

# Reversal of the complications of self-induced vitamin A deficiency

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A previous report (Fells and Bors, 1969) has described the case of a 25-year-old man who had deliberately, but illogically, omitted from his diet for 5 years all foods containing vitamin A or the precursor carotenoids, in response to his own idea that vitamin A was responsible for his grand mal epilepsy.

He was observed from the onset of ocular symptoms in March, 1968, to July, 1969, during which time he consistently refused to take vitamin A systemically or even locally. In this interval he developed progressive bilateral corneal xerosis and stromal vascularization, conjunctival xerosis, and severe retinal damage with yellow spots in the fundus (Fig. 1, opposite), great restriction of visual fields, virtually no light-induced rise on electro-oculography and a small residual cone response only in the electroretinogram. Serum vitamin A and carotenoid levels were consistently lower than have been recorded previously in man (Table I).

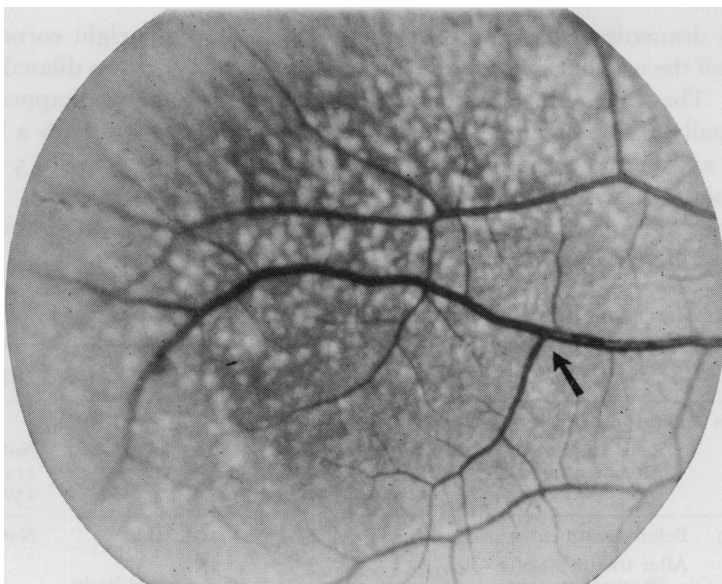
**Table I** *Blood levels of vitamin A and carotenoids*

<i>Date</i>	<i>Carotenoids (<math>\mu\text{g.}/100\text{ ml.}</math>)</i>	<i>Vitamin A (i.u./100 ml.)</i>	
8.5.68		13	
29.7.68	13	25.8	
30.9.68	3.9	13.6	
21.1.69	5	21	
12.5.69	3.6	21	
10.7.69	0	33	
24.7.69	4.8	115	
29.9.69	6.0	174	
2.2.70	13	190	

Normal levels in blood:  
100  $\mu\text{g.}$  per cent. carotenoids  
150 i.u. per cent. vitamin A

In April, 1969, he developed bilateral, paracentral, interpalpebral, shallow corneal ulcers. Although his visual acuity deteriorated and he was warned of the risk of corneal perforation he declined treatment.

He was admitted to hospital as an emergency 11 weeks later having been bedridden for 3 weeks with an intermittent pyrexia, increasing motor weakness, anorexia, and severe abdominal pain. For 10 days the visual acuity of the right eye had been very poor and the left eye was deteriorating rapidly. He was obviously very ill, with a peculiar greyish-coloured skin and follicular hyperkeratosis and extensive bilateral mid-stromal corneal



*FIG. 1 Yellow fundus dots before treatment. Arrow marks same vessel in Figs 1 and 3*

vascularization extending to a half-depth interpalpebral ulcer with very little infiltrate in the right eye (Fig. 2). There was no uveitis and vision was light perception in the right eye and 4/60 in the left.



*FIG. 2 Right cornea before treatment, showing vascularization and ulceration*

He finally agreed to have vitamin A therapy which was supervised by Prof. C. E. Dent. Initially vitamin A eyedrops (150,000 i.u./ml.) were given 2-hrly for 2 days with a symptomatic response of less photobia, pain, and watering. He was then given 200,000 i.u. vitamin A intramuscularly followed by vitamin A and D capsules orally four times a day (4,500 i.u. vitamin A, 500 i.u. vitamin D per capsule).

