Dermatological changes related to zinc deficiency
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Introduction
Although human deficiency of Zinc was not clearly established before 1969, since then it has been emerging as a nutrient of clinical importance through clinical trials and studies\(^1\). Zinc belongs to the group of essential trace elements which at present comprise Zinc, Iron, Copper, Manganese, Nickel, Cobalt, Molybdenum, Selenium, Chromium, Iodine, Fluorine, Tin, Silicon, Vanadium and Arsenic which are extremely vital for maintaining normal health\(^2\). As the metal component of more than 200 important enzymes such as alkaline phosphatase, alcohol dehydrogenase and several dehydrogenase and digestive enzymes it is involved in the synthesis and degradation of protein, lipid, carbohydrates and nucleic acids. It has recently been found to play an essential role in polynucleotide transcription and translation and thus in the processes of genetic expression. It's involvement in such fundamental activities probably accounts for the essentially of zinc for human and all other life forms\(^3\).

High Concentrations of Zinc are present in shellfish, legume, nuts, whole grain and green leafy vegetables, whereas fruits usually contain insignificant levels\(^4\). The Zinc supply depends largely on the protein content of the food and so protein under nourishment will lead to an insufficient Zinc supply. Phytate interferes with Zinc absorption and a high fiber content of the food also tends to decrease the bioavailability of the element\(^5\).c

The daily oral intake of Zinc should average 3 mg in infants less than 6 months, 5 mg in infants 0.5-1 yr. old, 10 mg in children 1-7 yr. old and 16 mg from the eleventh year and onwards. Pregnant and lactating omen should receive 20-25 mg zinc daily\(^5\).

Zinc deficiency
Zinc deficiency may be caused by a specific absorptive defect present in acrodermatitis enteropathica or by insufficient nutrition as reported from the Middle East and Turkey. These causes of Zinc deficiency are referred to as Primary. Zinc deficiency may also be consequent upon diseases of the gastrointestinal tract causing diarrhea and malabsorption. Such cases are called Conditional or Secondary Zinc deficiency.

In general common causes of Zinc deficiency are chronic liver disease, chronic alcoholism, cancer chemotherapy, intestinal disease, collagen disease, nephrotic syndrome, haemodialysis, burn, trauma, use of oral contraceptives and diabetes mellitus. Whatever the cause of Zinc deficiency is, it definitely causes a series of disorders as described in the following Table-1\(^6\).

| Primary zinc deficiency\(^7\) | Acrodermatitis enteropathica: The disease was recognized in 1936 by the Swedish dermatologist Thore Brandt. His findings were corroborated and further investigated by Danbolt and Closs who coined the name of the disease. It is the only known inherited Zinc deficiency disease in man, transmitted as an autosomal recessive trait. |
| Clinical features: The disease typically starts 4-6 weeks after weaning or earlier if the infant is not weaned. The child turns peevish, withdrawn and photophobic, develops a vesiculobullous dermatitis on hands, feet and peri-orificial areas and scalp hair is lost. Diarrhea is often present. Growth is stunted and there is a decreased resistance to infections. Wound healing is poor. |

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Without proper management the prognosis is usually fatal and in the past a lethal outcome without therapy has been described in most cases.

Treatment: Zinc sulphate supplementation is found to be the only treatment for acrodermatitis enteropathica and was first introduced in 1973-1974. Oral Zinc in a dose of 2 fig/kg daily was found to cure all clinical manifestations. Prolonged therapy at least up to adult age is necessary to prevent recurrence of Zinc deficiency.

Secondary (conditioned) Zinc Deficiency
Zinc depletion syndrome: Adults who receive 0.2 fig Zinc daily, which is 1.3% of the recommended allowance, become clinically Zinc deficient within three months. Where there is disturbed bowel function the Zinc loss is increased, and if combined with a decreased absorption and low dietary Zinc intake- Zinc depletion will develop. The Zinc depletion syndrome was originally identified because of the acrodermatitis enteropathica-like skin lesions of patients who received prolonged total potential nutrition for inflammatory bowel diseases and chronic diarrhoea. The cause of the depletion is often triple: pre-existing latent Zinc deficiency, prolonged total potential nutrition with a low Zinc content and a sudden weight gain provoked by high calorie supply with the parenteral nutrition. In most cases reported the parenteral nutrition was given for 2-3 months before signs of Zinc deficiency occurred. The semm Zinc level is significantly decreased, often less than 20 mg/100 ml, normal about 70-12 mg/100 ml equivalent to 11-19 mmol/L.

