing cycle in which the very illnesses that increase nutrient need simultaneously impair nutrient acquisition. A critical feature of vitamin A deficiency in these settings is its frequent co-occurrence with deficiencies of other micronutrients that are biologically linked to vitamin A metabolism. Among these, zinc deficiency is particularly relevant because zinc is necessary for both effective vitamin A absorption and for the hepatic synthesis of retinol-binding protein, which is the principal carrier responsible for transporting retinol within the circulation.[12] When zinc status is compromised, the efficiency of vitamin A utilization declines even if some dietary vitamin A is available, because retinol mobilization from hepatic stores and its intravascular delivery to target tissues becomes physiologically constrained. As a result, children in resource-limited regions may remain deficient despite marginal intake, since a concurrent zinc deficit can prevent vitamin A from being absorbed optimally and transported adequately.[12] This interplay illustrates how vitamin A deficiency frequently reflects a network of nutritional vulnerabilities rather than a single nutrient's shortfall, and it underscores the importance of considering combined deficiencies when evaluating etiology, risk, and potential interventions.

Infectious diseases endemic to low-resource regions further intensify vitamin A deficiency through mechanisms that involve acute reductions in circulating retinol and increased nutrient losses. Measles, in particular, has long been associated with severe nutritional deterioration and is still endemic in many regions where vitamin A deficiency is prevalent. Evidence indicates that measles infection can induce abrupt declines in serum retinol levels exceeding 30%.[13] Such decreases are clinically consequential because they may shift individuals who are marginally sufficient into overt deficiency or worsen existing deficiency into symptomatic disease. The pathophysiology described in relation to measles involves multiple interacting mechanisms: vitamin A deficiency is associated with reduced synthesis of retinol-binding protein, and measles infection is associated with increased urinary excretion of vitamin A, thereby accelerating depletion of already limited reserves.[13] In addition, the physiological demand for vitamin A rises during measles, in part because gastrointestinal epithelial tissues sustain damage, increasing the need for retinoids to support epithelial repair and immune function.[13] Thus, measles functions not only as a precipitating factor that acutely lowers serum retinol, but also as a condition that increases metabolic demand while simultaneously contributing to impaired nutrient retention, making it a potent accelerator of deficiency in susceptible populations. Maternal nutritional status also plays a central etiological role in infancy through its influence on breast milk vitamin A concentration. The vitamin A content of breast milk varies substantially depending on maternal intake and body stores, which means that the adequacy of infant vitamin A exposure is partially determined by maternal nutritional sufficiency. In resource-poor settings, breast milk vitamin A levels may only meet an infant's minimum daily requirement, thereby support basic physiological needs but not permitting the accumulation of substantial hepatic reserves.[14] This point is particularly important because infant and early childhood vitamin A status depends heavily on liver stores as a protective buffer during periods of dietary transition and illness. When breast milk provides only the minimal daily need, infants may fail to establish robust reserves, rendering them vulnerable to deficiency soon after weaning, when dietary sources may be insufficient or poorly absorbed.[14] In such cases, the weaning period becomes a critical etiological window during which vitamin A deficiency can emerge rapidly, especially if complementary foods are low in vitamin A, infections are frequent, or the child experiences poor overall nutritional intake.

By contrast, vitamin A deficiency is exceptionally uncommon in high-income countries, reflecting broader structural advantages in food systems and public health conditions. In the developed world, the rarity of vitamin A deficiency is attributed to widespread availability of vitamin A-rich foods, improved sanitation, access to clean water, and more comprehensive healthcare infrastructure, all of which reduce the prevalence of persistent enteric infection and enhance overall nutritional adequacy. Nonetheless, vitamin A deficiency does occur in these settings, and when it does, it is typically explained by primary or secondary malabsorption rather than absolute dietary insufficiency. The etiological profile in developed regions therefore shifts from environmental and infectious determinants to clinical conditions that disrupt digestion, absorption, storage, or transport of fat-soluble vitamins. In this framework, pancreatic, hepatic, and intestinal disorders are the leading contributors to vitamin A deficiency in high-income contexts, because they interfere with the physiological processes required to liberate, emulsify, and absorb vitamin A from the diet. Chronic inflammatory conditions of the intestine represent a prominent mechanism for vitamin A deficiency in developed settings, especially when they combine mucosal injury with reduced dietary intake. Inflammatory bowel disease provides a useful illustration: like the recurrent gastrointestinal infections common in resource-limited regions, inflammatory bowel disease is characterized by chronic inflammation of the intestinal mucosa and can disrupt absorption through epithelial damage and altered intestinal function.[15] Additionally, disease flares are frequently associated with reduced appetite, dietary restriction, and increased catabolic demand, factors that collectively diminish vitamin A intake while impairing assimilation. This dual burden—impaired absorption combined with inadequate consumption—creates a plausible pathway by which inflammatory bowel disease may precipitate clinically significant vitamin A deficiency in susceptible individuals.[15] The etiological relevance of inflammatory bowel disease also underscores that even in food-secure environments, intestinal integrity remains essential to maintaining vitamin A sufficiency [13][15].

Hepatic pathology constitutes another major etiological domain because the liver is central to vitamin A storage, metabolism, and mobilization. Chronic liver disease of various etiologies has been associated with vitamin A deficiency, though the precise mechanisms remain incompletely defined.[6] Proposed explanations include diminished bile acid production, which would compromise fat emulsification and thereby reduce vitamin A absorption, as well as altered hepatic storage patterns that may impair the body's ability to retain or mobilize vitamin A effectively.[6] Because bile acids are required for the intestinal absorption of fat-soluble vitamins, impaired bile synthesis or secretion can create a functional deficiency even when dietary intake is adequate. Simultaneously, changes in hepatic architecture and stellate cell function may disrupt normal storage dynamics, potentially reducing the availability of vitamin A during times of increased need. In this way, liver disease can influence vitamin A status through both absorptive and post-absorptive pathways. Pancreatic disorders, particularly pancreatic insufficiency, also contribute to vitamin A deficiency by undermining digestive enzyme production required for nutrient liberation and absorption. Pancreatic exocrine function is necessary to supply hydrolases that facilitate the processing of dietary vitamin A, and inadequate production of these enzymes can lead to poor absorption and progressive depletion.[16] This mechanism is especially relevant in chronic pancreatitis, cystic fibrosis, or other conditions associated with exocrine pancreatic insufficiency, where maldigestion of fats and fat-soluble vitamins is common. In these patients, vitamin A deficiency may develop insidiously, manifesting clinically only after substantial depletion has occurred, thereby emphasizing the need for vigilant nutritional monitoring in chronic pancreatic disease [16].

