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# Role of serum protein in the ocular manifestations of vitamin A deficiency

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The ocular lesions of vitamin A deficiency, in order of severity, are brown pigmentation of the conjunctiva, defective dark adaptation (clinically manifested as night blindness), Bitot's spot, xerophthalmia, and keratomalacia. The first four conditions are due to the mild chronic form of vitamin A deficiency and the last to the severe acute form.

Night blindness, xerophthalmia, Bitot's spot, and keratomalacia were identified and treated with liver and liver oil before the discovery of the vitamins, but the pathogenesis of these ocular manifestations of vitamin A deficiency are not yet known.

Supplementary protein in the diet causes early and complete disappearance of Bitot's spot and xerophthalmia (Yourish, 1953; Vaughan, 1954; Reddy, 1965; Gupta, Dhir, and Agarwal, 1968). This may be due to an interrelation of the metabolic functions of protein and vitamin A, and the present study seeks to elucidate this relationship.

## Materials and methods

Four groups of children aged 1 to 8 years, who were affected by keratomalacia, xerosis, Bitot's spot, and xerosis with Bitot's spot, were admitted to the Eye Ward of Gauhati Medical College Hospital. A complete nutritional and clinical examination, with estimation of serum vitamin A, total serum protein, serum albumin, and serum globulin was carried out.

The children received the standard hospital diet supplemented with a single mega dose of vitamin A (100,000 I.U. – Arovit, Roche) as recommended by the Indian Council of Medical Research (1967) and 1·5 g. milk protein (Casilan) per kg. body weight daily for 15 days, after which the examination was repeated.

Children with no signs of malnutrition were used as a control group and were treated and examined in the same way.

Serum vitamin A was estimated by the method of Kaser and Stekol (1943), using a Klett-Semmerson photoelectric colorimeter. Total serum protein, serum albumin, and serum globulin were estimated by the method of Wu (1920, 1922).

## Results

CONTROLS (Table I, opposite). After treatment there was no significant increase in the mean values . The mean total serum protein was raised from 7·31 to 7·63 g/100 ml. and the serum vitamin A rose by 11·8 per cent. The albumin/globulin ratio fell from 2·12 to 2·08 (Table II, overleaf).

KERATOMALACIA (Table I) The mean serum vitamin A level increased two-fold after treatment. The total serum protein in this group varied from 4·26 to 7·60 g./100 ml. (mean 5·82 g/.100 ml.). Along with the low serum protein level, the albumin/globulin

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**Table I** *Total serum protein, serum albumin, serum globulin, and serum vitamin A in eight normal healthy children, eleven with keratomalacia, six with xerosis, six with Bitot's spot, and six with xerosis and Bitot's spot before and after treatment.*

