THE BRITISH JOURNAL OF OPHTHALMOLOGY

SEPTEMBER, 1932

COMMUNICATIONS

RECURRENT INTRA-OCULAR HAEMORRHAGE IN YOUNG ADULTS (EAL'S DISEASE)

Being an account of the Disease, a Summary of
the Literature, a Report of Five Cases, and some
Speculations as to the Aetiology

BY

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Summary of the Literature and Historical Remarks

ALTHOUGH it is usually stated that Eales first defined this group of cases, it appears that von Graefe recognized the group 25 years before Eales' first publication. In 1855 von Graefe¹¹ (quoted from Krauss¹⁵) mentioned the disease, describing periodical intra-ocular haemorrhages in young individuals who had often had previous epistaxis.

In 1880, Henry Eales⁸ of Birmingham, published his first paper on "Cases of Retinal Haemorrhage Associated with Epistaxis and Constipation."

He described five cases of recurrent retinal and vitreous haemorrhage, all in young men, their ages ranging from 14 to 29 years. The fifth case differs from the others in many respects and is introduced "as a contrast." The other four were lads, the subjects of epistaxis and constipation. Eales described "symptoms of high arterial tension, such as slow pulse, and accentuation of the heart sounds." Two had traces of albumen in the urine, but no casts. In all the cases the left eye was mainly affected; in only one, was

the right eye also affected. He found no evidence of constitutional disease of any sort. He attributed the condition to a neurosis affecting the circulatory organs and digestive system, leading on the one hand to partial inhibition of the bowel movements, and to a vasomotor contraction of the vessels of the alimentary canal, causing dyspepsia and constipation, and on the other hand to a compensatory dilatation of the systemic capillaries, especially those of the head, and, in these cases, of the retina, with a tendency to rupture on the occurrence of any intensifying cause. He suggested that the limitation of the haemorrhages to the nose and the retina was due to a lack of counterpoising support in these situations.

Eales attributed the occurrence of the haemorrhages mainly in the left eye, to the facts that the left carotid artery arises more directly from the aortic arch than the right, and that the course of the left innominate vein is more lengthy and indirect than the right; these circumstances producing slightly greater capillary tension on the left.

He suggested that females are saved from this type of intra-ocular haemorrhage by menstruation.

In one of Eales' cases, vision in the left eye was completely lost through the occurrence of glaucoma.

Jonathan Hutchinson¹⁴ in 1880, a few months after Eales' publication, described a case of primary intra-ocular haemorrhage in the left eye, followed after a long interval by haemorrhage into the right eye. The left eye was excised as the condition was complicated by glaucoma. The right eye was affected over two years later. There were repeated relapses of haemorrhage in the right eye, but glaucoma did not occur. On one occasion a retinal vessel actually ruptured while the eye was being examined. The left eye, after excision, showed haemorrhages in the vitreous, between the retina and the vitreous, in the ciliary processes and in the retina near the disc.

This case and one other, described by Hughes¹⁵ in 1929 are the only two discovered in the literature in which it was possible to dissect an eye affected by this condition.

This (Hutchinson's) patient suffered from epistaxis and constipation; there was no sign of constitutional disease, but there was a strong family history of gout.

Hutchinson attached importance in these cases to "inheritance of the gouty state," and disagreed with Eales on the importance of constipation as a starting point.

In an appendix he described in less detail four other cases, in one of which there was a suspicion of syphilis.

In 1882 Eales⁹ published another paper on "Primary Retinal Haemorrhages in Young Men." He suggested the designation

"Primary Recurrent Retinal Haemorrhage." He outlined again the characters of the disease and described lassitude and dyspepsia as occurring in all his cases; he did not support Hutchinson's view of the gouty diathesis as a cause.

No fresh cases were found in 12,000 patients treated at the Birmingham and Midland Eye Hospital in one year.

The retinal haemorrhages were described in more detail as large and round, or irregular; *not* flame shaped; and as a rule, confined to the periphery of the retina, near the veins. Vision only suffered in proportion to the vitreous opacity, which often cleared very rapidly between attacks. The ultimate results were large, whitish glistening patches in the periphery of the retina, and branched vitreous opacities. Small retinal detachments occurred sometimes.

Glaucoma occurred in one case.

Eales referred to three further cases, less fully investigated, which confirmed his previous views.

Nieden¹⁹ (quoted from Krauss¹⁵) in 1882 reported that in 34,489 consecutive eye cases in 8 years 6 months, he found only six patients suffering from idiopathic recurrent vitreous haemorrhage. In three cases the second eye was not affected; in the other three, both eyes were affected alternately. He did not agree with Eales that the left eye was mainly affected, nor with Eales' argument to explain this. Of the nine eyes affected in his six cases, five were right and four left. There was no history of syphilis or tuberculosis; they were not constipated, but lacked appetite and energy. He believed the haemorrhage was from the choroidal vessels.

Mayweg¹⁶ (quoted from Krauss¹⁵) in 1889, reported the case of a boy, aged 17 years, who lost his left eye as a result of intra-ocular haemorrhage and detachment of the retina. The right eye was subsequently affected by haemorrhage, which was stopped by ligature of the right common carotid artery.

Henry¹² in 1894, described a typical case in a young man, aged 19 years, of "effeminate type," who had recurrent intra-ocular haemorrhages. The right eye was affected, the left remaining normal. He suffered from headache, constipation and epistaxis. He had several recurrences in four months, but in one year the vision had recovered to 6/8. The retinal haemorrhages were chiefly peripheral; the vitreous haemorrhages cleared quickly. Glistening white patches remained in the retina.

Krauss¹⁵ in 1908 reported a case in a young man, aged 23 years. The right eye alone was affected; he suffered from constipation, but never from epistaxis. Recurrent vitreous haemorrhages were frequently preceded by violent headaches. Rapid recovery of vision took place between attacks. Areas of "choroiditis" and vitreous veils were left by the disease.

