4. There is no evidence that with this dosage there is any permanent damage to other tissues, so that sodium iodate may be regarded as a selective poison to the retina.

5. By means of the method of vital staining with Kiton Fast Green it is shown that the retina is damaged by iodate in the albino rabbit though no pigmentary disturbances are seen ophthalmoscopically.

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THE NATURE OF EXPERIMENTAL DEGENERATION OF THE RETINA

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In the preceding paper an account was given of pigmentary degeneration of the rabbit's retina induced by intravenous injection of 5 c.c. of 2 per cent. solution of sodium iodate. It was shown that the essential lesion was damage to the neuro-epithelium, the pigmentary changes being absent in albino rabbits, and that furthermore in doses effective for retinal damage, sodium iodate acted as a selective poison for the retina.

The selective action of sodium iodate on the retina, raised the question whether some specific retinal metabolic process was disturbed by this chemical. The possibility presented itself that the iodate—a powerful oxidising agent—destroyed or disturbed the

FIG. 3.

Rabbit's fundus showing fine pigmentary degeneration induced by intravenous injection of sodium iodate.

FIG. 4.

Rabbit's fundus showing massive pigmentary degeneration caused by repeated subcutaneous injections of sodium perborate.

highly reducing vitamin C, present in exceptionally high concentration in the retina. *In vitro* the amount of iodate used experimentally destroys 266 mg. of ascorbic acid (vitamin C)—a considerable quantity in view of the small amounts normally present in the body. The high concentration of vitamin C in the retina is seen from its distribution in some tissues in man (Bessey and King, 1933), adrenals 2.0, liver 1.2, ovaries 1.5, heart 0.8, brain 1.8, mg. per cent., compared with the value of 18.9 mg. per cent. (Nakamura and Nakamura, 1936, for the retina and choroid in the rabbit).

Tahata, 1937, found that in a large series of mammals and amphibians the vitamin C content of the retina was high for all animals, being highest in toads (28.9 mg. per cent.), and lowest in dogs (10.7 mg. per cent.). The average content of the retina is about the same as for the lens, where the rôle of vitamin C in metabolism is well recognised. In view of these facts, an attempt was made to inhibit the development of pigmentary degeneration in the retina by the administration of vitamin C in doses of 0.25 gm. intravenously for three days prior to the injection of iodate. The results were completely negative. In animals thus treated pigmentary degeneration developed with the same regularity as it appeared in untreated animals. The action of sodium iodate cannot therefore be due to the destruction of vitamin C with a consequent actual or relative vitamin C deficiency in the retina, for the animals were saturated with the vitamin. The possibility of the iodate interfering with the consumption of available vitamin C remains. Fig. 1 shows the typical pigmentary degeneration observed in a rabbit treated with vitamin C prior to the administration of sodium iodate.

The possible rôle of vitamin C in retinitis pigmentosa is further suggested by the following note for which I am indebted to Dr. E. C. Dax.

“Controlled estimations of the urinary vitamin C output were made on five female and two male mental defectives with retinitis pigmentosa.

The output in the females was measured on three successive days, 300 milligrammes of ascorbic acid being given on the third morning. Both the cases with retinitis pigmentosa and the controls showed a vitamin deficiency. Accordingly 50 mgms. a day of ascorbic acid were given to each for a month and the estimations repeated. Four of five patients with retinitis pigmentosa and two out of the six controls still showed a gross vitamin deficiency.

The males were given 50 mgm. of ascorbic acid each day for a month before similar estimations were made. Both the experimental cases and the controls still showed a vitamin deficiency. After having 300 mgm. of ascorbic acid on the next three mornings, the controls excreted over 50 per cent. more vitamin C than did the cases with retinitis pigmentosa in the following 24 hours.

Thus six of seven patients with retinitis pigmentosa as against two of nine controls showed a vitamin C deficiency after supplementary feeding, although all had been having similar food for some years."