| *Diagnosis* | *Case No.* | *Age (yrs)* | *Sex* | *Total protein (g./100 ml.)* | | *Serum albumin (g./100 ml.)* | | *Serum globulin (g./100 ml.)* | | *Serum vitamin A (μg./100 ml.)* | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | *Before* | *After* | *Before* | *After* | *Before* | *After* | *Before* | *After* |
| Control | 1 | 1 | M | 7·80 | 7·80 | 5·44 | 5·98 | 1·90 | 1·82 | 56 | 60 |
| | 2 | 5 | M | 7·56 | 7·55 | 5·94 | 4·44 | 1·62 | 3·21 | 52 | 64 |
| | 3 | 3 | M | 5·80 | 7·85 | 3·80 | 6·16 | 2·00 | 1·69 | 60 | 66 |
| | 4 | 3½ | F | 7·50 | 7·80 | 4·50 | 5·62 | 3·00 | 2·18 | 50 | 66 |
| | 5 | 8 | M | 7·20 | 7·50 | 4·50 | 4·50 | 2·70 | 3·00 | 52 | 58 |
| | 6 | 6 | F | 7·65 | 7·65 | 5·25 | 5·05 | 2·40 | 2·60 | 60 | 62 |
| | 7 | 4 | M | 7·75 | 7·67 | 5·20 | 4·65 | 2·55 | 3·02 | 58 | 60 |
| | 8 | 2½ | M | 7·25 | 7·25 | 4·85 | 4·85 | 2·40 | 2·40 | 50 | 54 |
| | Mean | | | 7·31 | 7·63 | 4·93 | 5·16 | 2·32 | 2·49 | 34·75 | 61·25 |
| Kerato-malacia | 1 | 4 | M | 7·02 | 7·56 | 3·80 | 5·08 | 3·22 | 2·48 | 24 | 60 |
| | 2 | 8 | M | 6·50 | 8·52 | 4·25 | 4·90 | 2·25 | 3·62 | 10 | 38 |
| | 3 | 3 | M | 4·70 | 6·78 | 3·00 | 4·64 | 1·71 | 2·14 | 28 | 48 |
| | 4 | 2½ | M | 5·96 | 8·80 | 2·95 | 5·04 | 3·01 | 3·76 | 16 | 42 |
| | 5 | 6 | M | 5·06 | 7·28 | 3·32 | 4·74 | 1·74 | 2·54 | 23 | 52 |
| | 6 | 6 | M | 7·40 | 7·52 | 4·52 | 4·74 | 2·88 | 2·78 | 23 | 54 |
| | 7 | 8 | M | 5·64 | 7·28 | 2·00 | 3·48 | 3·64 | 3·80 | 48 | 65 |
| | 8 | 5 | M | 4·62 | 6·35 | 2·00 | 4·41 | 2·26 | 1·94 | 20 | 44 |
| | 9 | 6 | F | 6·30 | 7·80 | 2·20 | 4·39 | 4·10 | 3·41 | 23 | 52 |
| | 10 | 8 | M | 7·60 | 7·78 | 4·00 | 4·48 | 3·60 | 3·30 | 40 | 65 |
| | 11 | 8 | F | 4·71 | 6·78 | 3·60 | 4·64 | 1·71 | 2·14 | 34 | 60 |
| | Mean | | | 5·82 | 2·20 | 3·25 | 4·59 | 2·73 | 2·90 | 26·27 | 52·72 |
| Xerosis | 1 | 6 | M | 6·35 | 6·77 | 1·87 | 3·24 | 4·48 | 3·53 | 44 | 50 |
| | 2 | 5 | F | 7·01 | 7·20 | 5·32 | 5·98 | 1·69 | 1·22 | 34 | 49 |
| | 3 | 6 | F | 5·89 | 6·80 | 3·48 | 4·25 | 2·41 | 2·55 | 56 | 65 |
| | 4 | 4 | F | 6·82 | 6·92 | 5·20 | 5·28 | 1·62 | 1·64 | 52 | 60 |
| | 5 | 1½ | M | 6·60 | 7·29 | 2·60 | 5·98 | 4·00 | 2·31 | 46 | 50 |
| | 6 | 3 | F | 6·10 | 6·92 | 3·10 | 5·28 | 3·00 | 1·64 | 40 | 48 |
| | Mean | | | 6·46 | 6·98 | 3·59 | 5·00 | 2·87 | 2·15 | 45·33 | 53·67 |
| Bitot's spot | 1 | 3½ | M | 4·78 | 7·02 | 3·58 | 5·28 | 1·20 | 1·74 | 20 | 52 |
| | 2 | 5 | F | 5·20 | 7·02 | 3·80 | 5·21 | 1·40 | 1·81 | 40 | 56 |
| | 3 | 4 | F | 5·30 | 6·40 | 2·84 | 4·20 | 2·46 | 2·20 | 24 | 44 |
| | 4 | 4 | M | 6·40 | 7·02 | 3·10 | 5·21 | 3·30 | 1·81 | 40 | 56 |
| | 5 | 3 | M | 5·70 | 6·80 | 2·90 | 4·25 | 2·80 | 2·55 | 26 | 44 |
| | 6 | 1½ | M | 4·72 | 6·90 | 3·20 | 4·52 | 1·52 | 2·38 | 22 | 40 |
| | Mean | | | 3·35 | 6·86 | 3·23 | 4·77 | 2·11 | 2·08 | 28·66 | 49·00 |
| Xerosis and Bitot's spot | 1 | 6 | M | 6·03 | 7·28 | 4·02 | 4·44 | 2·01 | 2·84 | 30 | 52 |
| | 2 | 3 | M | 6·40 | 7·48 | 4·28 | 5·56 | 2·12 | 1·92 | 40 | 50 |
| | 3 | 2½ | M | 6·56 | 7·56 | 4·45 | 5·48 | 2·11 | 2·08 | 34 | 54 |
| | 4 | 5½ | M | 7·28 | 7·92 | 4·44 | 5·25 | 2·84 | 2·67 | 28 | 58 |
| | 5 | 8 | M | 6·25 | 7·28 | 4·20 | 4·62 | 2·05 | 2·66 | 40 | 57 |
| | Mean | | | 6·50 | 6·90 | 4·28 | 5·07 | 2·23 | 2·43 | 34·40 | 54·20 |

ratio was greatly altered even in cases in which the total serum protein was within the normal range (Cases 1, 2, 10). After treatment the mean serum protein level was raised to 7·20 g./100 ml. and the albumin/globulin ratio improved from 1·34 to 1·60 (Table II).