Krauss suggested the existence of a condition of local disease or weakness of the retinal or choroidal vessels, permitting rupture when other conditions were favourable. He stated that in individuals liable to epistaxis, the vessels of the nasal mucosa are near the surface, possibly with degenerated walls, and bleed easily. He suggested that such a condition might exist in the choroidal capillaries in the subjects of this disease. Any exciting cause, producing change in blood pressure (as indicated by severe headaches preceding the attacks in the above case) might then cause rupture of the weak vessels.

In this paper, Krauss quotes von Graefe¹¹ and Eales;⁸ also Nieden¹⁹ and Mayweg.¹⁶

Noll²⁰ (quoted from Finnoff¹⁰) in 1908, first suggested that the disease might be due to a tuberculous process.

Axenfeld³ (quoted from Finnoff¹⁰) in 1910 also suggested that these cases were often due to tuberculosis although no apparent tuberculous changes were present elsewhere in the eye; the lesions were due either to the bacilli themselves or to their toxins. The patients were frequently robust. Tuberculin was used for diagnosis and treatment, and improvement frequently followed its use.

Davis⁷ in 1912 reported a case in a young man, aged 22 years, the subject of dyspepsia but not of constipation. He had recurrent haemorrhages into the retina and vitreous of each eye, which began in the right. Within a year he lost the vision of the right eye almost completely, due to irreparable damage done by the haemorrhages; and the vision of the left eye was very seriously impaired, due to retinitis proliferans, and detachment of the retina. Davis observed "dense broad white bands" round the veins of the retina. There were some patches of white exudate between the veins.

In this case there were signs of kidney trouble at one time during the disease, shown by slight albuminuria, with many casts (red cells, granular and epithelial) in the urine; this however was only temporary, and the urine was again normal within three weeks.

Old tuberculin was used subcutaneously for diagnosis and treatment. General and local eye reactions resulted from the injection of 0.2 mgm. of old tuberculin, flushing of the sclera of each eye was observed.

Injections of human serum were tried without success.

Vitreous opacities, retinitis proliferans, and retinal detachment resulted from the disease. Davis concluded that tuberculosis was a definite aetiological factor, as also was indigestion and auto-intoxication. He considered that the haemorrhages arose from the retinal and not the choroidal vessels.

He favoured tuberculin and general hygienic management in the treatment.

Harrison Butler,⁵ in a discussion on the subject in 1912, quoted Axenfeld.³ He regarded a local reaction in the eye, following the injection of old tuberculin (subcutaneously) as conclusive evidence of tuberculous aetiology. He thought it reasonable that this condition might be due to local or remote tuberculosis.

Bennett⁴ in 1913 reported the case of a woman, aged 23 years, with retinitis proliferans in the left eye and incipient retinitis proliferans and some small retinal haemorrhages in the right eye. He regarded it as a case belonging to this group although he makes no actual mention of occurrence, of epistaxis, or of constipation. The right vision was reduced to 6/24, and the left to 6/60. Treatment was of no avail until thyroid extract was given, when the eye condition improved greatly, and the right vision became 6/6 partly and the left 6/18.

Ziegler,²³ in 1912, also advocated the use of thyroid extract in treatment.

Zentmayer,²² in 1920, outlined the disease as described by Eales. He quoted four cases of his own; in all, the Wassermann reaction was negative; in two the von Pirquet test was positive. Coagulation of the blood was delayed in two cases.

In view of the constant age incidence, the frequency with which males are affected, the physical condition of lassitude, the cold hands, and asthenia, and the benefit derived from the use of thyroid extract, Zentmayer suggested a disturbance in activity of the ductless glands as a factor in the disease. Possibly the adrenals were deficient in activity causing lack of tone in the venules and predisposing to haemorrhage.

Zentmayer did not wholly reject tuberculosis as a cause but thought some other factor must be found.

Aubineau² in 1920 reported five cases of intra-ocular haemorrhage in adolescents (apparently falling into this group). These cases were in hospital at the same time and were treated by the deliberate induction of anaphylactic shock by the injection of serum at suitable intervals. The injections were given under the skin and beneath the conjunctiva. In three cases no satisfactory general reaction was obtained. One case appeared to be definitely improved by each general reaction. (see also Candiotti.⁶)

Finnoff¹⁰ in 1922 reported five male cases; three of these were over the age of 30 years; one, aged 42 years, was the subject of pulmonary tuberculosis. Another had some central nervous disorder, with paraplegia and loss of sphincter control. It does not seem quite clear that these cases should be included in the group.

Finnoff concluded that this was not a specific disease and that tuberculosis of the retinal vessels, especially the veins, was one common aetiological factor. A focal reaction to the tuberculin test proved this.

Adams,¹ in a discussion on the significance of retinal haemorrhages in 1922 did not agree that tuberculosis was an aetiological factor.

Candiotti⁶ in 1922, described the case of a girl, aged 17 years, the subject of pulmonary tuberculosis and of albuminuria, who had recurrent vitreous haemorrhages. Anaphylactic reactions were deliberately produced by the injection of various sera, with apparent benefit to the eyes. However a severe recrudescence of the pulmonary disease also followed the treatment.

Foster Moore¹⁷ states in his book "Medical Ophthalmology" that there is no satisfactory evidence that the condition is due either to tuberculous infection or is associated with functional albuminuria.

He refers to the case of a woman in whom recurrences of the haemorrhage tended to occur at the menstrual periods and who had already lost the sight of one eye. The ovaries were removed in the hope of arresting the haemorrhage; the periods ceased but the retinal haemorrhages persisted, and total blindness resulted.

Hughes¹³ in 1929, reported a case in a youth, whose eyesight had been previously passed in a Board of Trade test.

