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Effect of Administration of Thyroid Extract and of α-Dinitrophenol upon Dark Adaptation.

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Previous studies[1, 2] have shown that the process of dark adaptation of the eye may be disturbed in certain patients having cirrhosis of the liver or renal stone. The abnormal dark adaptation was characterized by (a) elevation of the cone and rod thresholds, (b) reduction in the speed of the process, or (c) a combination of these two effects. Other studies[2, 3] have shown that simple Vitamin A deficiency, as from diets deficient in the vitamin or from obstructive jaundice, may produce threshold changes alone. However, the reduction in speed of adaptation appeared to be a different phenomenon. Since this latter change, like the elevated visual thesholds, responded favorably to Vitamin A therapy, the delay in adaptation was interpreted as possibly a manifestation of faulty utilization of the vitamin.

Attention, therefore, was directed to other factors which might influence the speed of dark adaptation and which thus might be involved in the intermediary metabolism of Vitamin A. The method and apparatus for measuring dark adaptation was similar to that previously employed.[2] Serum Vitamin A and carotenoids were determined by a modification of the method described by Kimble.[4] The usual hospital diet without Vitamin A concentrates was fed throughout the period of observations.

The oral administration of thyroid extract or of α-dinitrophenol to 3 patients with markedly prolonged dark adaptation produced sharp changes in both rod and cone functions. The effect of thyroid extract was tested 4 times in 3 patients, whereas the effect of α-dinitrophenol was tested 2 times in 1 of these patients.

Table I records values for dark adaptation and for serum Vitamin A and carotenoids in these 3 patients. Only the initial and final values for each test period are tabulated. The data show a marked increase in speed of adaptation and lowering of visual thresholds

1 Haig, C., Hecht, S., and Patek, A. J., Jr., *Science*, 1938, **87**, 534.

2 Patek, A. J., Jr., and Haig, C., *J. Clin. Invest.*, 1939, **18**, 609.

3 Hecht, S., and Mandelbaum, J., *Am. J. Physiol.*, 1940, **130**, 651.

4 Kimble, M. S., *J. Lab. Clin. Med.*, 1939, **24**, 1055.

TABLE I.
Values for Dark Adaptation and for Serum Vitamin A and Carotenoids Before and After Administration of Thyroid Extract and of α-dinitrophenol.

Patient	Exp. No.	Days of thyroid (T) or α-dinitrophenol (D)	Daily dose, gr.	Dark adaptation thresholds at various periods in dark *Log μμ lamberts* 2 min.	15 min.	40 min.	Cone/Rod transition point, *min.*	Serum Vit. A— I.U./100 ml.	Serum carot.— μg/100 ml.	B.M.R.
E.R., 55 yrs, ♀	1	0		**7.7***	6.9	4.7	15.0	105	56	— 2
Rheumatoid arthritis.		13 T	2	**6.3**	4.0	2.7	4.5	93	42	+12
Renal stone removed 7 yrs ago.										
J.C., 64 yrs, ♂	2	0		**7.4**	7.0	4.9	14.5	122	116	— 9
Cirrhosis of liver		42 T	1	**7.0**	5.1	4.2	8.1	64	116	+12
	3	0		**7.6**	7.0	4.5	14.8	190	149	—11
		9 D	1.1	**6.8**	5.4	3.7	9.0	134	166	+ 9
	4	0		**7.2**	6.7	4.4	13.5	—	—	—11
		8 D	1.1	**6.9**	3.9	2.1	4.2	—	—	—10
J.S., 35 yrs, ♂	5	0		**8.1**	6.7	5.0	12.8	0	458	—34
Cirrhosis of liver		121 T	1-3	**6.5**	4.4	4.2	4.5	9	99	— 4
Myxedema	6	0		**7.6**	5.6	4.8	9.8	70	200	—24
		56 T	1-3	**6.8**	4.7	4.2	5.5	56	158	—10

*Cone readings in bold face type.

after feeding either thyroid extract or α-dinitrophenol. The type of response is similar to that observed with Vitamin A therapy, but it is accelerated. For example, in previous experiments[1, 2] patient J. C. required 250,000 to 500,000 I.U. Vitamin A daily for 2 months before normal values for dark adaptation were attained. In the present study such values were reached in 3 to 10 days after feeding of either thyroid extract or α-dinitrophenol.

In 4 out of 5 experiments the serum Vitamin A level was lowered by therapy. In the exceptional case (Exp. 5) a rise in serum A occurred concomitantly with a striking reduction in serum carotenoids from abnormally high to normal levels. It is possible in this case that the conversion of carotene to Vitamin A was facilitated by thyroid extract. This possibility is suggested by the studies of Fasold and Heidemann,[5] and of Clausen and McCoord.[6]

The mechanism by which the feeding of thyroid extract or α-dinitrophenol accelerates the rate of dark adaptation and lowers the visual thresholds is not clear. The fact that both substances bring

[5] Fasold, H., and Heidemann, E. R., *Z. ges. Exp. Med.*, 1934, **92**, 53.
[6] Clausen, S. W., and McCoord, A. B., *J. Pediat.*, 1938, **13**, 635.

about the same response suggests that the visual changes, like the basal metabolic rate, are functions of general metabolism. Similarly, it is known that the rate (although not the extent) of regeneration of visual purple *in vitro* is increased by raising the temperature of the system.[7] It may be stated, however, that maximal visual responses occurred in experiments 4 and 6 before changes in the basal metabolic rate took place. Moreover, no general correlation was found between the level of the basal metabolic rate and the speed or extent of dark adaptation in other subjects. In one patient with classical myxedema (B.M.R. −26) the dark adaptation was normal. In 4 control subjects, whose basal metabolic rates were −17, −19, −16, and −15, respectively, the dark adaptation curves were normal.

An increase in the circulating available Vitamin A does not account for the visual response, since in all experiments but one the serum Vitamin A fell to lower levels during therapy.

The improvement in speed and extent of rod adaptation was greater than that of cone adaptation. In this respect the response resembles that to Vitamin A therapy,[7] and is in contrast to the slight and equal lowering of the rod and cone thresholds observed to accompany recovery from anoxemia.[8] The changes appear, therefore, to represent an alteration in the speed and extent of visual purple regeneration rather than a local effect upon the nervous mechanism. The decrease in serum Vitamin A level accompanying the improvement in dark adaptation suggests that the feeding of thyroid extract or of α-dinitrophenol to these patients facilitated the utilization of Vitamin A by the visual mechanism.

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Hemolytic Effect of Gramicidin.

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Gramicidin, a bactericidal agent isolated by Dubos[1] from cultures

[7] Zewi, M., *Act. Soc. Sc. Fenn.*, 1939, New Series B, **2**, 1.

[8] McFarlane, R. A., and Evans, J. N., *Am. J. Physiol.*, 1939, **127**, 37; McDonald, R., and Adler, F. H., *Arch. Ophth.*, 1939, **22**, 1.

[1] Dubos, R. J., *J. Exp. Med.*, 1939, **70**, 1, 11; *Ann. Int. Med.*, 1940, **13**, 2025.