Neuro-fibroma of the eyeball and its appendages / by E. Treacher Collins and Rayner D. Batten.

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Neuro-fibroma of the eyeball and its appendages.

By E. Treacher Collins and Rayner D. Batten.

Clinical Notes by Rayner D. Batten.

Alice S—, æt. 14 years, has been under observation since June, 1902. When first seen the right eye was buphthalmic to a marked degree. The cornea very large with deep anterior chamber. There was some haze of the cornea somewhat resembling an interstitial keratitis. The pupil reacted to light. There was some projection of uveal pigment round the lower margin of the iris. Vision in right eye = $\frac{1}{60}$. Tension normal. No satisfactory view of the fundus was obtainable. In addition to the above there was marked hypertrophy of the right upper lid and skin covering the orbit, together with a soft doughy swelling over the temporal fossa. The upper lid was large and thick, covering the globe. The lower margin of the palpebral conjunctiva protruded. The skin over the affected parts was coarse and thick.

The left eye appeared normal.

History.—The condition was noticed at birth. The mother was told that if she "licked the eye regularly" it would get better, which advice she followed for some years. The father and mother are healthy and there is no history of any defect amongst her brothers and sisters. There is no evidence of syphilis.

In December, 1902, as the right eye was irritable and the upper lid unsightly, a portion of the palpebral conjunctiva was excised, but not examined.

The patient was shown at a meeting of this Society in July, 1904, when Mr. Treacher Collins diagnosed the true nature of the condition.

As the eye was unsightly, irritable, and painful, and the mother was anxious for its removal, the eye was excised, together with a wedge-shaped portion of the upper lid, on July 18th, 1904. These were sent to Mr. Collins and his report forms the subject of this paper.

The patient was seen a month ago. There was no apparent increase in the growth. The general appearance was improved.

Pathological Report by E. Treacher Collins.

The specimens consist of a piece of the upper eyelid and a right eyeball.

Examination of the eyelid.—The eyelid is much thickened; at its cut surface several thick cords of a greyish white colour are seen in section.

Microscopically, the papillæ of the skin, and also of the conjunctiva at the lid margin, are seen to be much enlarged; the epithelium overlying them is much thickened.

There is extensive hypertrophy of the fibrous tissue of the corium. Towards the conjunctival surface and in the vicinity of the Meibomian glands, there are areas of dense round-cell inflammatory infiltration; there are also numerous multi-nucleated giant cells.

The alveoli of the Meibomian glands are seen as irregular spaces lined by degenerate, vacuolated, epithelial cells. In some places the protoplasm of several of these cells seems to have run together so that they look like giant cells (Plate XVIII, fig. 1). Some of the spaces enclosed by these cells are empty, others are filled, or partly filled, with a homogeneous or faintly granular material. The subcutaneous tissue, like the corium, is much hypertrophied; in it many nerves are seen in section, with extensive thickening of their endo- and perineurium (Plate XVIII, fig. 2).

Pathological examination of eyeball.—Diameters measure—antero-posteriorly 33 mm., vertically 25 mm., laterally 26 mm. The cornea is enlarged and globular, measuring

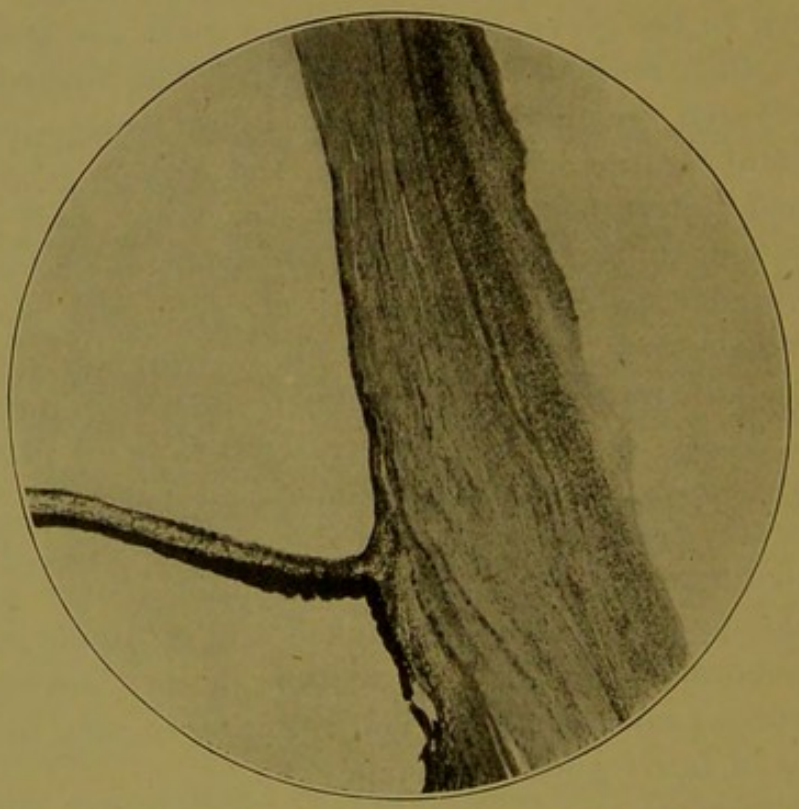
laterally 15 mm., vertically 14 mm. Its upper and outer margin is very ill defined; extending into it from the outer margin are several narrow opaque lines which become smaller as they approach the centre. The anterior chamber is very deep. The pupil is oval in shape, being wider laterally than vertically; there is well-marked ectropion of the uveal pigment at its margin. The optic nerve and its sheath appear normal. The ciliary nerves external to the globe at its posterior pole are somewhat thicker than normal, and convoluted. The eyeball, after being frozen, was divided into two by an antero-posterior horizontal section. On section, the lens is seen to be flattened antero-posteriorly. In the lower half of the globe about its centre and a little in front of the equator is a circular patch of choroidal atrophy, the white of sclerotic showing brightly through. Over this area the retina is adherent and in its centre is some deep pigmentation. There are also some scattered dots of choroidal atrophy and pigment disturbance, just posterior to the ora serrata, in the outer part of the upper half. Behind the equator in the outer part of the globe, over a large area, the choroid is much thickened and its tissue appears to be abnormally dense. On section in its thickest part it measures 1 mm. across. The retina is *in situ* and the vitreous of fairly good consistency.

