

THE BRITISH JOURNAL
OF
OPHTHALMOLOGY
FEBRUARY, 1926

COMMUNICATIONS

INFLAMMATORY PSEUDO-TUMOUR OF THE ORBIT*

BY

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THE term "inflammatory pseudo-tumour of the orbit" has a clinical rather than a pathological significance. It denotes a condition which outwardly resembles an orbital tumour—giving rise to proptosis, limitation of movement, increase in bulk of the orbital tissue and possibly swelling of the lids. The onset is slow and there are none of the usual signs or symptoms of inflammation. Frequently it is only when the orbital contents are submitted to microscopical examination that the true condition is revealed—and then not always with certainty as we shall see later. Macroscopically, the appearance of the orbital contents, if removed *en bloc*, may strongly suggest the presence of a tumour.

These cases are somewhat rare, and in a recent paper by Benedict and Knight⁽¹⁾ of the Mayo Clinic, it is stated that since Birch-Hirschfeld's⁽²⁾ original description in 1910 only five cases have been reported. One hopes that with further refinements in diagnosis the cases will become rarer still, since, by definition, only those cases which so closely resemble an orbital tumour as to be indistinguishable from it come into this category.

Though not strictly a pseudo-tumour, in that the condition was diagnosed and the eye saved, it may be of interest to refer to the case

*A paper read at a meeting of the Section of Ophthalmology, Royal Society of Medicine, February, 1925.

mentioned by Mr. Trotter, in the 1923 discussion on proptosis⁽³⁾. This case was sent to him by Mr. Harrison Butler with a history of prominence of the right eye for four years. The trouble began with some kind of inflammatory condition which subsided, leaving the proptosis which was thought to be increasing of late. Though there was serious reason to fear a slowly developing malignant growth the eye was left, and three years later Mr. Butler reported that vision and fundi were normal, though the proptosis was still severe.

With regard to cause, Benedict and Knight are inclined to attribute the occurrence of these pseudo-tumours to focal infection elsewhere in the body, such focal infections being overlooked as they produce no symptoms and no leucocytosis. This of course may be possible, but the evidence in each case would require very careful sifting. One cannot help feeling that the presence of a focal infection is no great rarity in otherwise normal individuals. I know for instance of a dental surgeon who has been nursing an apical abscess for the last few years. Its presence was discovered accidentally by X-rays, and as he has never had any symptoms referable to it, he has every intention of keeping the offending tooth unless such symptoms arise. I have no wish to underestimate the importance of focal infection, and the excellence of the results one has seen following its elimination, but one must avoid any tendency to making it a sort of scrap heap for otherwise undiagnosable types of disease.

Birch-Hirschfeld gave a useful classification of pseudo-tumours.

GROUP 1.—Those in which the recovery is spontaneous or occurs after the administration of drugs, such as potassium iodide, mercury or quinine.

GROUP 2.—Those in which an operation is performed and no tumour is found.

GROUP 3.—Those in which the macroscopical appearances of the orbital contents suggest the presence of a tumour, but the microscopical appearances show the tissue to be a chronic inflammatory mass.

The cases I propose to discuss are three in number, and I am indebted to the surgeons under whose care they were for permission to refer to them. The pathological examinations were carried out at the Central London Ophthalmic Hospital.

The first case occurred in a man, F.B., aged 25 years. He attended hospital on July 17, 1924, with marked proptosis of the right eye, and a lot of conjunctival injection. The movements were full and normal. Rhinological examination being negative and the proptosis considerable, he was ordered mercury and iodide without waiting for a Wassermann test. Three weeks later some

limitation was noted in the movement of the right eye, and the proptosis became more marked. The eye appeared to be otherwise normal and the vision with glasses was 6/12, the same as in the left eye.

