was discharged from the hospital three weeks after operation. Approximately six weeks after operation a post operative fundus photograph was secured. This is shown in the second illustration in which the peculiar “S” blood vessel may serve as a guide in orientation. The vision in this eye with correction has remained 20/25—and was so recorded when last seen, May 19, 1943. The fundus view does not show the areas of choroiditis which the multiple electro-coagulation punctures produce since these lesions are located a little more peripherally. A study of the post operative visual field is also included in this case report.

STUDIES IN DARK ADAPTATION AS A MEANS OF DETECTING DEFICIENCY OF VITAMIN “A”*

BY

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and

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The implication of a dietary factor in the production of a pathological state is determined by the use of certain “diagnostic criteria” (Yudkin, 1944a):

1. The demonstration of the existence of a deficiency of the dietary factor in subjects with the specified condition.
2. The production of the condition by a deficiency of the dietary factor.
3. The cure of the condition by replacement of the deficient dietary factor.

The use of studies of dark adaptation as a means of assessing nutritional status in respect to vitamin A is based on these criteria. It has been shown that:

1. Impaired dark adaptation is frequently found in groups whose diet is deficient in vitamin A (Jeans and Zentmire, 1936), (Harris and Abbasy, 1939), (Steven and Wald, 1941), (Hunt, 1941).

2. Experimental deprivation of the vitamin often results in a deterioration in dark adaptation (Booher et alia, 1939), (Hecht and Mandelbaum, 1939, 1940), (Wald and Steven, 1939), (Wagner, 1940), (Wald et alia, 1942).

3. The administration of vitamin A to individuals with poor

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Dark Adaptation as a Means of Detecting Deficiency of Vitamin "A"

Dark adaptation frequently results in improvement in dark adaptation (Hecht and Mandelbaum, 1939, 1940), (Wald and Steven, 1939), (Oldham et alia, 1942), (Wald et alia, 1942).

Beginning with the earliest reports of Jeans and Zentmire, (1934, 1936) in America and of Maitra and Harris, (1937) in England, many surveys of dark adaptation have been carried out amongst various groups, with a view to assessing the level of nutrition in respect to vitamin A. In some of these earlier studies, it had been thought that there was a narrow normal range of dark adaptation and that any value of the visual threshold beyond this range could be taken as presumptive evidence of deficiency in vitamin A. It became apparent, however, that the "normal" or rather average, range of dark adaptation was fairly wide. For example, the range of threshold of the completely adapted eye (the final rod threshold), was more than ten times or 1 log unit, so that in the general population, individuals with the best visual performance in the dark could perceive a light less than one-tenth of the intensity of that perceived by those with the worst visual performance. Two results emerged from these findings; first, that many individuals with poor dark adaptation were not improved with vitamin A and were thus presumably within the normal range, and second, that many individuals with only moderately poor dark adaptation and still apparently within the normal range, were improved with vitamin A. In other words, the normal range adopted by the earlier workers excluded some individuals with no deficiency of vitamin A and included some with such deficiency. As a result, workers have recently tended more to use the therapeutic test and to take as the criterion of deficiency the improvement of dark adaptation following administration of the vitamin (S. Yudkin, 1941, Steven and Wald, 1941). Thus, Steven and Wald diagnose deficiency by a "vitamin A-labile threshold," that is, one which improves by 0.3 log units (about two-fold) after administration of the vitamin; they do not attempt to define "normal" dark adaptation.

In conducting nutrition surveys in the field, however, it is not always possible or practicable to carry out the therapeutic test, which involves (i) the administration of doses of the vitamin for a period up to 3 weeks, (ii) the testing of dark adaptation before and after the administration of the vitamin and (iii) the use of some of the individuals as controls receiving "dummy" pellets. Nevertheless, it seems possible to adduce at least presumptive evidence of deficiency of vitamin A in groups of individuals without the necessity for determining the vitamin A-lability of their dark adaptation. If there is a significant difference in the average values of dark adaptation in two strictly similar groups, it seems
legitimate to conclude that the group with the inferior dark adaptation is, on the whole, probably at a lower level of vitamin A nutrition, provided there is no reason to suspect other causes for the difference. Such other causes include not only disease (retinitis pigmentosa, defective metabolism, e.g., hepatic cirrhosis, etc.) but also physiological causes, the most important of which is increasing age. It has been shown that there is a progressive deterioration of dark adaptation with age, amounting to about 0.12 log units in the final rod threshold for an increase of 10 years (Robertson and Yudkin, 1944), and it is necessary to allow for this in making comparisons of the dark adaptation of different groups.