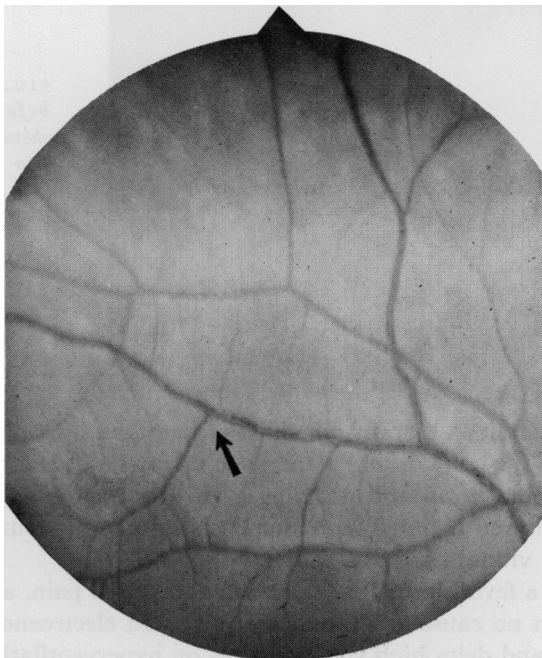
For the next 4 days he had a fever up to 103°F., severe abdominal pain, and anorexia. Despite intensive investigation no cause was found and repeated electroencephalograms were normal except for theta and delta high voltage waves on hyperventilation.

There was a dramatic ocular improvement; within 4 days the right corneal ulcer had decreased to half the original size and the intracorneal vessels were less dilated with closure of some loops. The "crocodile skin" conjunctival pattern had almost disappeared and the eyes were virtually asymptomatic. After 7 weeks only ghost vessels with a little cellular flow remained and the vision had improved to 6/24 in the right eye and 6/5 in the left.

Electrodiagnostic tests were performed before and after treatment. The results (Table II) show a very marked improvement with only a small residual disability. It had been feared that these retinal functions were irreversibly lost.

**Table II** *Electrodiagnostic tests before and after treatment*

<i>Eye</i>		<i>Right</i>	<i>Left</i>
Electro-oculogram	Light-induced rise (per cent.)		
	Before treatment	Not detected	Not detected
	After treatment of : 7 wks 11 mths	133 130	114 150
Electroretinogram	Before treatment	Not recordable	Not recordable
	After treatment of 7 wks:		
	Photopic response	Within normal limits	
	Scotopic response	b wave slightly small with double top	
	After treatment of 11 mths:		
	Scotopic a wave ( $\mu\text{v.}$ ) : 5 min. 10 min.	40 100	30 100
	Scotopic b wave ( $\mu\text{v.}$ ) : 5 min. 10 min.	90 210	220 210
Flicker fusion (c.p.s.)	40	40	
Dark adaptation	Before treatment	Grossly abnormal both rod and cone sectors	
	After 11 months	Down to 1 log unit at 25 min.	



**FIG. 3** *Similar area of fundus 5 months after treatment started. Arrow marks same vessel in Figs 1 and 3*

The yellow fundus dots decreased in size and disappeared after 3 months' treatment (Fig. 3), at which time visual acuity was 6/9 in the right eye and 6/5 in the left.

The patient continued the same dose of vitamins A and D for 4 months and then reduced the dose to two capsules per day.

When last seen he was feeling well with normal texture and colour of the skin, inactive corneal scarring, and fine intracorneal ghost vessels. The fundi appeared normal. He has maintained his strange diet which accounts for the persistently low level of serum carotenoids despite normal vitamin A levels. The external appearance of the eye is shown in Fig. 4.