He was taken into hospital on August 21, mercury inunctions and potassium iodide being continued for a further fortnight without any diminution of the proptosis. The condition was deemed urgent because the proptosis might be due to an orbital neoplasm. An exploratory incision was therefore made and revealed a hard

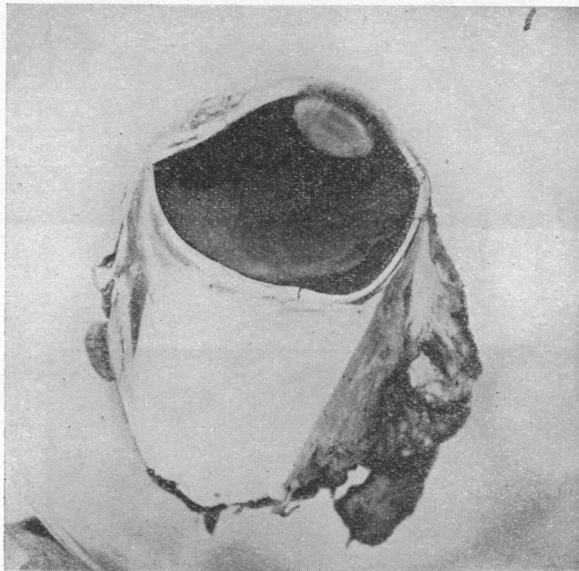


FIG. 1.

mass of tissue in the orbit and no pus. Exenteration was deemed advisable, and was performed on September 11, 1924.

Fig. 1 shows the general macroscopic appearances of the orbital contents. There is a large white mass within the cone of muscles moulded closely over the posterior surface of the sclerotic and completely surrounding the optic nerve.

A section of the anterior portion of the mass containing the optic nerve (Fig. 2) shows marked thickening of the dura which is in contact on one side with orbital fat, and on the other is continuous with the dense fibrous tissue mass. This section is stained with iron haematoxylin and van Gieson's stain, so that the fibrous tissue shows up conspicuously. The nerve itself does not seem to have been affected—the apparent separation of the fibres being an artefact produced during cutting of the sections.

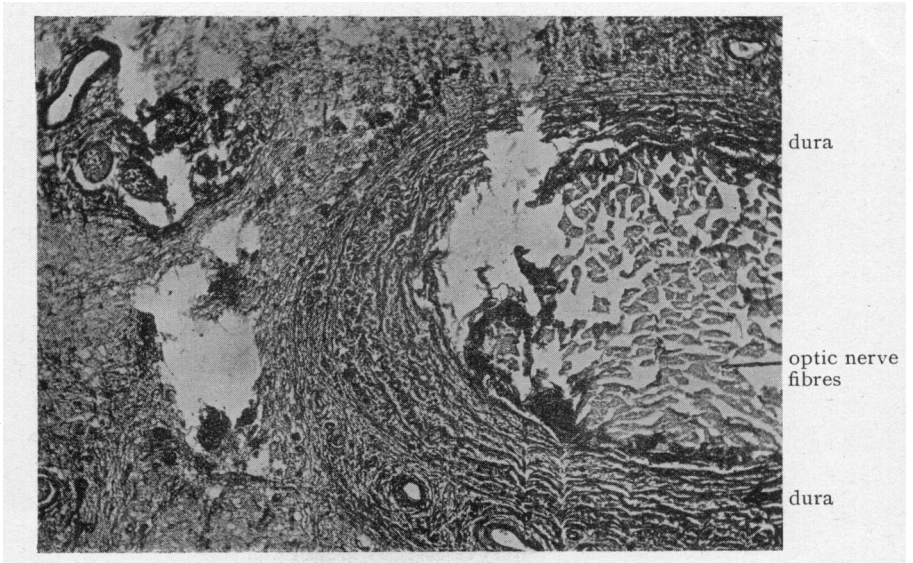


FIG. 2.