Both eyes were affected; recurrent haemorrhages occurred during a period of about 2 years. The left eye was chiefly affected, became blind and glaucomatous. Hughes removed this eye. The retina was completely detached by haemorrhagic subretinal exudate. There were many areas of haemorrhage in the choroid. There is no mention of microscopic examination. The general health was good. Nearly 3 years after the onset, the right vision (corrected) was 6/6.

Young²¹ in 1930 reported three cases of recurrent haemorrhage into the retina and vitreous in adolescents. One case showed deficiency in blood calcium, and seemed to benefit from the administration of calcium.

From this survey of the literature it is evident that many theories have been put forward to account for the occurrence of the haemorrhages in this group of cases, but no theory has been proved beyond doubt.

Many forms of treatment have been tried but no consistent success has been reported. Our ignorance of the cause of the disease must be the greatest obstacle to the discovery of effective methods of prevention and treatment.

General Account of the Disease

Incidence and Aetiology.—The disease is very rare. Niden¹⁹ found only six in 34,489 consecutive eye cases. Aubineau³ found eight in 25,000. It occurs in young men between the ages of 15

and 25 years. Women are not immune, but are affected much more rarely than men. In the cases reported in the literature the ratio is about nine to one.

Although one eye alone is first affected, the other one usually shows signs of the disease or is involved later. Eales⁸ found that the left eye was more often affected, but the cases reported in the literature show that both eyes are affected in the majority and cases in which one eye alone is affected are divided evenly between right and left.

The aetiology of the disease is still unknown; various theories have been put forward. Eales⁸ suggested a neurosis affecting the alimentary and circulatory systems. Hutchinson¹⁴ suggested an inherited gouty state. Delayed blood coagulation, deficient blood calcium, haemophilia, local weakness of the retinal or choroidal vessels, endocrine disorder, the effects of the tubercle bacillus or its toxins, and helminthiasis have at various times been suggested as the cause of the haemorrhages.

Precipitating causes of haemorrhage in the subjects of the disease are the recumbent position, coughing, sneezing and any sudden strain.

Morbid Anatomy and Pathology.—Very little is known of the morbid anatomy of the disease, as the necessity to remove an affected eye rarely arises. In only two cases in the literature has an affected eye been dissected; in each case the eye was removed because of glaucoma. The first case was described by Hutchinson;¹⁴ haemorrhages were found in the retina near the disc, in the ciliary processes, between the retina and the vitreous, and in the vitreous. The second case was described by Hughes,¹³ the eye removed showed the retina completely detached by haemorrhagic subretinal exudate and the choroid engorged with many areas of haemorrhage in it. No mention is made, in either case, of microscopic examination.

Clinical Features; Signs and Symptoms.—The subjects of Eales' disease are as a rule spare youths, fairly well nourished and apparently in good health, but they are very frequently lacking in spirits and energy. They have a poor appetite and often suffer from discomfort and flatulence after food. Constipation is common but not always present. They very often suffer or have suffered from attacks of epistaxis. Apart from these conditions there is no sign of constitutional disease; syphilis, haemophilia, anaemia, nephritis, heart disease and diabetes are not found. The blood is usually normal to all tests. The pulse is sometimes slow, the blood pressure low or normal. Functional albuminuria has occasionally been found. Some cases have suffered from pulmonary or lymphatic tuberculosis, but the relation of tuberculosis to the intra-ocular haemorrhages has not been conclusively proved.

The disease is characterised by the sudden occurrence of intra-ocular haemorrhage, for no obvious reason, producing dimness of vision. One eye is usually primarily affected and the patient may only notice this accidentally when the other eye happens to be covered. There is no pain or change in the external appearance of the eye.

The patient comes to the doctor and complains that a short time previously he noticed a mist, or floating shadows, before one eye; he may even describe a red glare, obscuring the vision of one eye. Frequently he takes little notice of the first attack, as he is but slightly inconvenienced by it; but the recurrence of his symptoms within a few days or weeks ultimately causes him alarm, and he seeks advice.

On examining the affected eye with the ophthalmoscope, it is found that the cause of the loss of vision is intra-ocular haemorrhage. The haemorrhages occur in the retina, and may or may not break through into the vitreous humour. Unless the macula itself is affected, which is uncommon, loss of vision seems to be in proportion to the degree of opacity resulting from haemorrhage into the vitreous. Quite extensive haemorrhages in the retina may not cause the patient to notice anything wrong.

It is often impossible at first to discover the full extent and characters of the retinal haemorrhages on account of the blood present in the vitreous. When the vitreous has cleared and the fundus can be examined, the retinal haemorrhages are found to be mainly peripheral, often situated near or beneath the retinal veins. They are less commonly seen near the disc or macula. The haemorrhages are usually large and irregular, often with serrated edges. Flame-shaped, striated, and punctate haemorrhages are seen, but not commonly. The haemorrhages show brown discolouration as they degenerate.

Semi-circular subhyaloid haemorrhages are sometimes seen.

White patches of exudate have been described, but are not common. A star figure at the macula does not appear. White bands along the course of the retinal vessels (usually the veins) are sometimes present at the periphery of the fundus.

Pigmentary disturbance is not seen, except at the site of old haemorrhages.

The retinal veins are usually dark, full and tortuous.

When the patient is first examined the vitreous chamber may be so full of blood that the fundus cannot be seen except at the extreme periphery. The vitreous then appears quite black when the ophthalmoscope is used, a dull red glare being seen by oblique illumination, or there may be numerous branched opacities in the vitreous, having the appearance of floating black cobwebs, between which a red reflex from the fundus is seen.

The conjunctiva, cornea, sclera, anterior chamber, iris, pupil, and lens are normal, unless such complications as glaucoma and iritis set in.