**Table II** *Albumin/globulin ratio in different groups of cases before and after treatment*

| *Group* | *No. of cases* | *Albumin/globulin ratio* | |
|---|---|---|---|
| | | *Before* | *After* |
| Control | 8 | 2·12 | 2·08 |
| Keratomalacia | 11 | 1·34 | 1·60 |
| Xerosis | 6 | 1·25 | 2·57 |
| Bitot's spot | 6 | 1·53 | 2·24 |
| Xerosis with Bitot's spot | 6 | 1·92 | 2·09 |

XEROSIS (Table I) The mean serum vitamin A level rose from 45·33 to 53·67 µg./100ml. There was no increase in the total serum protein level. The albumin/globulin ratio improved from 1·25 to 2·57 (Table II).

BITOT'S SPOT (Table I) The mean serum vitamin A level rose from 28·66 to 49·00 µg./100 ml. and the mean serum protein level rose by 28·2 per cent.
The albumin/globulin ratio rose from 1·53 to 2·24 (Table II).

XEROSIS AND BITOT'S SPOT (Table I) There was a significant increase in the serum vitamin A level and, although there was no significant change in the mean serum protein level, the albumin/globulin ratio increased from 1·92 to 2·09 (Table II).

## Discussion

McLaren (1964) suggested that the eyes were affected if the serum vitamin A level fell below 20µg./100 ml., but in the present series keratomalacia, xerosis, and Bitot's spot occurred in patients with levels as high as 56 µg./100 ml., suggesting that hypovitaminosis A is not the only aetiological factor in the ocular lesions which accompany malnutrition. Dhir, Gupta, and Agarwal (1968) demonstrated that the administration of vitamin A alone was incapable of curing the ocular lesions of hypovitaminosis A.

Though hypovitaminosis A was not frequently found in the present series, hypoproteinaemia with altered albumin/globulin ratio was noted almost in every case. Similar observations of hypoproteinaemia in cases of keratomalacia and xerophthalmia were made by Yap-Kie-Tiong (1957) and Gopalan, Ventakachalan, and Bhavani (1960). In our cases the serum protein level increased and the albumin/globulin ratio became normal after treatment, with clinical improvement of the ocular lesions.

The importance of giving protein as well as vitamin A in the treatment of hypovitaminosis A has been studied by various workers (Yourish, 1953; Vaughan, 1954; Bagchi, Halder, and Chowdhury, 1959; Reddy, 1965; Gupta and others, 1968). Yap-Kie-Tiong (1956) observed that the serum protein levels were lower in patients with keratomalacia than in those with xerophthalmia, while the concentration of vitamin A was approximately the same. It has also been reported that xerosis, Bitot's spot, and keratomalacia may occur when the serum vitamin A level is normal but the serum protein level is low (Cecil and Loeb, 1951; Sen, 1954; Yap-Kie-Tiong, 1956; Venkataswamy, 1967).

Protein deficiency produces a fatty infiltration of the liver and impairment of the normal functions of the liver cells. As the liver is a vital organ for vitamin A metabolism, protein deficiency prevents the availability of vitamin A to the body. Factors which influence the absorption, biosynthesis, and storage of vitamin A all tend to lower the serum vitamin A level (Abboud, Osman, and Massoud, 1968). Protein deficiency causes the rapid exhaustion of stored vitamin A, the impairment of digestion and malabsorption, and the reduction of power to utilize the small amounts of vitamin A and provitamins (Moore, 1960) which are still available in the body. Our study has shown that where the total serum protein level is low, the serum vitamin A level is also low. It is clear that protein plays a vital role in the prevention of the ocular manifestations of vitamin A deficiency, and that in the treatment of such cases protein and vitamin A should be given together.

## Summary

Children with various ocular lesions due to hypovitaminosis A were treated with one mega dose of vitamin A and 1·5 g. milk protein per kg. body weight daily for 15 days. In almost every case the clinical condition improved, and the serum vitamin A and protein concentration and the albumin/globulin ratio became normal. Both protein and vitamin A should be used in the treatment of the ocular manifestations of vitamin A deficiency.

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