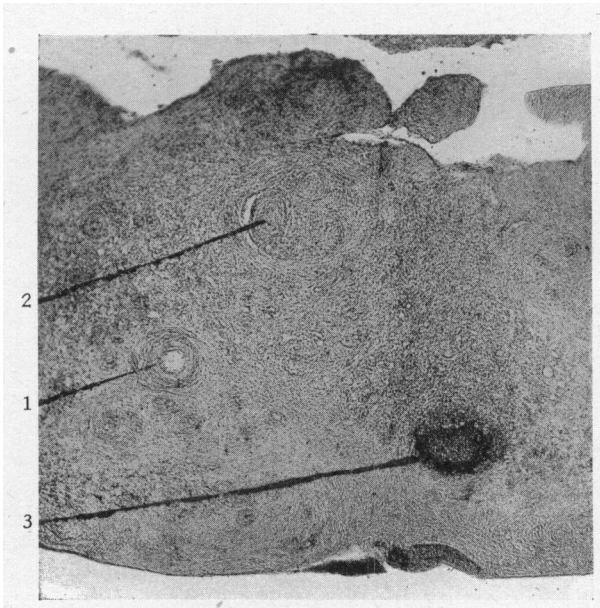


FIG. 3.

1. Vessel showing thickening of walls;
2. Obliterated vessels;
3. Focus of lymphocytic infiltration.

Fig. 3. The next section is fairly typical of the greater portion of the mass. It is stained with iron haematoxylin and van Gieson and is composed almost entirely of lamellae of fibrous tissue, staining deep red, with here and there, some foci of lymphocytic infiltration. An important feature of this section is the condition of the vessels. They show great thickening both of the intima and adventitia, in other words a definite endarteritis and periarteritis. In some portions, this condition has progressed to an extent sufficient to cause obliteration of the vessels. Areas of necrosis were conspicuously few. In parts the fibrous tissue had



Area of necrosis in muscle fibres.

FIG. 4.

rather an indeterminate and gummatous-looking structure, but the only area showing any definite break-down of tissue was in one of the muscles. This is shown in Fig. 4, where one notes a gap in the structure of the muscle surrounded by an infiltration of lymphocytes.

Summing up then, there can be little doubt that the apparent tumour in this case was a gumma so that the condition can be classified as an inflammatory pseudo-tumour.

It bears a strong resemblance to a case described by Hine in 1922⁽⁴⁾, when the orbit was exenterated and found to be occupied by a large mass of tissue. There was similar thickening and infiltration of the dura round the optic nerve, and the arteries showed extreme thickening. The mass also contained patches of lymphocytic infiltration. The opinion of the pathologist who

examined the slides was that "the tumour was a chronic inflammatory mass, the absence of giant cells making tuberculosis unlikely, and the presence of changes in the vessels suggesting a syphilitic origin." The Wassermann reaction was negative, and the condition was regarded as being possibly neurofibromatosis. With regard to the value of a negative Wassermann in tertiary syphilis, Harrison⁽⁵⁾ states the following :

"A negative report is of little value in excluding syphilis, since there is practically no stage of the disease in which 100 per cent. of positive reactions are obtained. Considering only the tertiary stage, it is stated that out of 255 untreated cases 98.4 per cent. were positive, if treated cases were included, the percentage fell to 83." These figures presumably apply to cases presenting clinical manifestations of active disease. "It is a very frequent occurrence to obtain a negative reaction in cases of syphilis where there is just one small lesion, as for example, an ulcer on the side of the tongue. . . . Help is sometimes obtained in doubtful cases by the effect of a provocative injection of salvarsan or one of its derivatives."