It seems possible, therefore, to determine the probable relative status of different groups in regard to vitamin A by measuring their dark adaptation, provided there is present in none of the groups a pathological condition other than dietary deficiency which might affect their dark adaptation and provided that the groups are of similar age or that allowance is made for the difference in age. This presumptive method for detecting deficiency in vitamin A is clearly not so conclusive as that involving the therapeutic test. In addition, there is evidence that exceptions may exist to each of the three criteria enumerated above. First, a lack of correlation has been reported in certain surveys between the dietary vitamin A and dark adaptation (Thomson et alia, 1939), (Oldham et alia, 1942). Secondly, in some experiments, deprivation of vitamin A produced no deterioration in dark adaptation even after several months (Steffens et alia, 1939), (Isaacs et alia, 1940), (Dann and Yarborough, 1941). Thirdly, the improvement of impaired dark adaptation does not always occur, or occurs incompletely, following administration of vitamin A, even though the impairment may have been produced by dietary depletion of the vitamin (Hecht and Mandelbaum, 1940), (Hunt and Hayden, 1942). In view of these findings, it is sometimes suggested that studies of dark adaptation are of no value in assessing nutritional status in regard to vitamin A. However, these findings cannot vitiate the many positive results which have been accumulated and prove definitely that there is a relationship between vitamin A and dark adaptation. They do, however, indicate that this relationship is possibly more complex than is commonly accepted. For this reason, therefore, evidence of poor dark adaptation alone, such as we have suggested might be obtained for the comparison of the vitamin A status of different groups, must be accepted as a less certain criterion than if it is combined with evidence of improvement following administration of the vitamin.

In this paper are reported studies of dark adaptation of both
types, carried out since June, 1941, on some 1,500 individuals. In some of the studies, the effect of the administration of vitamin A has been observed; in the remainder, the relative values for the dark adaptation of various groups have been compared.

Technique

The instrument used was a modified and improved form of the adaptometer described in (Haines, 1938). Its reliability has been demonstrated by Yudkin (1941), Yudkin et alia (1943) and Robertson and Yudkin (1944).

The subject is instructed to look along a tube 14 inches long, whitened on the inside, which can be illuminated by a bright lamp for the preliminary bright adaptation. The 60 watt lamp in the original instrument was replaced by one of 75 watts; the bright adapting light is then of the order of 500 millilamberts. The test objects are arrows subtending an angle of 6 degrees at the eye, cut out of a plate at the further end of the tube. The plate may be rotated by the observer so that either a blank white surface is presented (for bright adaptation) or one of four arrows pointing in one of four different directions (for dark adaptation). The intensity of the test light, which illuminates the arrows from behind, may be controlled by a combination of neutral filters and a pair of polaroid discs. The two polaroid discs are arranged so that one may be rotated and thus reduce by a desired amount the intensity of the transmitted light. The neutral filters, of which there are three with transmission of about 1/10, 1/100 and 1/1000, are fixed on a rotating wheel with four apertures. Thus, by using the polaroid discs alone or in combination with one of the three filters, the illumination may be varied continuously over the range from about 10^7 down to 10^3 or less micro-micro-lamberts (i.e., from 7 to 3 log µµl).

1. Measurement of course of dark adaptation in individuals. (See Yudkin et alia, 1943.)

After a standard intensity and duration of exposure of a bright light, the minimal perceptible illumination is recorded at intervals over a period of 40 minutes. No difficulties have been experienced in doing this with adults or with children down to 9 years of age.

2. Measurement of final rod threshold in groups of subjects. (See Robertson and Yudkin, 1944.)

Groups of three or four subjects enter a dark room directly from their work, without any previous light adaptation. If other investigations are to be made on the same subjects, they may be
provided with goggles of a density of 3, i.e., transmitting one-thousandth of the incident light. A low-powered (25 watt) red bulb with a reflector may then be used at a table. This will provide enough light for the observer to work and, for example, to make records of clinical or dietary history, take samples of blood for the determination of haemoglobin, etc.