Iatrogenic causes also occupy a significant etiological place in developed settings, most notably following bariatric surgical procedures designed to reduce energy absorption. Many bariatric surgeries intentionally bypass the duodenum and proximal small intestine or otherwise decrease fat absorption, thereby impairing uptake of fat-soluble vitamins, including vitamin A. Because vitamin A absorption is linked to fat digestion and emulsification, surgically induced malabsorption can precipitate deficiency if supplementation and clinical follow-up are not adequately implemented. Thus, vitamin A deficiency in this context is not merely a dietary issue but a predictable metabolic consequence of altered gastrointestinal anatomy and physiology, reinforcing the importance of structured post-operative nutritional surveillance. Finally, prematurity represents a distinct etiological pathway in early life, rooted in developmental physiology rather than environmental deprivation or chronic disease. Premature neonates are particularly vulnerable to vitamin A deficiency because they possess an immature gastrointestinal tract that is not yet optimized for efficient vitamin A absorption, they begin life with minimal hepatic vitamin A stores, and they have elevated physiological requirements during a period of rapid organ development.[17] This combination of limited reserves, reduced absorptive capacity, and high developmental demand creates a biologically plausible and clinically important risk profile. In neonatal care, this vulnerability has implications for both nutritional planning and the prevention of deficiency-related complications, highlighting that vitamin A status is not only influenced by dietary exposure but also by gestational maturity and the timing of nutrient accretion in fetal life. Across these diverse contexts, the etiology of vitamin A deficiency can be understood as the outcome of intersecting forces that include inadequate intake, malabsorption due to mucosal or enzymatic dysfunction, impaired transport related to associated micronutrient deficits, altered storage in hepatic disease, and increased requirements during infection or rapid growth. The relative contribution of each factor is strongly shaped by geography, socioeconomic status, disease prevalence, and healthcare access, explaining why vitamin A deficiency remains primarily a condition of disadvantaged populations globally while persisting in developed countries mainly as a complication of specific pathological or iatrogenic states [17].

Epidemiology

Vitamin A deficiency remains a major global public health concern, with its epidemiological burden distributed unevenly across age groups, physiological states, and geographic regions. The vast majority of cases worldwide occur in children under five years of age living in developing countries, where dietary insufficiency, recurrent infection, and limited access to healthcare converge to create conditions that favor micronutrient depletion. Despite notable progress over recent decades through supplementation programs and improved public health strategies, vitamin A deficiency continues to affect a substantial proportion of young children globally. Current estimates suggest that approximately 30% of children younger than five years are vitamin A deficient, and this deficiency is implicated in roughly 2% of all deaths within this vulnerable age group.[18] These figures underscore the persistent significance of vitamin A deficiency as a contributor to child morbidity and mortality, particularly in settings where infectious diseases remain prevalent and nutritional resilience is limited. The epidemiological concentration of vitamin A deficiency among young children reflects a combination of biological vulnerability and environmental exposure. Early childhood is characterized by rapid growth, heightened nutritional requirements, and immature immune defenses, all of which increase susceptibility to the adverse effects of inadequate vitamin A intake. In many low-income regions, complementary feeding practices following weaning are frequently inadequate in both quantity and quality, often lacking sufficient vitamin A content. When these dietary limitations are compounded by repeated episodes of diarrhea, respiratory infections, or other illnesses that impair absorption and increase metabolic demand, the risk of deficiency escalates further. Consequently, vitamin A deficiency in early childhood is not merely a marker of poor diet but an indicator of broader systemic challenges affecting food security, sanitation, and healthcare delivery [17].

Pregnant and lactating women represent another epidemiologically important group at elevated risk for vitamin A deficiency, owing primarily to increased physiological demands. During pregnancy, vitamin A is required to support maternal tissue expansion, fetal growth, and immune function, while lactation places additional demands on maternal stores to ensure adequate vitamin A transfer through breast milk. In resource-limited settings, where baseline maternal nutritional status may already be compromised, these increased requirements can precipitate or exacerbate deficiency. Evidence from a 2019 study conducted in rural Ethiopia highlights the severity of this problem, reporting vitamin A deficiency in 76% of lactating mothers.[19] Such findings illustrate that maternal vitamin A deficiency remains highly prevalent in certain populations and has important intergenerational implications, as inadequate maternal status directly influences the vitamin A content of breast milk and, by extension, infant vitamin A exposure. Despite its high prevalence in children and women of reproductive age in developing countries, vitamin A deficiency does not appear to exhibit a consistent gender predilection across populations.[20][21] Rather, risk is primarily shaped by age, physiological status, dietary patterns, and disease burden. This absence of a clear gender bias suggests that observed differences in prevalence are more likely attributable to sociocultural, economic, and biological factors that influence nutrient intake and requirements, rather than to inherent sex-specific susceptibility. Accordingly, epidemiological patterns of vitamin A deficiency should be interpreted within the broader context of population-level determinants rather than individual demographic characteristics alone. In contrast to the global situation, vitamin A deficiency is uncommon in the general population of high-income countries, reflecting the protective effects of diversified diets, food fortification, and robust healthcare systems. In the United States, for example, the estimated prevalence of vitamin A deficiency in the general population was only 0.3% in 2013.[7] Notably, vitamin A toxicity is reported to be more prevalent than deficiency in this context, a finding that reflects widespread access to vitamin A-rich foods and supplements.[7] When vitamin A deficiency does occur in developed countries, it is rarely due to absolute dietary insufficiency. Instead, symptomatic deficiency is most often associated with malabsorptive conditions or severely restrictive dietary practices that limit intake or impair utilization [7].