In view of this and the change described, I think one may regard this case as similar to the one I have described and as being an orbital gumma. A somewhat similar case is included in the paper by Benedict and Knight, where a mass was removed from the orbit. Microscopically, it was composed of fibrous tissue, infiltrated with lymphocytes collected into groups resembling follicles. Practically all the smaller vessels showed endarteritis, progressing in some parts to complete obliteration. Here again the Wassermann was negative. If this tumour were also in reality a gumma, it goes to show the immense clinical importance of this condition and to emphasize the necessity for a thorough anti-syphilitic treatment even in face of a negative Wassermann. An important case in this connection was alluded to by the late Mr. Johnson Taylor in the *Transactions of the Ophthalmological Society*⁽⁶⁾, where the administration of mercury had to be pushed to such an extent as to give the patient a diarrhoea resembling dysentery before the condition cleared up.

The second case occurred in a middle-aged man, who in December, 1922, consulted Dr. Hewkley, to whom I am indebted for the history. He had had influenza in February of that year and coincidentally severe hemicrania spreading down the left arm and left side of the chest. The pain was severe for three days, and finally ceased at the end of a fortnight. The patient could not say exactly when diplopia commenced, but had noticed inability to play bowls or snooker, at both of which he had been expert. When seen by Dr. Hewkley both eyes were prominent and the left showed definite proptosis, the vision with correction being 6/9,

while that of the right with correction was 6/6. The left fundus was normal, and there was paresis of the superior rectus and levator palpebrae; there was also some weakness in closure of the lid. As time went on this weakness increased and there was more marked chemosis and proptosis. Owing to the exposure of the cornea, due to the proptosis, a small ulcer developed on it. The

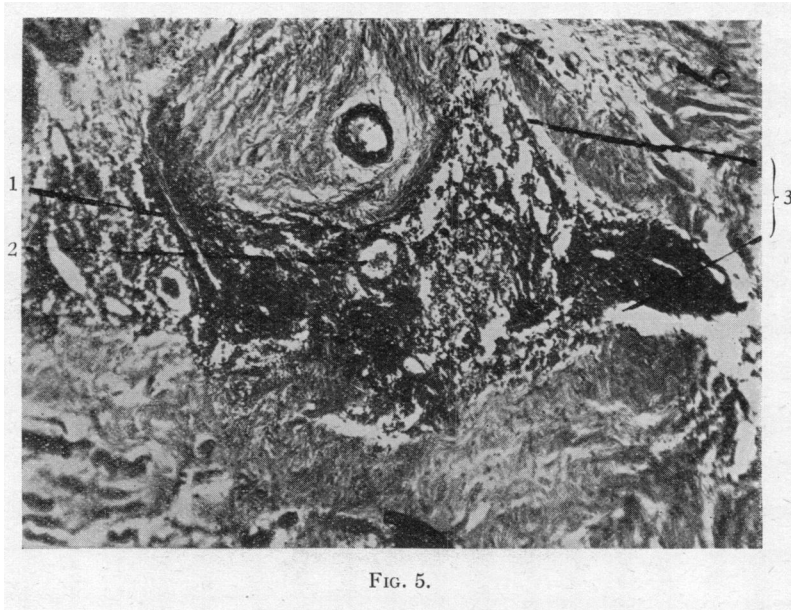
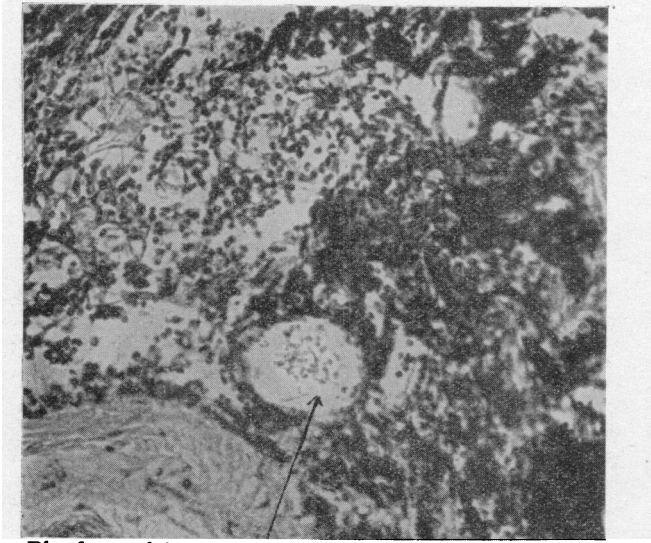


FIG. 5.