It is a curious characteristic of the disease that the blood in the vitreous is absorbed with surprising rapidity, the remaining opacities sink to the bottom of the vitreous chamber, leaving the upper part of the vitreous comparatively clear. Thus a vitreous haemorrhage may reduce the visual acuity suddenly to perception of light only or to counting fingers, but in two or three weeks vision may be restored almost to normal.

The course of the disease is characterised by recurrences of haemorrhage, which occur over a period of months or years. The second eye is very frequently affected. After the first attack, although vision may have been very much reduced, it may recover almost to normal within a few weeks. Then, suddenly, fresh haemorrhages occur, sometimes quite spontaneously, or as a result of a violent cough or sneeze, and vision is again greatly obscured by a large vitreous or subhyaloid haemorrhage. In spite of all treatment, recurrences may occur for several years with depressing regularity. They are sometimes accompanied by deterioration in the general health, recurrence of dyspepsia, constipation, epistaxis and bradycardia, and finally, again for no obvious reason, the haemorrhages cease.

The final condition of the eye, or eyes affected, after the haemorrhages have ceased, depends on the magnitude and number of the haemorrhages and the resultant damage to the eye, the extent to which they are absorbed and the presence or absence of complications.

The vitreous haemorrhages may clear almost completely, but as a rule some opacity remains. There may be a diffuse haze, or there may be branched floating opacities, attached in places to the retina. The vitreous opacities often sink to the bottom of the vitreous chamber. Subhyaloid haemorrhages are usually absorbed completely.

The retinal haemorrhages undergo gradual absorption; they may leave behind them pigmented patches or glistening white areas of atrophy in the retina. Veil-like opacities may come forward from the retina into the vitreous, carrying with them delicate newly-formed blood vessels.

Complications.—Retinitis proliferans is probably the commonest complication and is often described in the literature. White bands of connective tissue form on the retina and in the vitreous.

Detachment of the retina is fairly common and is a great menace to vision after the haemorrhages have ceased. It is associated with retinitis proliferans, the contracting bands of connective tissue pulling on the retina and detaching it.

Chronic glaucoma and iritis are uncommon complications.

Glaucoma has been reported in two cases in the literature and iritis in one.

Prognosis.—The disease is confined to the eye and is not necessarily associated with any constitutional disorder. There is therefore no danger to life.

The immediate prognosis as regards vision is bad. Both eyes are usually affected, one less severely than the other.

Recurrences are likely to occur for months or years, with greater or less obscuration of vision. Between the attacks, vision may return almost to normal.

The ultimate prognosis, as mentioned before, depends on the magnitude of the haemorrhages and their damage to the retina and vitreous; the duration of the disease and the occurrence of complications. A number of large haemorrhages may do irreparable damage to the eye, producing extensive scars in the retina and permanent opacities in the vitreous. On the other hand, very large vitreous haemorrhages, if not too frequently repeated, may be almost completely absorbed and good vision recovered. However, even if this occurs there is grave danger that the retina may be detached by the growth and contraction of fibrous bands attached to it, and the eye is almost certain to become blind in time. The eye may be lost through the occurrence of chronic glaucoma while the disease is still progressing, but this is uncommon.

Diagnosis and Differential Diagnosis.—Eales' disease is very rare, and before the diagnosis is made in a case of recurrent intra-ocular haemorrhages in a young adult, it is necessary to exclude a number of other conditions in which such haemorrhages may occur. Such conditions are nephritis, diabetes, the anaemias, leukaemias, purpuras, and syphilis. The stools should be carefully searched for the ova and segments of parasitic worms, since retinal haemorrhages are frequent in cases of bothriocephalus anaemia. However, anaemia is not the rule in Eales' disease, whereas it is always present in cases of retinal haemorrhage caused by worms in the alimentary canal.

Subcutaneous injections of Old tuberculin have been used for diagnosis; a focal reaction in the eye, with flushing of the bulbar conjunctiva being taken as evidence of tuberculous aetiology.

Trauma should, of course, be excluded as a cause and the possibility of malignant intra-ocular growths should always be borne in mind.

Treatment.—No consistently successful method of treatment has yet been discovered.

(a) *Local Treatment.*—This consists of giving the eyes complete rest so long as the haemorrhages continue. Reading should be

forbidden and dark glasses ordered. It is probably wise to keep the eyes under the influence of atropine while the disease is active.

Both hot and cold applications have been used with the object of promoting absorption of the blood. Subconjunctival injections of dionine and saline have been tried, without great success.

(b) *General Treatment*.—The patient should not be allowed to work while the disease is progressing. It is advisable to give complete rest in bed while the general investigation is being done. At the same time it is possible to judge whether complete rest is beneficial to the patient. In most cases it seems better to allow and encourage reasonable exercise; confinement to bed tends to increase mental depression and lassitude, and low spirits are common characteristics of the disease. Moderate exercise will increase the appetite which is often poor and possibly aid the sluggish digestion. Moreover, it is usually found that the haemorrhages occur just as frequently when the patient is in bed as when he is up and about. On the other hand, strain of any sort, physical or mental, should be avoided. A "change of air" is probably beneficial if the patient becomes depressed by the tedious course of his disease.

General hygienic measures should be adopted; the constipation corrected by the use of mild laxatives and an occasional saline purge if necessary. Every effort should be made to improve the appetite and digestion by suitable diet and the use of bitter tonics.

Thus far and no farther, can one go in the treatment with any confidence of definitely doing good. Various other forms of medical treatment have been tried. Potassium iodide has been given, in the hope of promoting absorption of the haemorrhages. Thyroid extract has been administered, and several writers have found it beneficial.^{4, 22, 23.}

When the blood calcium is reduced, calcium and parathyroid extract may be tried;²¹ indeed this treatment has been employed even when the blood calcium was normal, as it usually is.