Within the United States and similar settings, specific clinical populations demonstrate markedly higher prevalence rates of vitamin A deficiency, highlighting the importance of disease-specific epidemiology. Children diagnosed with inflammatory bowel disease represent one such group, with studies indicating that 16% have vitamin A deficiency at the time of diagnosis.[15] The prevalence is higher in Crohn disease than in ulcerative colitis, a difference that likely reflects the greater extent of small intestinal involvement and malabsorption typically seen in Crohn disease.[15] These data emphasize that even in nutritionally abundant environments, chronic inflammatory disorders of the gastrointestinal tract can substantially increase the risk of vitamin A deficiency, particularly in pediatric populations with ongoing growth demands. Liver disease is another condition strongly associated with vitamin A deficiency in developed countries. Among patients with liver cirrhosis who are eligible for transplantation, the prevalence of vitamin A deficiency has been reported to reach 70%, with a positive correlation between the severity of cirrhosis and the likelihood of deficiency.[22] This high prevalence underscores the central role of hepatic function in vitamin A storage and metabolism and illustrates how progressive liver dysfunction can severely compromise vitamin A status. In these patients, deficiency may contribute to further immune impairment and epithelial dysfunction, potentially exacerbating clinical outcomes in an already vulnerable population. Pancreatic disorders also feature prominently in the epidemiology of vitamin A deficiency within high-income settings. Among patients with chronic exocrine pancreatic insufficiency, 35% have been found to be vitamin A deficient, despite the fact that 84% were receiving pancreatic enzyme replacement therapy.[16] This observation suggests that standard therapeutic interventions may not fully correct fat-soluble vitamin malabsorption in all patients, and that subclinical deficiency may persist even with treatment. Similarly, surgically induced malabsorption following bariatric procedures represents a significant epidemiological risk. Studies indicate that 70% of patients who underwent biliopancreatic diversion developed vitamin A deficiency within three years of the procedure.[23] These findings reflect the profound and sustained impact of altered gastrointestinal anatomy on fat-soluble vitamin absorption and highlight the need for long-term nutritional surveillance in post-surgical populations [16].

Neonates born prematurely constitute a distinct epidemiological subgroup with exceptionally high rates of vitamin A deficiency. At birth, approximately 66% of premature infants are vitamin A deficient, and by 36 weeks post-menstrual age, this proportion increases to 82%.[17] This high prevalence reflects the combined effects of limited transplacental vitamin A transfer during late gestation, immature gastrointestinal absorption, and elevated requirements during a period of rapid growth and organ development. As a result, prematurity introduces a unique set of risk factors that place infants at significant risk for deficiency, even in settings where overall nutritional resources are sufficient. Collectively, the epidemiology of vitamin A deficiency reveals a condition that is globally pervasive yet contextually specific. While it remains predominantly a disease of young children and women in resource-limited regions, it persists in developed countries within well-defined clinical populations characterized by malabsorption, chronic disease, or altered gastrointestinal physiology. These patterns underscore the importance of tailoring public health and clinical strategies to the populations most at risk, informed by an understanding of the diverse epidemiological pathways through which vitamin A deficiency arises [16].

Pathophysiology

Vitamin A plays a central and multifaceted role in maintaining normal physiological function across several organ systems, most notably the visual apparatus, epithelial tissues, and the immune system. At the molecular level, vitamin A and its active metabolites, collectively referred to as retinoids, are essential for cellular differentiation, gene regulation, and tissue integrity. Through these mechanisms, vitamin A supports the regeneration of visual pigments in the retina, preserves the structural and functional integrity of mucosal membranes, and modulates both innate and adaptive immune responses. When vitamin A availability becomes inadequate, these tightly regulated processes are disrupted, leading to a cascade of functional impairments that underlie the clinical manifestations of vitamin A deficiency. One of the earliest and most characteristic consequences of vitamin A deficiency occurs within the visual system. Vitamin A is an indispensable component of the visual cycle, particularly in the regeneration of rhodopsin, the light-sensitive pigment found in retinal rod cells. Rods are responsible for vision under low-light conditions, and their function depends on the continuous availability of 11-cis-retinal, a vitamin A–derived chromophore. In states of deficiency, insufficient retinal is available to regenerate rhodopsin following photobleaching, resulting in impaired dark adaptation. Clinically, this dysfunction manifests night blindness, often one of the first observable symptoms of vitamin A deficiency.[24][25] At this stage, visual impairment may still be reversible with timely vitamin A repletion, as structural damage to retinal cells has not yet occurred. However, when vitamin A deficiency is prolonged or severe, the pathophysiological changes within the retina become more profound and less reversible. Persistent deprivation leads to degeneration of rod photoreceptors, reflecting both functional exhaustion and structural deterioration. As rod cells degenerate, the retina's capacity to respond to low-light stimuli is progressively lost, and the visual impairment deepens. Concurrently, deficiency-related changes in the conjunctival and corneal epithelium give rise to xerophthalmia, a pathological condition characterized by dryness, keratinization, and loss of normal epithelial integrity.[24][25][26] In advanced stages, corneal ulceration and scarring may occur, ultimately leading to irreversible blindness. These ocular manifestations represent the most severe end of the vitamin A deficiency spectrum and remain a major cause of preventable childhood blindness in regions where deficiency is endemic [25][26].

Beyond the visual system, vitamin A deficiency exerts widespread effects on epithelial tissues throughout the body. Vitamin A is essential for the maintenance and differentiation of mucosal epithelial cells, which form a critical barrier against environmental pathogens. In the absence of adequate vitamin A, normal columnar and mucus-secreting epithelium is progressively replaced by stratified, keratinized epithelium. This pathological transformation leads to xerosis and breakdown of mucosal surfaces in the gastrointestinal and respiratory tracts.[27][28] As a result, the protective barrier function of these membranes is compromised, facilitating microbial invasion and increasing susceptibility to infection. The loss of mucosal integrity also impairs normal secretory and absorptive functions, which may further exacerbate nutritional deficiencies and perpetuate a cycle of malnutrition and illness. The immunological consequences of vitamin A deficiency are closely linked to these epithelial changes but also involve direct effects on immune cell development and function. Vitamin A plays a regulatory role in both innate and adaptive immunity, influencing lymphocyte proliferation, differentiation, and cytokine production. Deficiency is associated with impaired antibody responses, altered T-cell–mediated immunity, and diminished function of natural killer cells. These immunological impairments reduce the host’s ability to mount effective responses to pathogens, contributing to increased frequency, severity, and duration of infections.[29][30] In populations already burdened by infectious disease, such immune dysfunction significantly amplifies the morbidity associated with vitamin A deficiency and increases the risk of adverse outcomes, particularly in young children. Chronic infection and sustained immune activation in the context of vitamin A deficiency can also contribute to the development of anemia of chronic inflammation. Recurrent infections driven by mucosal breakdown and immune compromise lead to persistent inflammatory signaling, which alters iron metabolism and suppresses erythropoiesis. Vitamin A deficiency has been associated with impaired mobilization of iron stores and reduced hemoglobin synthesis, further compounding the anemic state.[27][28][29][30] This interaction between nutritional deficiency, immune dysfunction, and inflammation illustrates the systemic nature of vitamin A deficiency and its capacity to disrupt multiple physiological pathways simultaneously. In summary, the pathophysiology of vitamin A deficiency reflects the essential role of retinoids in maintaining visual function, epithelial integrity, and immune competence. Initial functional disturbances, such as night blindness, may progress to irreversible structural damage and blindness if deficiency persists. Concurrently, widespread mucosal breakdown and immune impairment predispose affected individuals to recurrent infections and chronic inflammatory states, including anemia. These interrelated mechanisms explain the broad clinical spectrum of vitamin A deficiency and highlight why timely prevention and correction are critical to preserving vision, immunity, and overall health .[27][28][29][30]