1. Vessel cut longitudinally; 2. Vessel cut transversely; 3. Patch of lymphocytic infiltration.

eye was eventually removed and the orbit exenterated as there was a strong suspicion of a malignant growth.

The orbital contents were removed piecemeal and small portions were embedded in paraffin and sectioned. There was nothing in the appearances to suggest a neoplasm and having recently read the article I have alluded to by Benedict and Knight, I was much inclined to make the diagnosis of inflammatory pseudo-tumour, especially when I came across a portion of tissue presenting the appearance shown in Fig. 5. There are three blood-vessels, one cut longitudinally, two transversely, and surrounding them is a fairly dense infiltration of cells which under the high power prove to be lymphocytes. It therefore appeared to be a clear case of some chronic blood-borne infection with the tissue reaction most marked around the blood-vessels. Closer inspection, however, revealed a somewhat different state of affairs. In the first place



Blood vessel in section, surrounded by lymphocytes and containing red blood corpuscles.

FIG. 6.

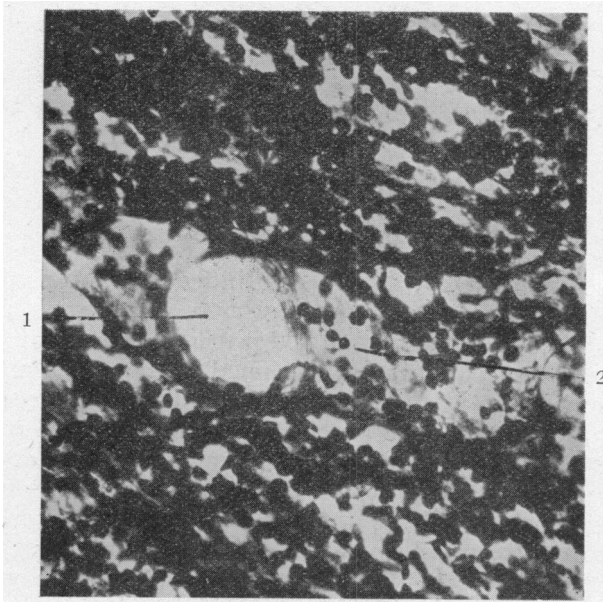
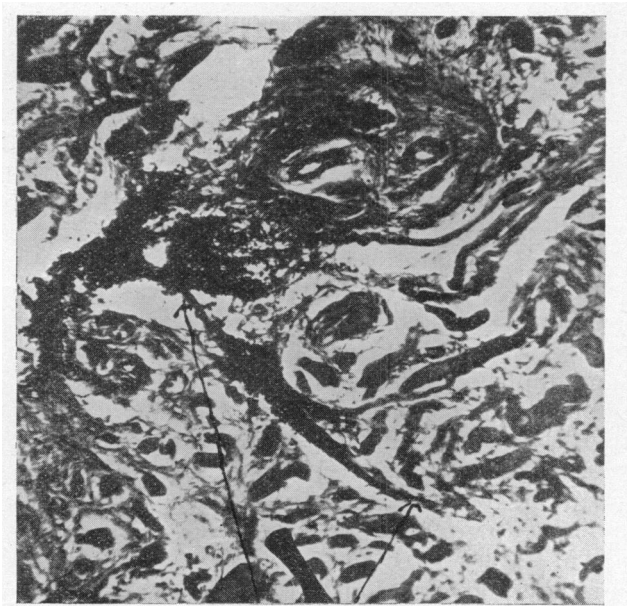


FIG. 7.