Injections of human serum have been used;⁷ and apparent success has been reported from the deliberate production of anaphylactic shock by the injection of anti-diphtheritic serum.^{2, 6.}

The injection of Old tuberculin in cases giving a local or general reaction to the intradermal or subcutaneous test may be tried.^{7, 10.}

The galvanic current, applied locally to the eye, has been used.

Report of Five Cases (for full notes, see Appendix)

The cases investigated have all been treated as in-patients in the Ophthalmic Ward at St. Bartholomew's Hospital, London. One of the cases was admitted and treated while the writer was

House Surgeon to the Ophthalmic Department. (This case is still under observation, as the disease remains active.) The records of the ophthalmic cases for the past 7 years 6 months (*i.e.*, from December, 1923 to May, 1931, inclusive) were examined and the notes of the four other cases discovered. Of these four cases, three have attended hospital as out-patients since their discharge and further notes have been made of their condition from time to time. Of the three who have attended as out-patients, two were recently re-examined by the writer, the third could not be traced, and has not been seen at the hospital for nearly four years.

The fourth patient, who has never attended as an out-patient since his discharge, has been examined at intervals by Mr. Arthur Cooke, at Addenbrooke's Hospital, Cambridge. I am greatly indebted to Mr. Cooke for his kindness in giving me further notes of this case.

The following are the important facts about the five cases collected:—Five cases of Eales' disease were admitted to the Ophthalmic Ward in 7 years 6 months, during which time 2,559 eye cases were admitted to the hospital. (1,255 males and 1,304 females.) These figures, however, are practically valueless, since all five cases were sent to the hospital from considerable distances in the country, as cases of exceptional interest, for investigation.

The age of the patients at the onset of the disease was between 17 and 25 years.

Four cases were males, one female.

Two patients were definitely lacking in spirits and energy.

In two there was a history of epistaxis; in one other case epistaxis occurred during the course of the disease, although it had never happened before. In one case there was no epistaxis; and in one it is not mentioned. In no case was there any other tendency towards prolonged bleeding or bruising. In no case was constipation present. Discomfort and flatulence after food were complained of in two cases. Frontal headache was a feature in two cases, and was present occasionally in a third. Bradycardia was not present except in one case, in which the pulse frequency was usually about 60 in the mornings but more rapid in the evenings. The blood pressure was within normal limits in each case.

In no case was any sign of tuberculosis found. An intradermal tuberculin test was done in the worst and most recent case, and was negative. In one case only was there a family history of tuberculosis, a sister being suspected of pulmonary infection.

There was no suspicion of syphilis, congenital or acquired, in any case. The blood Wassermann and Sigma reactions were negative in each case.

Urine examinations and the blood coagulation time were normal in each case.

Blood counts were done in four cases and were found normal.

The blood platelets, blood calcium and bleeding times were estimated in two cases and also found normal.

No case had had any previous trouble with the eyes.

In all five cases both eyes were involved to a greater or less extent; in two cases, in the less affected eye, one small retinal haemorrhage was the only discoverable sign of disease.

In one case (the worst) both eyes were affected equally; in another case the left eye was mainly affected, and in the other three the right eye was mainly affected.

Vitreous haemorrhage occurred in all cases; in three, only in the eye chiefly affected, and in the other two, in both eyes.

In one case the vitreous haemorrhage was slight and the vision after recovery was good. In the other four cases the vitreous haemorrhages were large and the vision after recovery very poor. (In the case in which the disease is still active, the final result is of course not known, but it seems certain that vision will be very poor.)

The retinal haemorrhages in three of the cases were mainly peripheral; in two the haemorrhages were situated both near the disc and at the periphery. The haemorrhages were in two cases large and irregular; in three small and circumscribed. Flame-shaped and striated haemorrhages were not seen.

The retinal veins were full, dark and tortuous in one case. In another, they were surrounded by thin white bands near the periphery. Apart from this the retinal vessels were normal.

In each of three cases, a patch of white exudate was seen in the retina.

The total period during which the haemorrhages took place, varied from six months to four years. From three to five recurrences of haemorrhage occurred as a rule; except in the case of the patient most recently seen whose disease is still progressing and who has already had repeated haemorrhages in both eyes. One patient, whose disease lasted two years, is known to have been free from haemorrhages for three years. Another, who had recurrences for four years, has now been free for two years.

In three cases in which large vitreous haemorrhages occurred, permanent vitreous opacity has resulted; vision was reduced in the affected eye to 6/60 in one case and to even less in the other two patients.

In the case in which the vitreous haemorrhage was slight the vision is now 6/6 in both eyes, three years after the last haemorrhage. What opacity is left in the vitreous, sinks to the bottom of the chamber, causing no disturbance of vision. A few veil-like

opacities with delicate new vessels project from the retina into the vitreous of the affected eye in this case.

Two other patients are now usefully employed at work which requires good eyesight; they rely on the less affected eye.

Complications, such as detached retina, chronic glaucoma, and iritis have not occurred so far in any case.

Discussion

The results of the investigation of these five cases, in the main, agree with the facts already established about the disease.

That the male sex is chiefly affected is confirmed, but the female sex is not immune. The age incidence, 17 to 25 years, is also in agreement with previous findings. The general characters of the disease in the cases investigated are the same as those previously described, except for a few minor points of difference. Constipation, for instance, was not a feature of these cases. The prognosis as regards vision in the eye chiefly affected is perhaps not so good as is indicated by some writers; gross vitreous opacities remained in at least three cases. No sign of tuberculosis was found in any of the patients.

The chief matter of interest in Eales' disease is its aetiology, which is still unknown.

Eales' own theory as to the importance of constipation and intestinal disturbances as a starting point, does not seem to have received much support. It is difficult to believe that a neurosis producing partial inhibition of the bowel movements and vasomotor contraction of the blood vessels of the alimentary canal could produce a compensatory dilatation of the systemic capillaries sufficient to cause rupture and haemorrhage in the eye, on the occurrence of any slight intensifying cause.