History and Physical

A meticulous clinical history is often the most valuable starting point for identifying individuals at risk of vitamin A deficiency, particularly because early manifestations may be subtle and laboratory confirmation is not always immediately available. Suspicion should be heightened when the patient’s background or medical history suggests either inadequate intake, impaired absorption, diminished hepatic reserves, or increased physiological requirements. In contemporary clinical practice, vitamin A deficiency is most commonly encountered in association with malabsorptive states and chronic illness, and therefore a careful review of gastrointestinal, hepatobiliary, pancreatic, infectious, and developmental histories is essential. Conditions that compromise intestinal absorption, such as inflammatory bowel disease, chronic gastrointestinal infections, cirrhosis, pancreatic insufficiency, or a history of bariatric procedures, are particularly relevant, as they can prevent adequate uptake of fat-soluble vitamins even when dietary intake appears sufficient. Likewise, prematurity should prompt consideration of deficiency due to limited hepatic stores, immature gastrointestinal function, and high nutritional demands during rapid postnatal development. A history of rubeola infection (measles) is also clinically significant because acute illness can precipitate a rapid decline in vitamin A status, especially in individuals who are already marginally nourished. Beyond medical diagnoses, social and geographic history remains critical; prior residence in, or prolonged travel to, resource-poor regions where food insecurity and recurrent infections are common should raise concern for vitamin A deficiency. Finally, pregnancy and lactation in the setting of poor nutritional intake represent important physiological contexts in which vitamin A requirements increase, making deficiency more likely if dietary quality and overall caloric adequacy are not maintained. The symptomatic evolution of chronic vitamin A deficiency typically follows a recognizable pattern, and eliciting this progression through targeted questioning can provide strong diagnostic clues. One of the hallmark early symptoms of hallmarks is the gradual onset of night blindness, reflecting impaired regeneration of visual pigment and reduced rod function. Patients may report difficulty seeing in dim light, trouble adjusting when entering dark rooms, or impaired night driving, although in children the history may be indirect and obtained from caregivers. In parallel, a history of increased frequency of infections should be actively explored, particularly gastrointestinal, pulmonary, and urinary tract infections, as mucosal barrier compromise and immune dysfunction predispose to recurrent illness.[30][31] These infectious episodes are not merely coincidental findings; rather, they can reflect an underlying vulnerability that accompanies vitamin A depletion and may further accelerate deficiency through inflammation and reduced intake during illness. Dermatologic symptoms can also accompany the chronic course. Patients may describe progressive skin dryness, roughness, or a "bumpy" texture, often corresponding clinically to xeroderma and to phrynoderma, a pattern of follicular hyperkeratosis that is frequently distributed over extensor surfaces and may be prominent on the shoulders and buttocks.[30][31] While these findings are not exclusively diagnostic of vitamin A deficiency, their presence in the appropriate clinical context strengthens suspicion, particularly when they occur alongside visual complaints and recurrent infections.

The physical examination should be directed toward identifying ocular, cutaneous, and systemic signs that reflect the severity and chronicity of deficiency. Ocular inspection is especially important, as the eye findings of vitamin A deficiency can progress from subtle conjunctival changes to vision-threatening corneal pathology. As deficiency becomes more advanced, xerophthalmia develops, and classic features may be identified on careful examination. Bitot spots are a characteristic finding and appear as foamy, triangular or oval lesions on the conjunctiva, typically associated with conjunctival dryness and keratinization.[26] Conjunctival xerosis may be observed as a dry, dull conjunctival surface with visible wrinkling, reflecting loss of normal tear film function and epithelial integrity. These findings suggest that deficiency has progressed beyond early functional impairment and has begun to produce structural changes in ocular tissues. If vitamin A deficiency persists or deepens, corneal involvement becomes increasingly likely, and the condition may enter stages associated with a high risk of irreversible vision loss. Corneal xerosis represents further progression, in which the corneal surface becomes dry, hazy, and vulnerable to breakdown. This may evolve into corneal ulceration, a serious complication that can rapidly compromise visual acuity and, in severe cases, threaten the integrity of the globe. With continued progression, keratomalacia may develop, reflecting corneal softening and tissue necrosis. Even when ulcers heal, corneal scarring can occur, and this scarring may result in permanent blindness. These advanced ocular manifestations demand urgent recognition because timely treatment may prevent catastrophic outcomes, whereas delays can lead to irreversible damage. Clinical history must also consider that vitamin A deficiency does not always follow the gradual progression classically described, particularly in the setting of acute systemic infection. In patients with an acute decline in vitamin A status, especially during measles infection, ocular complications may present abruptly and severely. In this context, corneal xerosis and ulceration may develop without preceding night blindness or the typical earlier conjunctival signs such as Bitot spots, reflecting the rapid depletion of already limited stores and the heightened physiological demand associated with infection.[26] This presentation is clinically important because it may lead clinicians to underestimate vitamin A deficiency if they rely exclusively on a stepwise symptom sequence. Therefore, the presence of severe ocular findings during or shortly after measles should prompt immediate consideration of vitamin A deficiency even if classic early symptoms are absent.

Fig. 1: Signs and symptoms of Vitamin A deficiency.