Zinc depletion observed in infants on total parenteral nutrition. Premature infants are particularly at risk of developing such a state because they are born with negligible Zinc stores and undergo rapid growth within their first months of life. Apart from cutaneous lesions of zinc deficiency they may show gastric retention and paralytic ileus which resolves promptly following Zinc therapy. Chronic Zinc deficiency may develop in patients suffering from malabsorption- malnutrition associated with alcohol liver cirrhosis and alcoholic pancreatitis. It may also develop following bypass surgery.

Skin changes related to Zinc deficiency
Systemic Zinc deficiency causes lesions including alterations in nail and hair growth. The findings are similar whether the cause is primary or secondary.

Acute Zinc deficiency: General symptoms include septicemia, photophobia and mental depression. There is an acute eczematous eruption on hands and feet, in the anogenital regions and around the body openings. The volar aspects of the fingers show characteristic flat bullous lesions on the flexural creases. There are various degrees of paronychial inflammation on fingers and toes. Oozing lesions may be seen on the heels of bedridden patients. Some lesions are black and necrotic and burn-like skin changes may be seen. There is angular stomatitis with perioral lesions sparing the vermilion border.

Chronic Zinc deficiency: Chronic Zinc deficiency lesions are typically seen on skin areas subject to pressure and minor trauma such as elbows, knees, knuckles and malleolar regions of the ankles. The lesions are sharply demarcated, thickened and of a red-brown color. Lichenification is present as an important clue to distinguish it from psoriasis. Seborrhoeic dermatitis-Like changes may be seen on the face of adult patients. Pre-existing acne vulgaris tends to flare. A severe reticulate non-itchy scaly dermatitis on the trunk has been described in chronic Zinc deficiency of alcoholics. It remains unresponsive to topical steroid treatment but clears rapidly with oral Zinc.

Hair and nail changes related to Zinc deficiency
In acute Zinc deficiency diffuse thinning of the scalp hair becomes progressive and eventually leads to total alopecia. In chronic Zinc deficiency the hair growth is poor and sparse. Structural changes of the hair may be observed with the microscope, e.g. broken spearhead-like endings, transverse striation of the shaft, pseudomonilethrix, longitudinal spits and bayonet hairs. Severe Zinc deficiency usually leaves deep transverse
depressions (Beau's lines) on the finger nails. White transverse bands may be seen alone or in association with the depressions.\textsuperscript{17}