After the subjects have been in the dark for 35 or 40 minutes, the dark adaptation of each subject is measured by noting the minimal amount of light which he can just see.

The three or four subjects in each group are tested in turn and then tested a second time in the same order. It is the second value which is taken as the measure of dark adapting capacity.

In about 400 of the 1,500 subjects who were investigated, complete curves of dark adaptation have been determined. Since, however, the final rod threshold is the best single measure of visual performance of the dark adapted eye (Yudkin et alia, 1943), only values for this stage of adaptation are quoted in this paper.

Results

1. *Comparison of the dark adaptation of various groups.*

Because of the effect of age on dark adaptation, the results are presented in three parts. In the first are compared groups of school-children aged 9 to 12 years; in the second, groups of young adults aged 15-22 years and in the last, older subjects over 22 years.

*School children.*—In addition to children from the Cambridge Senior School who were included in the nutrition survey described elsewhere (Yudkin, 1944b), children from three other schools were examined. Two of these schools were in Cambridge and one in a village a few miles outside Cambridge. The results are shown in Table I, Fig. 1. It will be seen that the results were similar

<table>
<thead>
<tr>
<th>Table 1</th>
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<tbody>
<tr>
<td><strong>Mean dark adaptation values for children</strong></td>
</tr>
<tr>
<td>Group</td>
</tr>
<tr>
<td>School 1</td>
</tr>
<tr>
<td>School 2</td>
</tr>
<tr>
<td>School 3</td>
</tr>
<tr>
<td>School 4</td>
</tr>
</tbody>
</table>
DARK ADAPTATION AS A MEANS OF DETECTING DEFICIENCY OF VITAMIN "A"

DARK ADAPTATION OF SCHOOL CHILDREN

in all three Cambridge schools but were distinctly poorer in the village schools (School 4). These findings are interesting in view of the differences in economic level and diet of the children. School 1 was a Senior School in a fairly well-to-do part of Cambridge. School 2 was in one of the poorest areas of the town where many of the children were clearly undernourished. School 3 was a home for waifs and strays with which our laboratory had been in close contact for several years and in which the diet of the children was of a high standard. Nevertheless, there was no appreciable difference in the dark adaptation of the children in these schools. The slightly lower performance in School 3 is not significant with the small numbers studied (31). On the other hand, children from the village school, whose diet in respect of vitamin A might have been expected to be better than that of the town children, showed a significantly poorer dark adaptation.

Young adults.—One of these groups comprised Birmingham factory workers (see Yudkin, 1944c). The other groups of similar age were 100 Cambridge medical students, 95 students from one of the Cambridge women's colleges, 53 nurses from Addenbrooke's
Hospital (of a group which included 73 older nurses) and 28 workers from a Sheffield steel factory (of a group which included 32 older workers). A comparison of these groups shows that the nurses and both groups of students were equally good, and all were better than the two groups of factory workers (Table II, Fig. 2).

**Table II**

*Mean dark adaptation values for young adults.*

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Mean final rod threshold, log. µA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical students</td>
<td>100</td>
<td>3.19</td>
</tr>
<tr>
<td>Women students</td>
<td>95</td>
<td>3.17</td>
</tr>
<tr>
<td>Nurses</td>
<td>53</td>
<td>3.14</td>
</tr>
<tr>
<td>Sheffield workers</td>
<td>28</td>
<td>3.28</td>
</tr>
<tr>
<td>Birmingham workers</td>
<td>346</td>
<td>3.36</td>
</tr>
</tbody>
</table>

**DARK ADAPTATION OF YOUNG ADULTS**

Older subjects.—Owing to the fact that the effect of age on dark adaptation becomes increasingly evident with increasing age and that comparatively small numbers of subjects over the age of 22 years were comprised within each age interval, the values for the
older subjects have been compared with the average values for the Birmingham factory workers, which was the largest group examined (Yudkin, 1944c), (Robertson and Yudkin, 1944). The two groups which were thus compared with the Birmingham workers were the 73 older Cambridge nurses and the 32 older Sheffield workers. The results are shown in Figs. 3 and 4. On the whole, the dark adaptation of the Sheffield workers was about the same as that of the Birmingham workers, whilst that of the nurses was better than either group of factory workers. Of the 32 Sheffield workers, 16 were better and 16 worse than the average values for the Birmingham workers; of the 73 nurses, 43 were better and 30 worse.