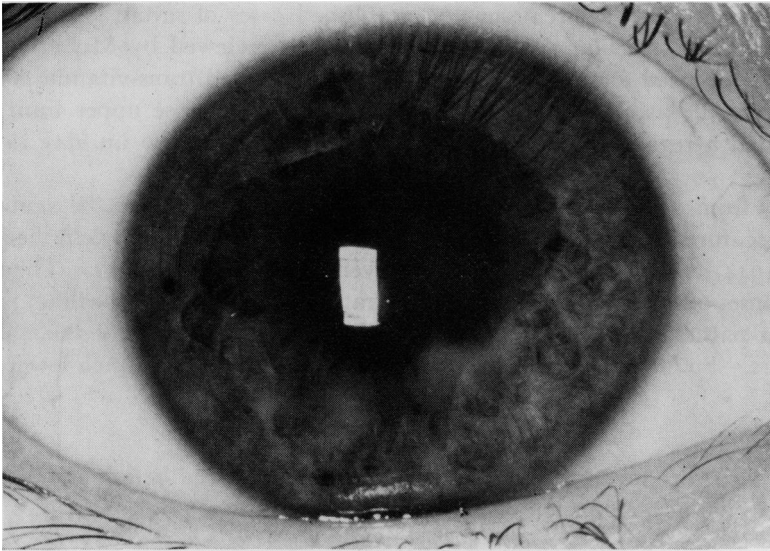


FIG. 4 *Right eye 5 months after treatment*

### Discussion

Several features of this case are apparently unique.

The mechanism of the production of the deficiency was extraordinary: a deliberate and successful attempt to eliminate carotenoids and vitamin A from the diet for 5½ years in a country in which a routine diet provides these in abundance.

The very low levels of serum vitamin A have not been previously reported (Sharman, 1969). In the Medical Research Council trial (Hume and Krebs, 1949), restriction of intake to less than 70 i.u. vitamin A per day in sixteen subjects with normal commencing levels resulted in a drop to a minimum level of 20 i.u. per cent. after 24 months in only one subject, the other levels being higher. The only clinical ocular change in those subjects was a mild change in dark adaptation in a few.

The ocular lesions were severe but only very slowly progressive through prexerosis, xerosis and vascularization, and only late corneal ulceration which did not advance rapidly and destructively and was not accompanied by uveitis. This is at variance with the descriptions given of keratomalacia by Sweet and K'ang (1935) and Duke-Elder (1965). However, the epidermal features of this patient were similar to other descriptions, and correspond to the experimental results reported by Fell (1960) in which, in organ cultures of embryonic skin, deficiency of vitamin A induces keratinization of epithelium of mucous type.

The mechanism of action of vitamin A is unknown, but it is known to retard the maturation of cells of the prickle cell layer of the epidermis and the formation of keratin. Excess of vitamin A causes some disruption of fatty protein cell membranes (Fell, 1963).

The acute illness following initial therapy is not similar to that previously reported in nondeprived subjects given massive doses of vitamin A. Reports by Moore (1957) and Oliver and Havener (1958) describe nausea, headache and vomiting, vertigo, diplopia, and papilloedema, presumably all due to a rise in cerebrospinal fluid pressure. The cause of the illness in this patient remains speculative. The recovery of ocular function has been remarkable. Only fine corneal stromal scars remain with retinal function within normal limits (Table II), after very severe damage before treatment.

Previous reports of the treatment of established cases of severe vitamin A deficiency with reversal of the ocular deficiency features were reviewed by McLaren (1963), who emphasized the need for urgent treatment with preformed trans-vitamin A systemically, and felt from the available evidence that there was no precise upper limit to the dose. He suggested a regime of 100,000 i.u./day initially then 30,000 i.u./day to the stage of full healing.

Toxicity from treatment is reported by many observers and can be acute or chronic. The acute features have been noted; the chronic effects were initially described in a child by Josephs (1944) and later by Oliver and Havener (1958) and others. They include the insidious onset of hepatomegaly, painful migrating bone and joint swelling, papilloedema, and ocular palsies. The dose to produce this in adults is probably 100,000 i.u./day for 1 to 2 years. So far this patient has shown no toxic effects on a much lower dose.

### Summary

A patient with very severe vitamin A deficiency was observed before and after treatment. The progression and regression of the ocular features are noted.

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