1. Transverse section of lymphatic vessel ;
2. Vessel passing obliquely through thickness of section.

(Fig. 6), the blood-vessels, though surrounded by lymphocytes, showed no evidence of any proliferative activity in their walls. Secondly, although there was some patchy infiltration of the extra-ocular muscle fibres, they were not broken up and they also did not show any proliferative activity. Thirdly (Fig. 7), there were several patches without a blood-vessel in their centre, but with a clearly marked lymphatic occupying this position, as shown in this slide, where one can see a lymphatic vessel passing obliquely



Lymphatic vessel in longitudinal section.

FIG. 8.

through the thickness of the section. In another part of the section (Fig. 8) I was lucky in cutting one of these vessels longitudinally and here one can see the cells passing along in the line of the wall of the lymphatic. These appearances suggest that the condition may be a lymphoma, and not inflammatory. Unfortunately, I have not been able to obtain any figures relative to the blood count which might have been of assistance in the diagnosis. Ewing⁽⁷⁾ in his account of this form of tumour refers to the difficulty of diagnosis between lymphocytic proliferation due to inflammatory change, and due to neoplastic activity. In fact, one to a certain extent merges into the other. Thus, according to Paltauf, the regeneration of lymphocytes following an acute infection may be

excessive and prolonged, giving rise to a tumour-like overgrowth which persists long after the removal of the bacteria and their products. The tumours form solid masses, with little or no tendency towards necrosis. After reaching a certain limit of growth they may remain stationary for months or years. The structure is dominated by diffuse overgrowth of small lymphocytes—a conspicuous feature of the present case. In a case described by Richardson Cross in 1916⁽⁸⁾ as lymphoma, there was symmetrical proptosis, swelling of the eyelids, slight impairment of vision, and some defect in movement of the eyes. He was first seen in August, 1915. The blood count was practically normal. Graves' disease was excluded and in spite of searching investigations nothing could be found to account for the condition. He was watched for a year during which time no change occurred in the proptosis. No pathological examination was made as there was no indication for operation.

Cross refers to several other cases. One of them reported by Treacher Collins, occurred in an infant, aged $1\frac{3}{4}$ years, who came with proptosis of the left eye on January 9; it had been noticed for about three weeks. On March 13 there was marked bilateral proptosis. Death occurred four days later. Separate tumours were found in the two orbits, consisting of small nucleated cells resembling lymphatic gland tissue. Similar nodules were scattered over the body in almost every organ.

Lagrange⁽⁹⁾, in an account of 24 cases, notes that in all there was proptosis of the two eyes. If this is to be taken as a criterion of the condition, then the diagnosis of lymphoma in the present case would have to go, as, up-to-date, proptosis has been noted in only one eye.

The most likely explanation in the case I am describing would seem to be the following. The patient had influenza in February, 1922, which lowered his resistance to bacterial attack. In consequence he developed an infection at the back of the orbit, possibly the result of transference of organisms by the blood stream from some distant focus. The left hemicrania might be due to involvement of the branches of the ophthalmic division of the fifth nerve. The patient's resistance improves and within a fortnight the infection subsides. There is left, however, a mass of lymphocytes, which, as in the tuberculous cases, continue to multiply long after the infecting organisms and their products have been removed. A case showing similar histological characters is described in the paper already alluded to, by Benedict and Knight. It shows leucocytic infiltration of the muscles, most dense around the vessels where there are also numerous endothelial cells. It has been shown that lymphocytes arise by metamorphosis of the proliferated endothelial cells so that the condition represents a

slightly earlier stage than that exemplified in the case I have described.