Cutaneous findings on examination can further support the diagnosis, although they must be interpreted cautiously given their overlap with other nutritional and dermatologic conditions. Phrynoderma, a form of follicular hyperkeratosis, may be evident as rough, keratotic papules centered around hair follicles, often affecting extensor surfaces.[31] While this finding is compatible with vitamin A deficiency, it is also associated with other nutritional deficiencies, meaning that it should be treated as suggestive rather than definitive.[31] Its diagnostic value increases when it occurs in combination with ocular symptoms, recurrent infections, and a history consistent with malabsorption or dietary inadequacy. Overall, a comprehensive history and targeted physical examination can provide a strong clinical basis for suspecting vitamin A deficiency. Identifying risk factors such as malabsorptive disease, chronic infection exposure, liver or pancreatic dysfunction, prematurity, measles, residence in resource-poor settings, or pregnancy and lactation in the context of poor nutrition is essential. Equally important is recognizing the typical symptom trajectory from night blindness and recurrent infections to dermatologic changes and progressive xerophthalmia. Because advanced ocular disease may develop rapidly in acute infection and may lead to permanent visual impairment, clinicians must maintain a high index of suspicion and prioritize prompt evaluation and intervention when clinical features are consistent with vitamin A deficiency.[26][30][31]

Evaluation

The evaluation of vitamin A deficiency relies on an integrated approach that combines clinical assessment with targeted laboratory investigations, recognizing that no single test is sufficient in all circumstances. In many cases, the diagnosis can be made on clinical grounds when characteristic signs and symptoms are present, particularly in individuals with well-established risk factors. Certain physical findings, especially ocular manifestations, carry substantial diagnostic weight and may allow clinicians to identify vitamin A deficiency even in the absence of laboratory confirmation. Among these findings, xerophthalmia is considered nearly pathognomonic for vitamin A deficiency and strongly supports the diagnosis when observed in the appropriate clinical context.[32] Because xerophthalmia reflects advanced depletion of vitamin A stores and structural changes in ocular tissues, its presence typically indicates clinically significant deficiency that warrants prompt intervention. In patients whose history and physical examination findings are less definitive, laboratory evaluation can provide additional support for the diagnosis. Measurement of serum retinol concentration is the most commonly used biochemical test in clinical practice and can be readily ordered to assess vitamin A status. Deficiency is conventionally defined as a serum retinol level below 20 micrograms per deciliter.[8] This threshold is widely applied in both clinical and epidemiological settings and serves as a practical indicator of inadequate vitamin A availability. However, interpretation of serum retinol values requires careful consideration of physiological and pathological factors that may influence circulating concentrations independent of total body stores. Because vitamin A is stored primarily in the liver, hepatic reserves can buffer short-term fluctuations in intake and maintain serum retinol levels within the normal range until stores are substantially depleted [8].

As a result of this homeostatic regulation, serum retinol concentrations may remain normal despite significantly reduced total body vitamin A stores, particularly in early or subclinical deficiency. This limitation reduces the sensitivity of serum retinol as a standalone diagnostic tool, especially in populations with chronic marginal intake. Furthermore, serum retinol levels can be influenced by acute phase responses during infection or inflammation, which may transiently lower circulating retinol concentrations independent of actual vitamin A status. Consequently, laboratory findings must be interpreted alongside clinical features, dietary history, and risk factors rather than in isolation. In individuals with high clinical suspicion but normal serum retinol levels, the absence of biochemical confirmation should not preclude consideration of vitamin A deficiency or delay appropriate management. The definitive assessment of total body vitamin A status is achieved by quantifying hepatic retinol concentration, as the liver serves as the primary storage site for vitamin A. Measurement of liver retinol content obtained through biopsy is regarded as the gold standard for evaluating vitamin A reserves.[33] This method provides a direct and accurate reflection of total body stores and allows precise differentiation between adequate, marginal, and deficient states. However, the invasive nature of liver biopsy, along with its associated risks, ethical considerations, and limited feasibility, restricts its use in routine clinical practice. Consequently, hepatic retinol measurement is generally confined to research settings or highly specialized investigations and is not recommended for standard diagnostic evaluation of vitamin A deficiency. Given these constraints, the evaluation of vitamin A deficiency in clinical practice emphasizes a pragmatic balance between clinical judgment and available diagnostic tools. Recognition of near-pathognomonic signs such as xerophthalmia, combined with an understanding of the limitations of serum retinol testing, allows clinicians to identify deficiency with reasonable confidence in most cases. Ultimately, assessment strategies should prioritize timely diagnosis and intervention, particularly in high-risk populations, to prevent progression to irreversible complications while acknowledging that definitive quantification of total body vitamin A stores is rarely necessary or practical outside of research contexts.[8][32][33]

Treatment / Management

The cornerstone of management for vitamin A deficiency is vitamin A supplementation (VAS), implemented with the dual aims of restoring adequate retinoid status and preventing the well-recognized complications of deficiency, particularly ocular morbidity and infection-related mortality. In populations where deficiency is prevalent, supplementation functions not only as an individual therapeutic intervention but also as a population-level preventive strategy. A substantial body of evidence has demonstrated that vitamin A supplementation in vitamin A–deficient communities yields clinically meaningful reductions in childhood morbidity and mortality, supporting its longstanding role as a major public health measure in high-burden settings.[34] The therapeutic benefit is most apparent in individuals with biochemical evidence of deficiency. Specifically, VAS produces a definitive clinical effect among patients with serum retinol concentrations below 20 micrograms per deciliter, consistent with established thresholds for deficiency.35 Conversely, individuals whose serum retinol concentrations are greater than 30 micrograms per deciliter are not expected to derive benefit from supplementation and should instead meet requirements through adherence to recommended dietary allowance targets, thereby minimizing unnecessary exposure and reducing the risk of hypervitaminosis.35 In regions where vitamin A deficiency is highly prevalent, international policy emphasizes universal supplementation for selected high-risk groups rather than reliance on individualized biochemical screening, which is frequently impractical in low-resource settings. The World Health Organization (WHO) recommends universal VAS for young children living in high-risk areas, reflecting the disproportionate burden of deficiency and its severe consequences in this age group. The recommended regimen includes a one-time dose of 100,000 IU for children aged 6 to 11 months, followed by 200,000 IU doses administered every four to six months until five years of age.[36] This schedule is designed to replenish liver stores periodically and to provide sustained protection during the years of greatest vulnerability to deficiency-related infectious and ocular complications. The use of intermittent high-dose supplementation in these settings reflects an evidence-informed balance between feasibility, safety, and efficacy, particularly where continuous dietary adequacy cannot be reliably ensured [36].