Deficiency in blood calcium, prolonged bleeding time and delayed blood coagulation, seem to be ruled out in almost every case in which these points have been investigated.

Zentmayer's theory²² that there might be disturbance of ductless gland activity, does not seem to have been tested sufficiently in actual practice. The fact that thyroid extract benefits some cases gives some support to the theory. Zentmayer suggested that adrenal deficiency might cause lack of tone in the venules and and predispose to haemorrhage. It would be interesting to try the effect on the disease, of injections of adrenalin or of ephedrin given by mouth.

The theory that tuberculosis is an aetiological factor lacks any concrete evidence in its support, and although several writers have

favoured the theory, none has offered any pathological explanation of the process whereby the tubercle bacillus, either by its local presence in the eye or by the toxæmia produced by its remote presence in the body, could produce the hæmorrhages characteristic of this disease.

Tuberculous toxin does not produce hæmorrhages in other parts of the body.

In any condition characterized by hæmorrhage, one must assume that there is an abnormality either of the blood vessels, or of the blood itself, or of both. In Eales' disease, there is so far no pathological evidence of either. Krauss¹⁵ has suggested a condition of weakness or local disease of the choroidal or retinal vessels permitting rupture when other conditions are favourable. If this is the case, why does the condition start so abruptly in adolescence, only to cease, also abruptly, after some months or years? If an abnormality of the blood causes the hæmorrhages, why does it affect only the eye and the nose? Is it because there is lack of counterpoising support in these situations? (as suggested by Eales), or do hæmorrhages occur, unrecognised, in other parts of the body?

It appears most likely that there is some abnormality of the blood, as yet unrecognized by pathological tests: it might be a deficiency of some normal constituent, producing reduced viscosity or altered osmotic pressure; or it might be the presence of some abnormal toxic constituent, absorbed from the bowel. The general condition of lassitude and low spirits, so common in the subjects of the disease, supports this view. Such a condition of the blood might conceivably have a harmful effect on the venules and capillaries of the body, so that they allow diapedesis to occur or even actual rupture. Foster Moore¹⁸ believes that most retinal hæmorrhages (not specially in Eales' disease) are brought about by diapedesis. Leakage of blood from the vessels in the eye would soon produce symptoms and easily recognized signs. It may be that the hæmorrhages occur only in the eye and the nose because of a lack of supporting tissue around the vessels in these situations.

Another possibility is that the disease might be a manifestation of vitamin deficiency, allied to scurvy. This idea was suggested by the frequency with which reported cases of Eales' disease have occurred in youths in some way connected with the sea; this circumstance can, of course, have no bearing on the matter in these days. In scurvy, epistaxis and constipation are common, conjunctival hæmorrhages not uncommon, but retinal hæmorrhages are quite unusual. There is nothing else suggestive of scurvy in Eales' disease.

Conclusions

1. The disease is rare, affecting young men between the ages of 17 and 25 years. The female sex is not immune.
2. Epistaxis is common, but does not always occur.
3. Constipation and dyspepsia are not invariably present.
4. There is no general constitutional disease, but a condition of lowered vitality is often present.
5. One eye is chiefly affected, either right or left, but the second eye is almost always affected to a greater or less degree.
6. The retinal haemorrhages are chiefly peripheral.
7. Vitreous haemorrhage is the rule, in the eye chiefly affected.
8. The prognosis as regards vision in an affected eye, depends mainly on the extent of the vitreous haemorrhages: large and recurrent haemorrhages tend to produce permanent opacities with much impairment of vision.
9. There is no satisfactory evidence that tuberculosis, either local or remote, is a cause.
10. The disease is probably due to deficiency in some blood constituent, or to the presence of some toxic product, causing damage to the endothelium of the smaller branches of the retinal vessels, with resultant diapedesis.
11. The occurrence of the haemorrhages chiefly in the eye may be due to the lack of supporting connective tissue around the retinal vessels.

Appendix

NOTES OF CASES

CASE I.—J. R., male, hatter. First attended the out-patient department on April 20, 1926, then aged 25 years. Admitted to hospital on April 23, 1926.

History: Eight days previously had noticed a black blur over the right eye. Four days previously, black blur changed to a green mist, which since then had been clearing. No previous trouble with the eyes; no bruising; epistaxis when younger; no jaundice; no constipation; no dyspepsia.

Examination: General physical examination revealed nothing abnormal. Blood pressure: 130 systolic, 80 diastolic.

Right eye: External examination, normal. Vision 6/12. Vitreous: blood was present, but the opacity did not greatly obscure the fundus. Fundus: two or three large irregular haemorrhages were seen in the retina near the disc, at its lower and nasal margins; two other elongated irregular haemorrhages were seen, one around the lower temporal vein and the other near the lower nasal vein. The haemorrhages showed brownish discolouration. A brownish elongated patch was seen on the nasal side of the disc, apparently the remains of an older haemorrhage. An elongated haemorrhage with brownish discolouration at its centre was seen directly above the disc, about two disc-diameters from it. The vessels, optic disc and macula were normal.

Left eye: Normal, except one small haemorrhage seen in the lower temporal quadrant of the retina. Vision 6/6. Blood coagulation time: normal. Wassermann and Sigma reactions: negative.

The patient was discharged after eight days in hospital. The right vision had improved to 6/9. Potassium iodide, grains v, three times a day, were given; also mild aperients. A fresh retinal haemorrhage appeared on May 21, 1926. On July 19, 1928, more than two years after the onset, there was a recurrence of symptoms, but no detailed note of ophthalmoscopic appearances was made. Since that time, no recurrence has occurred. The patient was examined again on April 21, 1931. He had no complaint and was following his occupation without difficulty. He suffered from indigestion but not from constipation. Vision was 6/6 in each eye. Greenish-grey opacities were seen in the lower part of the right vitreous chamber and greyish films projected into the vitreous from the retina; one of these veils was accompanied by delicate blood vessels. No fresh haemorrhages were seen, but a pigmented patch remained at the site of one of the early haemorrhages. The left eye was normal.