The third case is an example of a small mass of young connective tissue forming as a result of irritation induced by the presence of cholesterin crystals. It was discovered by accident in a blind eye removed for a supposed intraocular tumour. The intraocular mass turned out to be an old organizing blood clot, and I reported the case to the Ophthalmological Society in 1922⁽¹⁰⁾. The patient died some two years later from sarcoma of the ilium. It is unlikely that

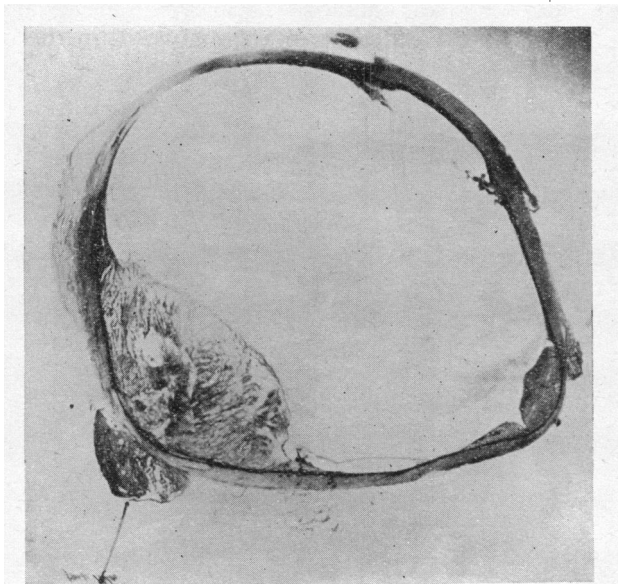


FIG. 9.

Mass outside sclera.

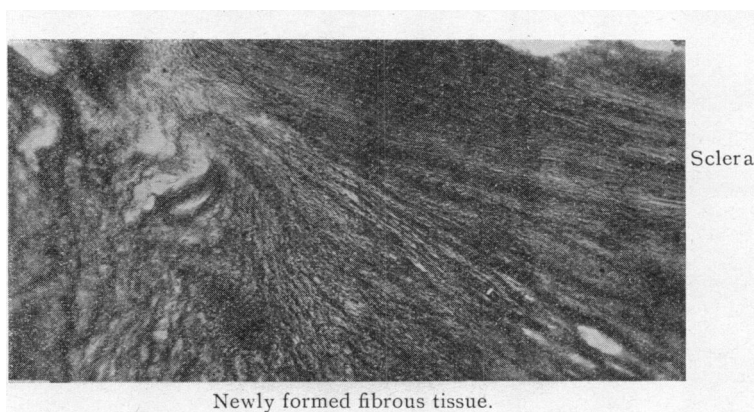
this was a metastatic deposit from the eye, when one takes into consideration the local appearances.

The point to which I wish to call attention is the presence, outside the sclera of the mass of tissue shown in Fig. 9. It is comparatively small and probably did not produce any definite exophthalmos, as there is no note of this condition in the history, though marked chemosis was observed.

Examination under a higher power (Fig. 10) shows a fairly cellular type of connective tissue arranged in lamellae which enclose spaces. The shape of these suggests that in the fresh state they were occupied by crystals of cholesterin, which were dissolved out during fixation. This supposition is strengthened

by the fact that the intraocular change was probably the result of repeated haemorrhages.

There is little doubt that if the intraocular condition had not necessitated enucleation, the continued growth of this mass of tissue would soon have brought about proptosis and the condition of inflammatory pseudo-tumour of the orbit. It may, at first sight, seem a little far fetched to label this inflammatory. It represents, however, the reaction of tissue to injury, though in this case the exciting substance is non-bacterial. Lafon⁽¹¹⁾ reports a more advanced case, probably of the same type. He states that, excluding subperiosteal haemorrhages which are nearly always scorbutic, blood extravasated spontaneously within the orbit is in



Newly formed fibrous tissue.