DARK ADAPTATION OF OLDER SHEFFIELD WORKERS

Curve from Robertson and Yudkin, 1944: variation of dark adaptation with age in Birmingham factory workers.

Fig. 3.
2. Effect of vitamin A on dark adaptation.

Laboratory workers.—A small number (fourteen) of research workers and laboratory assistants received supplements of vitamin A in the form either of the vitamin itself (24,000 I.U. daily) or carotene (half a pound of carrots, containing about 20,000 I.U. carotene, daily). Details of the effect on the whole course of dark adaptation have been described elsewhere (Yudkin et alia, 1943). Taking a decrease of 0.20 log units in the threshold as the criterion of improvement it was found that the dark adaptation of 6 of these
subjects had improved after taking the supplements for three weeks (Table III). The proportion in this group which showed improvement was exceptionally high and has not been equalled in any other group studied. The reason for this is not clear: it may have been coincidental in view of the small number of subjects.

**Table III**

*Effect of Vitamin A or Carotene on Dark Adaptation of Laboratory Workers*

<table>
<thead>
<tr>
<th>Subject</th>
<th>Final rod threshold log µµL</th>
<th>Significant improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>1</td>
<td>3.45</td>
<td>3.45</td>
</tr>
<tr>
<td>2</td>
<td>3.35</td>
<td>3.00</td>
</tr>
<tr>
<td>3</td>
<td>3.30</td>
<td>3.00</td>
</tr>
<tr>
<td>4</td>
<td>3.35</td>
<td>3.15</td>
</tr>
<tr>
<td>5</td>
<td>3.50</td>
<td>3.40</td>
</tr>
<tr>
<td>6</td>
<td>3.60</td>
<td>3.60</td>
</tr>
<tr>
<td>7</td>
<td>3.20</td>
<td>2.90</td>
</tr>
<tr>
<td>8</td>
<td>3.10</td>
<td>2.90</td>
</tr>
<tr>
<td>9</td>
<td>3.25</td>
<td>3.30</td>
</tr>
<tr>
<td>10</td>
<td>3.10</td>
<td>2.90</td>
</tr>
<tr>
<td>11</td>
<td>2.90</td>
<td>2.90</td>
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<tr>
<td>12</td>
<td>2.95</td>
<td>2.95</td>
</tr>
<tr>
<td>13</td>
<td>2.90</td>
<td>2.90</td>
</tr>
<tr>
<td>14</td>
<td>3.10</td>
<td>3.10</td>
</tr>
</tbody>
</table>

Factory workers.—From October, 1941, until May, 1942, some of the Birmingham factory workers (see Yudkin, 1944c), were given vitamin pellets similar to those taken by the Cambridge school children; that is, they received a daily supplement of 5,000 I.U. vitamin A, 1 mg. vitamin B₁, 25 mg. vitamin C and 500 I.U. vitamin D (Yudkin, 1944b). When they were re-examined in June, 1942, it was found that many of those given the pellets had not taken them regularly. At the examination, therefore, each subject was asked in confidence whether he had in fact regularly taken the pellets and in the analysis of the results, those who admitted that they had not done so were included with those who had not been given the pellets. The analysis revealed that these 188 "controls" showed no appreciable alteration in dark adaptation (average improvement of 0.002 log units), whilst the 147 subjects who claimed to have taken the pellets regularly showed an average improvement of 0.073 log units. Statistical analysis
shows that the change in the vitamin group is significant whilst that in the control group is not. Taking again a decrease of 0·20 log units as an index of improvement and an increase of 0·20 log units as an index of deterioration, it was found that, of the control group, 58 improved, 71 were unchanged and 49 deteriorated; of the vitamin group, 73 improved, 46 were unchanged and 28 deteriorated. The difference between the results in these two groups is statistically significant.

School children.—At three of the schools where tests on dark adaptation were carried out, the effects of vitamin supplements were studied. The schools were the three Cambridge town schools described above (see Fig. 1). The first of these was the Senior School in which the survey reported previously (Yudkin, 1944b), so that the examination of dark adaptation was repeated, as were the other examinations, after half of the children had been given the multiple vitamin preparation for a year. The children from the other two schools were also divided into two groups, alternate children receiving daily for 3 weeks capsules containing 100,000 I. U. of vitamin A. In none of these schools did the supplements produce any alteration in dark adaptation.