CASE II.—J. H., male, in "Naval Service." Admitted to ophthalmic ward on April 20, 1927, then aged 19 years.

History: One year previously, loss of vision in right eye; small specks in line of vision; clear in two weeks. Ten months previously, following excitement, a number of black specks appeared before the right eye. Admitted to Naval Hospital and treated by complete rest in bed. Very slight improvement; could only count fingers (with right eye) at this time. Left eye unaffected. Appetite and digestion good; no constipation; had only had one attack of epistaxis in his life; no headaches; no history suggesting syphilis or tuberculosis.

Examination: A healthy looking youth; general physical examination revealed nothing abnormal. Urine, normal; blood pressure: 108 systolic, 65 diastolic.

Right eye: External examination, normal. Vision 6/12. Vitreous: cloudy, with floating opacities (blood). Fundus: seen indistinctly; no visible haemorrhages in retina; disc, normal.

Left eye: External examination, normal. Vision 6/12. Vitreous: clear. Retina: several small haemorrhages in the temporal half and one patch of white exudate with a central pigmented area. Disc and macula normal. Blood count and coagulation time: normal. Wassermann and Sigma reactions: negative.

Treatment: Full diet: calcium lactate, gr. x, three times a day, and tab. parathyroid, gr. $\frac{1}{2}$, at night.

After three weeks in hospital the patient was discharged, not improved. He was examined again on May 22, 1927; there had been a recurrence of haemorrhage in the right eye and vision was reduced to finger counting; the right vitreous was completely opaque with blood. The left eye was as before, the vision being improved from 6/12 to 6/6 by correction of refractive error. On June 10, 1927, no improvement had taken place. Since this time the patient has not been traced.

CASE III.—W. M., male, assistant store-keeper. Admitted to ophthalmic ward on July 10, 1929, then aged 21 years.

History: Sent to the hospital by Mr. Arthur Cooke, of Cambridge, with the following notes:—Four years previously: while working as a stone mason, had a right vitreous haemorrhage; right vision reduced to finger counting. Three years previously: fresh effusion of blood in front of right retina. Two years previously: large floating opacities in both vitreous chambers. Five months previously: haemorrhage in left vitreous and retina; admitted to Addenbrooke's Hospital, Cambridge, under the care of Mr. Arthur Cooke. Blood count showed over 6 million red cells per cubic millimetre. Wassermann reaction: negative. Blood coagulation time: normal. Vision improved slightly to 6/60 (right) and 6/18 (left). One month previously: left vision reduced to perception of hand movements. Appetite good; digestion good; no constipation (epistaxis not mentioned). No history suggestive of tuberculosis or syphilis. A sister had been suspected of phthisis.

Examination: A healthy looking youth. General physical examination revealed nothing abnormal. Urine, normal; blood pressure: 124 systolic, 82 diastolic.

Right eye: External examination, normal. Vision 6/60. Vitreous: contained black branched opacities and many floating specks. Fundus; disc normal; several

small dark haemorrhages in retina on the temporal side, near an artery; on the nasal side was an oval white patch of exudate crossed by an artery.

Left eye: External examination, normal. Vision 6/12. Vitreous: contained many black opacities. Fundus: disc normal; above the disc was a large white patch with small haemorrhages in it; many small haemorrhages seen near the arteries; below the disc, a grey pigmented patch. Blood count and coagulation time: normal.

The patient was discharged after ten days in hospital; further notes supplied by Mr. Arthur Cooke stated:—"The patient has been well and at work since discharge; has complained of headache; no recurrence of haemorrhage. March 25, 1931, vision with glasses was barely 6/60 right and 6/12 left. In the right fundus, two broad white streaks, with small patches of pigment were visible in the temporal half, beyond the macula. The disc was normal. No marked opacities in the vitreous. In the left eye, vitreous opacities were well marked; the disc was pale with rather vague margins; a few faint pigmented patches were seen around the disc."

CASE IV.—A. A., female, clerk. Admitted on January 24, 1930, then aged 25 years. *History:* Three weeks previously: woke up one morning to find the left vision misty; the condition had remained ever since. Right vision normal. No headaches; no previous eye trouble; no dyspepsia; no constipation; no epistaxis. Had always been healthy. No history suggestive of tuberculosis or syphilis.

Examination: Healthy looking. General physical examination revealed nothing abnormal. Urine, normal; blood pressure: 130 systolic, 90 diastolic.

Right eye: External examination, normal. Vision 6/6. Vitreous: clear. Fundus: normal, except one small retinal haemorrhage discovered at the periphery at "6 o'clock."

Left eye: External examination, normal. Vision, less than 6/60. Vitreous: diffuse central opacity, with several smaller floating opacities. Fundus: only the periphery visible; a few white patches and many small haemorrhages, especially at 3 and 6 o'clock. Blood count, platelet count, bleeding time, coagulation time and blood calcium all normal. Wassermann and Sigma reactions: negative.

The patient was discharged after two weeks in hospital. She was examined again on March 7, 1930. The vitreous opacities (left) had sunk to the bottom of the chamber and a good deal of absorption had taken place. Two large irregular haemorrhages were visible in the retina, near the disc. The patient was sent for again and examined on April 21, 1931. She reported that the left eye was worse, one or two recurrences of symptoms having occurred after she was last seen. No change had taken place for several months. The right eye was normal so far as she could tell, and she was following her occupation without difficulty. General health, very good. The right visual acuity was 6/5 partly. The left visual acuity was reduced to perception of hand movements. The right fundus was normal except for some fine sheathing of the finer vessels, which was seen at the periphery, especially below. The left vitreous appeared to be full of blood; indirect illumination showing a dull red opacity behind the lens; the fundus was invisible.