FIG. 10.

general quickly absorbed, causing disappearance of the exophthalmos. In some cases, however, the eye remains proptosed. This may be due to the blood becoming encysted or to a proliferative reaction of the orbital connective tissue. He gives details of one such case which occurred in a man, aged 34 years. Two years previously on rising in the morning he had noted unilateral proptosis, which steadily diminished during the day and disappeared during the course of the next few days. Since then, the condition had recurred about ten times, clearing up again within a few days. Each attack, however, was a little worse than the preceding one. No ecchymosis occurred. A month before seeing Lafon he had had his worst attack. During this, vision was temporarily deranged, and the exophthalmos persisted to a considerable degree. When seen, the movements of the globe were good but not quite full, vision and fundi normal; there was 8 mm. of exophthalmos. The condition improved as the result of treat-

ment, but there was a bad recurrence two months later, and the orbit was exenterated. The muscles were enlarged and covered with a species of fibrous tissue. The main mass of the pseudo-tumour was composed of bundles of fibrous tissue, in some parts enclosing collections of red blood cells. Microscopical investigation showed that the reaction was in all probability caused by the repeated haemorrhages. He has been unable to find more than two similar cases. A point of interest in Lafon's case is that the blood coagulation time was markedly increased and that there was slight anaemia. Otherwise there was nothing abnormal.

Summing up then we have three cases of pseudo-tumour of the orbit in which the aetiology seems fairly clear. In the first the inflammation is gummatous, in the second there is lymphatic hyperplasia following on a post-influenzal orbital infection, and in the third there is proliferation of fixed connective tissue cells consequent on their irritation by the products of haemorrhage.

The pre-operative diagnosis and treatment of this condition are at once the most important and the most difficult part of the subject. A negative Wassermann test does not necessarily exclude the presence of a gumma, though the effect of a heroic course of mercury, as in Johnson Taylor's case, may settle the diagnosis. With regard to blood counts Marbaix and van Duyse⁽¹²⁾, in a report of a case of pseudo-blastoma of the orbit, found lymphocytopenia in a differential white count. The proportion of lymphocytes was not such as to allow of the diagnosis of lymphatic leukaemia, and it was deemed to be pseudo-leukaemia. Krönlein's operation had been performed previously with a negative result except that the lacrymal gland was enlarged and found to be infiltrated with the lymphocytes. Incidentally, neuro-paralytic keratitis developed as an after-result of the operation. These authors are of opinion that hyperplasia of the orbital lymphatic tissue may be the only manifestation of a general disease, apart from the blood changes which such a disease engenders.

In two of Benedict and Knight's cases, however, where a differential white count was done, there was no lymphocytosis.

Diagnosis of these cases is admittedly difficult and in a sense it involves consideration of all the possible causes of proptosis. I do not propose to go over these, as they have been exhaustively dealt with in the discussion on proptosis at the 1923 meeting in London of the Ophthalmological Society. It is of interest to note, however, that during this discussion the only case of inflammatory pseudo-tumour mentioned was that to which I have already alluded, and a possible one alluded to by Juler.

One must attempt then to outline some sort of procedure which would be of service in excluding this condition in cases of unilateral

proptosis simulating orbital tumour. As a basis of discussion, I should like to suggest the following, though the list seems rather formidable. Examination of the urine, especially for sugar. Performance of a Wassermann reaction which, if negative, should be repeated after a provocative dose of salvarsan. Exclusion of tuberculous infection, if necessary, by a complement fixation reaction or one of the tuberculin tests. Differential blood count, and estimation of blood coagulation time. Careful search for focal infections and radiographic examination of teeth and sinuses. The history, of course, as in Harrison Butler's case, may be of paramount importance, and one must always remember the possibility of early Graves' disease. Finally, an exploratory operation might be indicated before proceeding to a radical extirpation of the complete contents of the orbit.

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TWO CASES OF CEREBRAL ANEURYSM CAUSING OCULAR SYMPTOMS WITH NOTES OF OTHER CASES

BY

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I HAVE had recently several interesting cases of cerebral aneurysm. Two of them, being of a type somewhat rare, are described at length, and notes of some other cases are appended. The occurrence of these cases has raised in my mind the whole question of cerebral aneurysm, and I have found it to be of interest to collect and collate the data of all my cases and many others that have gone to post-mortem examination in the Glasgow