Sodium iodate is a relatively stable compound, but the question arises whether it is as stable in the bloodstream as *in vitro*. This involved testing for the stability of iodate in blood *in vitro*, in plasma, and in the bloodstream of the intact animal. Oxidising agents liberate free iodine from iodides in solution: the persistence of sodium iodate can therefore be shown by a blue colour when sodium iodide is mixed with a solution of starch to which a drop of dilute hydrochloric acid is added, and this mixture brought in contact with the fluid suspected of containing iodate. Both blood *in vitro* and plasma to which iodate in minute quantities (smaller than the amount that would be contained in a corresponding quantity of blood withdrawn from a rabbit previously treated with 5 c.c. of 2 per cent. solution of sodium iodate injected intravenously) did not destroy the iodate, for such blood and plasma still gave a distinct blue colour when added to a solution of sodium iodide and starch. It was otherwise with blood withdrawn from the rabbit after injection of sodium iodate. At least 20 drops of such blood withdrawn immediately after the injection of iodate were required before a doubtful blue colouration could be obtained in the test for iodine. The test repeated 10 minutes and 20 minutes later was completely negative. It would therefore appear that the iodate is immediately broken up in the bloodstream, and that its action on the retina is of an indirect character.

Another attempt at elucidating the nature of the action of sodium iodate was made by administering other oxidising agents to see whether a similar effect could be induced in the retina. The substances used were colloidal manganese dioxide, sodium perborate and potassium persulphate. The highest concentration of manganese dioxide that could be obtained in solution was 0.35 per cent., and with this concentration massive doses would have to be injected to obtain a quantity equivalent to the effective dose of sodium iodate. Repeated injections of smaller doses (7 c.c., 10 c.c., 12 c.c., 15 c.c., intravenously on four successive days, the last dose being combined with 20 c.c. injected intra-muscularly) gave a completely negative result. The use of sodium perborate and ammonium persulphate intravenously proved unfeasible, as 5 c.c. of the solution containing the equivalent amount of 2 per cent. sodium iodate (4.72 per cent. and 6.9 per cent. solutions respectively) were lethal, instantaneously in the case of perborate and within half-an-hour with persulphate. Persulphate also proved lethal when injected subcutaneously. Perborate was tolerated subcutaneously; 20 c.c. of the saturated solution were injected on two occasions at an interval of a week. Ten days after

the first injection there was some lack of lustre in the area below the opaque nerve fibres; peripheral pigmentary changes were observed four days later, when a further subcutaneous injection of perborate of the same dose and concentration was given, to be followed by two more at weekly intervals. In all, five injections amounting to 100 c.c. were thus administered over a period of five weeks. Definite ophthalmoscopic changes were present, as already noted, by the end of the first fortnight: these gradually intensified and the appearances seen in Fig. 4 illustrate the condition after two months. These changes are different from those obtained with septojod or sodium iodate; instead of appearances simulating retinitis pigmentosa, the lesions bear some resemblances to an inflammatory reaction.

The suggestions that emerged from these findings were that iodate probably acts by virtue of its oxidising properties, and that the different appearances of the perborate lesion were probably due to the different rate of action, perborate in the doses and method used taking longer to induce visible changes.

What significance these findings have in the interpretation of the range of pigmentary changes seen clinically, is difficult to assess. That two different oxidising agents should produce changes simulating retinitis pigmentosa in one case and chorio-retinitis in the other, raises the question as to whether clinically observed pigmentary changes with their great ophthalmoscopic variations, are not fundamentally identical lesions, modified by a different rate of development. There is no inherent improbability in the suggestion that retinitis pigmentosa is caused by an inborn metabolic disorder and chorio-retinitis by comparable tissue-poisons introduced extra-neously.

These results and observations are offered with considerable reserve. The work recorded presents the basis of a wider experimental study which is now indefinitely postponed. The results described have not been checked and they are published as a preliminary and unverified note.

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