Table 1: Vitamin A Treatment Regimens

INFANTS AND CHILDREN*	VITAMIN A DOSAGE (IU)
Young Infants, (0-5 months)	50,000
Older Infants, (6-11 months)	100,000
Children (males, ≥12 mo; females, 12 mo-12 y and >50 y)	200,000
WOMEN (13-49 Y)	
Xerophthalmia: night blindness, and/or Bitot's spots	10,000 daily or 25,000 weekly for at least 3 months
Active corneal lesions (rare)	200,000 on days 1, 2, and 14

Fig. 2: Vitamin A deficiency Treatment Plan.

Pregnancy introduces important considerations in vitamin A supplementation, as maternal deficiency may pose risks to both the mother and fetus, yet excessive dosing carries teratogenic potential. For pregnant women at increased risk of deficiency, the WHO recommends lower-dose supplementation strategies that are intended to improve maternal status while mitigating concerns related to fetotoxicity. The recommended dosing includes either 10,000 IU daily or 25,000 IU weekly for a 12-week period.[37] This approach reflects the need for cautious dosing during pregnancy, where the margin between correcting deficiency and exceeding safe upper exposure limits is narrower than in nonpregnant populations. In addition, it is important to recognize that supplementation guidelines have evolved in response to emerging evidence and safety considerations. The WHO no longer recommends universal supplementation for infants younger than six months of age or for postpartum women, indicating a shift away from routine blanket dosing in these groups in favor of more targeted approaches.[38][39][40] While population-level supplementation regimens are well defined in high-prevalence regions, guidance is less prescriptive for asymptomatic vitamin A deficiency in resource-rich settings. In these contexts, routine universal supplementation is generally unnecessary because dietary access and fortification practices reduce baseline risk. Instead, treatment decisions are typically individualized and guided by the severity of deficiency, the presence of clinical manifestations, and the underlying etiology, with dosing determined by clinician judgment and ongoing monitoring. The WHO provides clear therapeutic dosing recommendations for individuals with xerophthalmia, a manifestation of advanced deficiency that requires urgent correction to prevent irreversible ocular damage. In this circumstance, the recommended dosing is 50,000 IU for children younger than six months, 100,000 IU for children aged six to twelve months, and 200,000 IU for children older than twelve months, administered once daily for two consecutive days, followed by an additional dose two weeks later.[41] The staged dosing strategy reflects an intent to rapidly correct deficiency, replenish body stores, and reduce the risk of progression while accounting for age-related differences in safety and tolerance.

Measles represents a special clinical scenario in which vitamin A supplementation is recommended even when deficiency status has not been formally established, reflecting the robust association between measles infection and acute depletion of vitamin A reserves as well as the demonstrated clinical benefits of supplementation in severe disease. The WHO recommends that children with severe measles receive the same age-based dosing regimen described for xerophthalmia, given once daily for two days, regardless of whether vitamin A deficiency has been previously documented.[41] This recommendation underscores that treatment in measles is not merely corrective but also adjunctive, aimed at reducing complications and improving outcomes during an infection that substantially increases physiological demand and is associated with high risks of ocular and systemic sequelae. Effective management also requires attention to factors that may blunt the response to vitamin A supplementation. Zinc deficiency is particularly important because zinc is required for optimal vitamin A metabolism and transport, and individuals who are zinc deficient may respond poorly to vitamin A supplementation alone.[12] In such cases, concomitant zinc supplementation is advised to improve the efficacy of vitamin A repletion and to address the broader micronutrient deficiency context that frequently accompanies undernutrition.[12] Similarly, when vitamin A deficiency arises from malabsorption rather than inadequate intake, oral supplementation may be insufficient to restore adequate status. In these circumstances, clinicians should consider alternative delivery routes, including intramuscular formulations, to bypass impaired intestinal absorption and ensure reliable bioavailability. This approach is especially relevant in conditions characterized by fat malabsorption, pancreatic insufficiency, cholestatic liver disease, or severe intestinal pathology, where the absorption of fat-soluble vitamins is intrinsically compromised [12].

In resource-rich countries, particular patient populations warrant tailored supplementation strategies due to predictable risks of deficiency. Post-bariatric surgery patients represent a prominent example, as procedures designed to reduce nutrient absorption can lead to chronic malabsorption of fat-soluble vitamins. For this group, recommendations commonly include daily supplementation with 10,000 IU of vitamin A, with subsequent dose adjustment guided by periodic serum retinol monitoring. Some individuals require substantially higher doses to maintain adequate levels, and in certain cases, requirements may rise to as much as 100,000 IU per day, emphasizing the wide interindividual variability in absorption and the necessity of longitudinal biochemical surveillance.[42] The clinical imperative in post-bariatric populations is therefore twofold: ensuring consistent supplementation and implementing routine monitoring to prevent both deficiency-related complications and iatrogenic toxicity from excessive dosing. Premature infants constitute another high-risk group, although standardized guidelines for supplementation of vitamin A in this population have not yet been established. Nevertheless, emerging evidence suggests that supplementation may confer clinically significant benefits in vulnerable neonatal cohorts. Recent studies have reported that administration of 10,000 IU every other day for four weeks in very low birth weight neonates produced substantial outcome improvements, including a 56% reduction in all-cause mortality and reductions in oxygen requirement, sepsis, patent ductus arteriosus, and duration of hospitalization.[43] Additional research has indicated that supplementation with 1500 IU daily in extremely premature infants was associated with a significant reduction in retinopathy of prematurity, with reported rates of 1.6% versus 6.9%, and a near 50% reduction in bronchopulmonary dysplasia.[44] Although these findings are compelling, they also reinforce the need for careful clinical oversight, as neonatal physiology is uniquely sensitive to both deficiency and excess, and optimal dosing parameters may depend on gestational age, birth weight, baseline stores, and concurrent clinical conditions. Beyond these defined groups, vitamin A deficiency associated with other malabsorptive disorders is typically managed on a case-by-case basis, integrating the severity of deficiency, the presence of symptoms, the capacity for oral absorption, and the feasibility of monitoring. Across all settings, effective treatment extends beyond the act of supplementation itself and includes identifying and addressing root causes, such as chronic infection, inadequate dietary intake, or gastrointestinal disease. When appropriate, nutritional counseling to improve intake of vitamin A–rich foods and broader management of comorbid deficiencies can complement pharmacologic repletion and reduce the risk of recurrence. Ultimately, vitamin A supplementation remains the principal and most evidence-supported intervention for correcting deficiency and reducing adverse outcomes, but its successful implementation depends on context-sensitive dosing, attention to safety thresholds, and the recognition that certain populations require tailored regimens and ongoing monitoring.[34][36][41][42][43][44]