<table>
<thead>
<tr>
<th>TABLE -1</th>
<th>Zinc Deficiency May Cause The Following Disorders:\textsuperscript{2,3,6,11}</th>
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</thead>
<tbody>
<tr>
<td>GROWTH RETARDATION</td>
<td>Zinc deficient cells fail to divide and differentiate, with consequent growth impairment.</td>
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<tr>
<td>IMPAIRED SPERMATOGENESIS</td>
<td>Testicular zinc is critical for normal spermatogenesis and for sperm physiology; it preserves genomic integrity in the sperm and stabilizes attachment of sperm head to tail.</td>
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<tr>
<td>HYPOGONADISM AND SUPPRESSION OF SECONDARY SEXUAL CHARACTERISTICS</td>
<td>The development of primary and secondary sex organs in male, and all phases of the reproductive process in the female from estrous to parturition and lactation, can be adversely affected in zinc deficiency. Zinc deficiency results in a reduced gonadotrophin output and consequent fall in androgen production which in turn results in hypogonadism with suppression of secondary sexual characteristics.</td>
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<tr>
<td>CONGENITAL MALFORMATION</td>
<td>Zinc is essential for normal embryonic development. Deficiency results in malformation of brain, eyes, bones, heart, and other organs. Zinc deficiency significantly reduces the activity of thymidine kinase, an enzyme vital to DNA synthesis- results in congenital malformation.</td>
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<tr>
<td>IMMUNOLOGICAL DYSFUNCTION</td>
<td>Zinc is essential for the formation and function of the immune system. With zinc deprivation, the thymus atrophies and viable thymocytes are not formed. The function of macrophages and T -cells are impaired and lymphocyte concentration decreased-the ultimately result is an inability to respond to antigens or to defend the organism against infections.</td>
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<tr>
<td>RESPIRATORY TRACT INFECTION</td>
<td>In recent studies, it is evident that zinc deficiency increases the incidence of respiratory tract infection in children.</td>
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<td>DERMATOLOGICAL DYSFUNCTION</td>
<td>Zinc deficiency causes a wide variety of dermatological dysfunction includes of hyperkeratosis, parakeratosis and alopecia.</td>
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<td>DIARRHOEA</td>
<td>Zinc deficiency increases the incidence of diarrhea and its supplementation reduces the prevalence. The role of zinc in diarrhea may be mediated through several mechanisms, which include 1) membrane stabilization, 2) mucosal integrity, 3)electrolyte transport and water transport, 4) immune competence, 5)protein and essential enzyme synthesis.</td>
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<td>LOSS OF APPETITE AND ANOREXIA</td>
<td>Desensitization of the taste buds in zinc deficiency causes loss of appetite and anorexia.</td>
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<tr>
<td>OTHERS</td>
<td>Night blindness, Abnormal hair growd1, Deformed bone formation</td>
</tr>
</tbody>
</table>

**Pathology**

In acute vesiculobullos acrodermatitis-light microscopy reveals pronounced epidermal extracellular oedema with formation of suprabasal cysts and clefts. The horny layer is often separated or lost. Necrosjs of the outer epidermis may be seen\textsuperscript{18}, simulating inigratory necrolytic erythema. In chronic Zinc deficiency there is psoriasis-like acanthosis of the epidermis. In the dermis a slight perivascular infiltrate of lymphocytes, neutrophils and a few histiocytes is present. Electron microscopy of acute lesions shows degenerate basal calls with slender cytoplasmic protrusions and an intact basal lamina with multiple invaginations\textsuperscript{14,a}.  

**Diagnosis**

Server Zinc deficiency is usually suspected from the clinical findings and the history. The serum Zinc and alkaline phosphatase levels are low\textsuperscript{14,19} but rise promptly during Zinc administration. The parallel indices of the two parameters can be used for diagnosis and for control of the treatment\textsuperscript{14,20}. It is important always to consider the level of plasma
albulnin which binds 60-70% of circulating Zinc. Severe hypoalbuminaemia therefore is generally associated with low serum Zinc values which do not reflect a state of Zinc deficiency.

In suspect cases a therapeutic trial with oral or parenteral Zinc should be undertaken. If no clinical improvement occurs within 4-5 days and the serum alkaline phosphatase remains unaltered or even decreases despite a rise in serum Zinc the patient is not deficient in Zinc.

**Treatment**

In adult patients oral Zinc sulphate 0.2g are given two to three times daily (about 2 mg Zinc/kg). Similar doses on a kilogram basis are given to children. Parenterally 0.2-0.3 mg Zinc/kg daily (about 10-20 mg daily in adult patients) is sufficient in severe cases of acute Zinc deficiency. For prophylactic purposes total parenteral nutrition should supply no less than 70-80 J.lg Zinc/ kg. daily. Infants and premature babies on parenteral nutrition should receive a prophylactic does of 0.1- 0.3 mg/kg daily.21

**Conclusions**

Considering the decreasing level of Zinc in our soil and food grains, a patient having clinical features resembling Zinc deficiency, should be investigated and treated accordingly.

**References**

    c) Zinc in nutrition, Banladesh Agricultural Research Council, copy right 1988.