Discussion

The comparison of the values of dark adaptation recorded in the last section suggests that both groups of factory workers are inferior, in respect of vitamin A nutrition, to the Cambridge students and nurses. In addition, the children from the village school appear also to be deficient in vitamin A when compared with children from the three Cambridge town schools.

The former result is in part confirmed by the fact that the administration of vitamin A to the Birmingham factory workers resulted in a significant improvement in dark adaptation. The results with the Cambridge school children are less directly confirmed by the absence of improvement in the town children following the administration of the vitamin.

The fact that the dark adaptation of the village children was inferior to that of the town children was surprising, especially since some of the latter were obviously of a low nutritional standard. Nevertheless, the fact that the general nutritional level of the village children was higher than that of the children of at least one of the town schools, whereas their dark adaptation was inferior, does not imply that this could not have been due to deficiency in vitamin A. It is quite possible that from a nutritional point of view, one group may be worse than a second in one respect and better in another respect. For example, the poorer dark adaptation of the Birmingham factory workers compared with the
Cambridge students and the fact that the former improved with vitamin A suggests that the workers were worse than the students in regard to vitamin A intake; nevertheless the haemoglobin values of the workers were higher (Yudkin, 1944c).

Summary

Measurements of dark adaptation may be used to assess nutritional level in respect of vitamin A either by the determination of the effects of the vitamin on dark adaptation or by the comparison of the values of dark adaptation in various groups. The latter method, while not providing such conclusive evidence as the former, may sometimes provide presumptive evidence of the relative nutritional status in respect of the vitamin, and for technical reasons it may be the only feasible procedure.

Using the former method of measuring vitamin A-lability it was shown that deficiency of vitamin A existed in a small group of laboratory workers and in a large group of Birmingham factory workers. Of these workers, 147 who took vitamin supplements showed a statistically significant improvement in dark adaptation whilst 188 "controls" showed no significant change. Three groups of school children showed no sign of deficiency of vitamin A by this method.

By comparing the values of dark adaptation in various other groups, it was shown that the Birmingham factory workers and a group of Sheffield factory workers had significantly poorer dark adaptation than groups of students and nurses. Similarly, a group of village school children had significantly poorer dark adaptation than the three groups of school children whose dark adaptation had been shown to be unaffected by vitamin A.

We are indebted to Messrs. Glaxo, Ltd., and to Messrs. British Drug Houses, Ltd., for generous gifts of vitamin A and multiple vitamin pellets respectively.

REFERENCES


SNAKE VENOM OPHTHALMIA*

BY

Major Harold Ridley, F.R.C.S.

R.A.M.C.

Spitting has long been recognised as a method of defence of certain African snakes and injuries to the human eye are not uncommon. Few cases have been reported in the literature, and in view of certain peculiar characteristics a single instance is perhaps worth recording.

It will be recalled that there are two families of poisonous snakes, the viperine and the colubrine. The viperine, exemplified by the puff adder, Gaboon vipers, etc., has long thin movable fangs not unlike hypodermic needles from the apex of which is ejected a venom which is chiefly haemolytic though to some extent also neurotoxic. The colubrine, or more correctly the sub-family elapine, exemplified by the various types of cobra has strong fixed fangs sometimes grooved as opposed to hollow from which is discharged a mainly neurotoxic venom. In general colubrines have narrow bodies and heads and are very active, while viperines have broad bodies and angular heads and tend to be sluggish—sometimes being trodden on by barefooted natives.

*Naja nigricollis*, the black necked cobra frequently incorrectly called the black mamba, is the usual spitting snake, though other African cobras, *N. melanoleuca*, *N. haje* and *N. goldii* have to a less extent the power to eject venom. All these snakes are exceedingly poisonous, the venom being second only in virulence among African snakes to that of *P. reticulatus* the true mamba, an elapine tree snake. Death from neurotoxic venom is due to respiratory paralysis and 1/5th grain is said to be fatal. Generally 10-20 times the fatal dose is injected if the fangs remain in the tissues for a few seconds.

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