Differential Diagnosis

A rigorous differential diagnosis is essential when assessing suspected vitamin A deficiency because several ophthalmologic and nutritional conditions can mimic its early manifestations, and misattribution may delay appropriate investigations or lead to inappropriate supplementation. The earliest symptomatic feature of chronic vitamin A deficiency is often night blindness, a complaint that is not specific and may herald a variety of retinal or optical disorders. Retinitis pigmentosa classically presents with progressive nyctalopia and peripheral visual field constriction, and night blindness is frequently the first symptom that prompts clinical attention.[45] A similar presentation can occur in certain rare inherited retinal dystrophies, in which rod photoreceptor dysfunction precedes broader retinal degeneration, producing impaired dark adaptation that may be indistinguishable from deficiency-related nyctalopia on history alone.[46] In these settings, a detailed family history, the tempo of progression, and confirmatory ophthalmic testing such as electroretinography are often necessary to differentiate structural retinal disease from a potentially reversible nutritional etiology. In addition to retinal degenerations, common degenerative ophthalmologic conditions may present with symptoms that patients interpret as night blindness. Cataracts, through progressive lens opacification and light scatter, can cause reduced vision in dim environments and impaired contrast sensitivity, which may be described as difficulty seeing at night even though the pathophysiology differs from rod dysfunction. Myopia can also contribute to nocturnal visual difficulty because reduced distance acuity, glare, and suboptimal correction become more apparent in low-light conditions. These disorders are typically distinguished through routine visual acuity assessment, refraction, slit-lamp examination, and fundoscopy, which may reveal lens changes or refractive errors without the conjunctival and corneal abnormalities characteristic of advanced vitamin A deficiency [46].

Ocular surface findings likewise require careful interpretation. Bitot spots, frequently considered a classic sign of vitamin A deficiency, are not entirely exclusive and must be differentiated from other conjunctival lesions. Notably, Bitot spots have also been associated with niacin deficiency, a consideration that is clinically important in contexts of generalized malnutrition where multiple micronutrient deficiencies coexist.[47] Furthermore, benign degenerative conjunctival lesions such as pinguecula and pterygium can resemble Bitot spots on superficial inspection, particularly when lesions appear elevated or foamy and are located on the exposed interpalpebral conjunctiva. Distinguishing features may include the vascularity and triangular encroachment onto the cornea typical of pterygium, the yellowish elastotic appearance of pinguecula, and the broader clinical context in which vitamin A deficiency-related findings usually occur. In practice, the differential diagnosis is refined through integration of dietary and malabsorption history, presence or absence of systemic infectious susceptibility and cutaneous signs, and objective ophthalmologic assessment, ensuring that vitamin A deficiency is neither overdiagnosed nor overlooked [47].

Prognosis

The prognosis of vitamin A deficiency is strongly determined by the severity and duration of deficiency at the time treatment is initiated, as well as by the presence of established ocular or systemic complications.[26] When deficiency is identified in its early or subclinical stages, outcomes are generally favorable. Individuals who have biochemical evidence of reduced vitamin A status but have not yet developed major ocular surface disease typically experience excellent recovery following supplementation, without enduring sequelae. Importantly, clinical improvement can occur rapidly; treatment at any stage of severity has been reported to produce observable improvement within approximately one week, reflecting both restoration of circulating retinoid availability and early functional recovery in affected tissues.[48] Ocular prognosis follows a gradient in which reversible functional impairment precedes structural damage that may be only partially correctable. Early ophthalmologic manifestations—such as night blindness—are largely functional and tend to resolve with repletion when intervention occurs before significant photoreceptor degeneration. Similarly, conjunctival xerosis and Bitot spots generally resolve completely within roughly two months of supplementation, demonstrating that epithelial abnormalities can normalize when vitamin A becomes available for mucosal repair and differentiation.[49][26] In contrast, once the deficiency progresses to corneal xerosis and ulceration, the prognosis becomes more guarded. Even if active corneal disease improves after treatment, scarring may remain, and this scarring can result in permanent visual impairment or blindness despite correction of the underlying deficiency.[49][26] Thus, the timing of treatment relative to corneal involvement is a critical determinant of long-term visual outcome.

Beyond the eye, prognosis is also shaped by the systemic vulnerability that accompanies deficiency, particularly susceptibility to infection. Once visual manifestations occur, patients typically demonstrate increased risk of infectious morbidity, reflecting both compromised mucosal barrier integrity and immune dysfunction.[26] In preschool-aged children, the presence of ocular signs functions as an epidemiologic indicator of heightened overall mortality from gastrointestinal, pulmonary, and other mucosal infections associated with vitamin A deficiency.[26] Risk stratification data underscore the prognostic significance of these manifestations. Mortality among children with night blindness is approximately three times higher than mortality in children with subclinical vitamin A deficiency. Those who exhibit both Bitot spots and night blindness have mortality rates about nine times higher than children with subclinical deficiency. Most strikingly, keratomalacia is associated with extremely poor prognosis, with nearly two-thirds of affected children dying within months, highlighting keratomalacia as a marker of severe systemic compromise and advanced depletion.[26] These outcomes emphasize that vitamin A deficiency is not merely an ophthalmologic disorder but a systemic condition whose prognosis depends on rapid recognition and early intervention before irreversible tissue injury and severe infectious complications develop [26][46].

Complications

Complications of vitamin A deficiency reflect the vitamin's essential roles in vision, epithelial maintenance, and immune competence, and they become particularly severe when deficiency is profound or prolonged. The most feared complication is irreversible visual loss. Advanced ocular disease can progress from corneal xerosis to ulceration and keratomalacia, culminating in scarring that permanently impairs vision or causes complete blindness.[26] Such outcomes are especially devastating in early childhood, where visual impairment carries long-term consequences for development, education, and quality of life. Even when supplementation is provided, structural damage to the cornea may not fully reverse, making prevention and early treatment central to avoiding permanent disability. Systemically, vitamin A deficiency increases susceptibility to infection through impairment of mucosal barrier integrity and dysregulation of immune responses. Compromised epithelial surfaces in the respiratory and gastrointestinal tracts facilitate pathogen entry, while immune dysfunction reduces the body's capacity to contain and clear infections effectively. This combination predisposes affected individuals to recurrent or severe respiratory infections, diarrheal diseases, and other mucosal infections. In high-burden environments, these infections can precipitate a vicious cycle in which illness reduces appetite and absorption, further worsening deficiency and increasing vulnerability. The clinical consequence is not only higher infection frequency but also higher infection-related mortality, particularly among young children with ocular manifestations of deficiency.[26] In severe cases, the cumulative effect of blindness risk, recurrent infections, and impaired immune function contributes to markedly elevated mortality.[26] Thus, the complication profile of vitamin A deficiency extends beyond isolated organ involvement and should be recognized as a syndrome in which advanced ocular pathology often signifies broad systemic compromise. The prevention of complications depends on early identification of at-risk individuals, timely supplementation, and addressing underlying drivers such as malnutrition, malabsorption, and infectious disease exposure.