CASE V.—G. J., male, dockyard worker. Sent to St. Bartholomew's Hospital, London, by Dr. Heath, of Rochester, Kent, who had observed "every variety" of retinal haemorrhage in both eyes and marked alteration in the calibre of the retinal vessels. Admitted on March 11, 1931, then aged 19 years.

History: Five weeks previously: vision became misty in both eyes, left worse than right; this became slowly worse. Admitted to Naval Hospital, Chatham, and then transferred to St. Bartholomew's Hospital, Rochester, for investigation. The vision improved slightly. Sent to St. Bartholomew's Hospital, London, for admission under the care of Mr. Foster Moore. No history of injury or pain; two months previously, eyesight had been tested; vision then 6/6 right and left. Appetite good; troublesome dyspepsia and distension after meals; no constipation; no epistaxis; no bruising or prolonged bleeding. No history suggestive of syphilis or tuberculosis.

Examination: Healthy looking youth, but low in spirits and lacking in energy. General physical examination revealed nothing abnormal. Urine, normal; blood pressure: 110 systolic, 70 diastolic.

Right eye: External examination, normal. Vision 6/36. Vitreous: contained very many dark floating opacities; the bottom of the chamber was full of these.

Fundus only visible at the extreme periphery, above and to the nasal side; large irregular retinal haemorrhages, with serrated edges were seen in these situations.

Left eye: External examination, normal. Vision 6/9. Vitreous: Full of floating opacities, appearing to hang down from above; the lower part of the chamber was quite black. Fundus only visible at the periphery above, and to the temporal and nasal sides; a large irregular retinal haemorrhage visible on the temporal side.

March 13, 1931.—Vitreous opacities had cleared somewhat; various and extensive haemorrhages visible at periphery of retinae. March 31.—Recurrence of haemorrhage in both eyes, in spite of treatment and rest in bed. Vision 6/60 right, 6/24 left. April 4.—Vitreous humour even more opaque, especially left. April 6.—Practically no red reflex from left fundus, owing to increased vitreous opacity. April 11.—Right vision, 3/60; left vision, perception of hand movements only. April 17.—First attack of epistaxis; this occurred spontaneously while in bed. Second attack occurred two days later. April 28.—Right fundus more clearly visible; large irregular retinal haemorrhages noted. Left vitreous full of blood. May 1.—Right vitreous more opaque again. The disease is still progressing in both eyes.

Pathological tests: Blood count, blood platelets, bleeding and coagulation times and blood calcium, all normal. Wassermann and Sigma reactions, negative. Intradermal tuberculin test gave no local or general reaction.

Treatment adopted: Full diet; complete rest in bed at first, until it was seen that this had no beneficial effect; the discomfort after meals soon disappeared. Potassium iodide by mouth was tried without success for three weeks. Calcium lactate and parathyroid were then given but discontinued when it was discovered that the blood calcium was normal. Thyroid sicca was then given by mouth in doses up to gr. i, t.d.s.

I am indebted to Mr. Foster Moore for his kindness in allowing me to use the notes of these cases.

REFERENCES

1. Adams, P. H.—*Trans. Ophthalm. Soc. U.K.*, Vol. XLII, p. 211, 1922.
2. Aubineau, E.—*Ann. d'Ocul.*, Vol. CLVII, pp. 412-417, 1920.
3. Axenfeld—*Bull. de la Soc. Belge d'Ophtal.*, Vol. XXIX, p. 115, 1910-11.
4. Bennett, H. P.—*Ophthalmoscope*, Vol. XI, p. 20, 1913.
5. Butler, Harrison.—*Trans. Ophthalm. Soc. U.K.*, Vol. XXXII, p. 179, 1912.
6. Candiotti—*Arch. de Méd. et Pharm. Nav.*, Vol. CXII, pp. 334-336. Paris, 1922.
7. Davis—*Trans. Amer. Ophthalm. Soc.*, Vol. XIII, p. 235, 1912-14.
8. Eales, H.—*Birm. Med. Rev.*, Vol. IX, p. 262, 1880.
9. ——— *Ophthalm. Rev.*, Vol. I, p. 41, 1882.
10. Finnoff, W. C.—*Amer. Jt. of Ophthalm.*, Vol. V, p. 195, 1922.
11. Graefe, von.—*Arch. f. Ophthalm.*, Vol. I, 1855.
12. Henry, R. W.—*Birm. Med. Rev.*, Vol. XXXVI, p. 225, 1894.
13. Hughes, C. A.—*Trans. Ophthalm. Soc. U.K.*, Vol. XLIX, p. 490, 1929.
14. Hutchinson, J.—*Trans. Ophthalm. Soc. U.K.*, Vol. I, p. 26, 1880-81.
15. Krauss, F.—*Ann. of Ophthalm.*, Vol. XVII, p. 58. St. Louis, 1908.
16. Mayweg.—*Bericht der Ophthalm. Gesell.* Heidelberg, 1889.
17. Moore, Foster.—“*Medical Ophthalmology.*” 2nd edition, p. 287, 1925.
18. ——— *Trans. Ophthalm. Soc. U.K.*, Vol. XLII, p. 225, 1922.
19. Nieden.—*Bericht der Ophthalm. Gesell.* Heidelberg, 1882.
20. Noll.—*Arch. f. Augenheilk.*, Vol. LXIII, p. 213, 1909.
21. Young.—*Arch. of Ophthalm.*, Vol. III, p. 117, 1930.
22. Zentmayer, W.—*Amer. Jt. of Ophthalm.*, Vol. III, p. 652, 1920.
23. Ziegler.—*Trans. Amer. Ophthalm. Soc.*, Vol. XIII, p. 253, 1912-14.