Patient Education

Deterrence of vitamin A deficiency begins with nutritional sufficiency, and in individuals with normal absorptive capacity, a balanced, nutrient-dense diet is generally adequate to prevent deficiency. In resource-rich settings, most people have routine access to vegetables and animal-source foods that contain vitamin A or provitamin A carotenoids, and many staple products are fortified with vitamin A, further reducing population risk. Consequently, patient education in these environments often focuses on reinforcing dietary diversity, clarifying food sources of vitamin A, and identifying clinical contexts—such as malabsorptive disease or restrictive diets—where routine intake may not translate into adequate status. In resource-poor countries, deterrence strategies have historically emphasized large-scale vitamin A supplementation programs designed to deliver high-dose vitamin A at intervals recommended by the World Health Organization, particularly to young children in high-prevalence regions.[50] These programs are frequently coupled with public education initiatives that address nutrition, breastfeeding practices, and recognition of vitamin A deficiency symptoms, aiming to strengthen both prevention and early presentation for care. However, outcomes have been variable across regions, reflecting differences in infrastructure, program continuity, community engagement, and broader determinants such as food access and healthcare reach.[51][52] This variability has contributed to a growing emphasis on addressing upstream causes of deficiency rather than relying solely on episodic supplementation. In response, contemporary approaches increasingly integrate food fortification and education as sustainable deterrence strategies. Many staple foods are now fortified with essential micronutrients, including vitamin A, and advances in agricultural science have enabled genetic modifications in crops such as rice, potatoes, wheat, and soybeans to enhance vitamin A content.[53][54][55][56][57] These biofortified crops are particularly relevant because they can deliver provitamin A through foods that are already widely consumed, thereby reducing reliance on healthcare-based supplementation delivery. Evidence suggests that biofortification can be both economically and agriculturally viable, making it an attractive strategy for durable prevention in low-resource settings. Effective patient and community education therefore extends beyond dietary advice to include awareness of fortified foods, breastfeeding support, and recognition that persistent infections and poor dietary diversity increase risk, encouraging families and communities to seek preventive services when available.

Enhancing Healthcare Team Outcomes

Optimizing outcomes in vitamin A deficiency requires coordinated interprofessional care, because the condition often reflects intersecting nutritional, gastrointestinal, infectious, and ophthalmologic factors that exceed the scope of any single discipline. In resource-rich settings, the primary care physician commonly serves as the initial point of contact, identifying risk factors, recognizing early signs, initiating laboratory evaluation when appropriate, and coordinating treatment. Dietitians contribute critical expertise by assessing dietary adequacy, developing individualized nutrition plans, and addressing broader micronutrient needs, while pharmacists support safe supplementation practices by advising on dosing, formulation, interactions, and toxicity risk. When vitamin A deficiency is driven by malabsorptive pathology, specialist collaboration becomes essential. Gastroenterologists help evaluate and manage inflammatory bowel disease and other intestinal disorders that impair fat-soluble vitamin absorption. Bariatric surgeons play a key role in the long-term management of post-surgical patients, ensuring structured supplementation and monitoring. Transplant surgeons and hepatology teams contribute to care in advanced liver disease, where altered storage and absorption can predispose to deficiency. Ophthalmologists are indispensable in evaluating and managing the spectrum of vitamin A deficiency-related eye disease, from early conjunctival changes to corneal ulceration, where timely intervention may prevent irreversible blindness. Their involvement is particularly important when symptoms progress beyond night blindness or when corneal involvement is suspected, since ocular complications can evolve rapidly and require specialized assessment. Following acute evaluation and initiation of therapy, ongoing prevention and monitoring commonly return to the primary care setting, where longitudinal follow-up can address recurrence risk and adherence [58].

In settings with limited medical infrastructure, the interprofessional model often centers on public health delivery rather than specialty care access. Public health nurses are critical for administering high-dose vitamin A supplementation in rural communities and for facilitating appropriate referrals when severe ocular disease or complicated illness is identified. Government agencies and international health organizations provide essential funding, logistics, and coordination to sustain supplementation, education, and fortification initiatives, recognizing that the burden of vitamin A deficiency is shaped by systemic determinants that require organized public health responses.[34] Although vitamin A deficiency is often straightforward to diagnose and treat when resources are available, its continued impact on millions globally highlights the necessity of integrated healthcare and public health collaboration to achieve consistent prevention, early detection, and effective management across diverse settings.

Conclusion:

Vitamin A deficiency persists as a major public health challenge, disproportionately affecting vulnerable populations in resource-limited settings and select clinical groups in developed countries. Its systemic impact extends beyond ocular morbidity to include heightened susceptibility to infections and increased mortality, particularly among young children. Early recognition and intervention are paramount, as functional impairments such as night blindness are reversible, whereas advanced corneal disease often results in permanent blindness. Global strategies have demonstrated that high-dose supplementation programs significantly reduce child mortality and prevent severe ocular complications. However, reliance on episodic supplementation alone is insufficient for long-term eradication. Sustainable solutions require a multifaceted approach that addresses underlying determinants of deficiency, including poverty, dietary inadequacy, and recurrent infections. Food fortification and agricultural biofortification represent promising interventions to improve population-level vitamin A intake, while targeted supplementation remains essential for high-risk groups such as pregnant women, post-bariatric patients, and premature infants. Ultimately, combating VAD demands coordinated efforts across clinical care, nutrition policy, and public health infrastructure. By integrating preventive strategies with timely therapeutic interventions, healthcare systems can mitigate the profound consequences of VAD and advance progress toward global nutritional equity.

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