Microscopical examination of the eyeball.—Cornea: The surface epithelium and anterior limiting membrane present their normal appearance. The substantia propria is thin and between its layers are seen linear tracks of elongated cells; they are more numerous on one side of the section than the other, and are bigger and more conspicuous near the margin of the cornea than in its central parts. They are probably thickened nerve-fibres (Fig. 1). Descemet's membrane is thin. There is some dense laminated tissue in the position of the ligamentum pectinatum to which the root of the iris is adherent There are no spaces of Fontana and it is difficult to identify the canal of Schlemm.

Iris and ciliary bodies.—Some pigmented iris tissue, con-

tinuous with that of the stroma, is seen to be prolonged round the angle of the anterior chamber and to line the posterior surface of the cornea for some distance at its periphery (Fig. 1). The stroma of the iris, where it ceases to be adherent to the cornea, is very thin. There is marked ectropion of the uveal pigment, and also some

Fig. 1.



Photograph of section showing the periphery of the cornea and angle of the anterior chamber. The dark streaks seen in the anterior part of the cornea are probably thickened nerve-fibres. No spaces of Fontana or canal of Schlemm can be made out. Tissue like that of stroma of the iris is seen prolonged forwards round the angle of the anterior chamber.

bending forwards of the sphincter muscle at the pupillary border. The ciliary processes are attenuated and directed straight inwards towards the sides of the lens. The ciliary muscle, except for alteration in shape due to the dragging inwards of the ciliary processes, appears normal.

The *choroid* over nearly the whole of its extent is abnormally dense in structure. In one part it is quite

PLATE XVIII.

Illustrates Mr. E. Treacher Collins' and Dr. R. D. Batten's paper on Neuro-fibroma of the Eyeball.

For the photographs reproduced on the plate the writers are indebted to Mr. E. Collier Green.

Fig. 1.—Shows a section through the tarsus of the upper eyelid with one of the Meibomian glands greatly distended. There is considerable round-cell infiltration around it, and also marked hyperplasia of the fibrous tissue of the part. Some of the thickened nerve-fibres are shown in section.

Fig. 2.—Shows one of the nerves in the upper eyelid cut transversely under a higher power. All its fibrous tissue elements are greatly increased in amount.

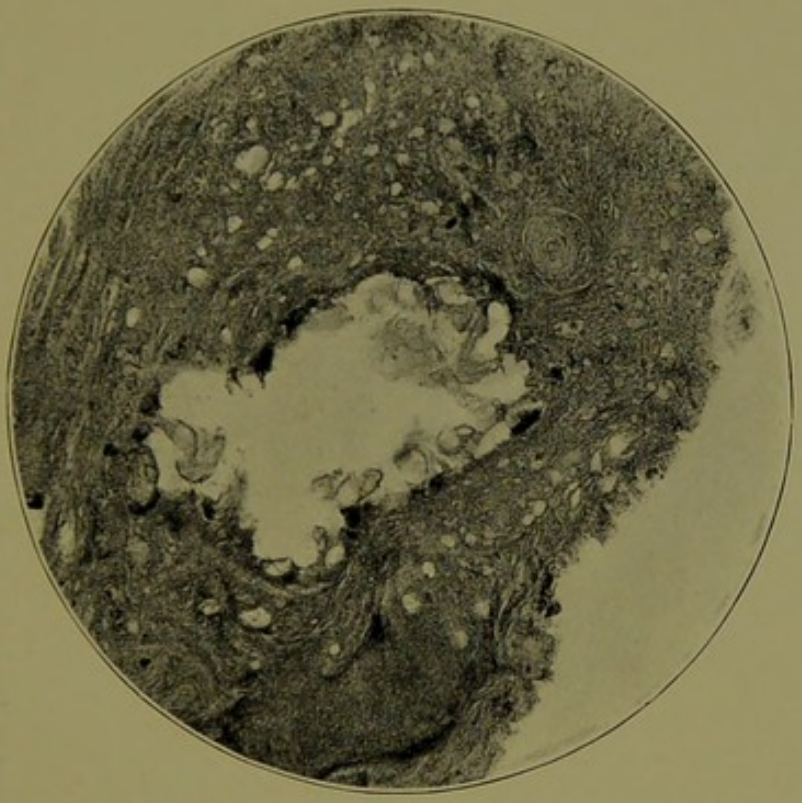


Fig. 1.

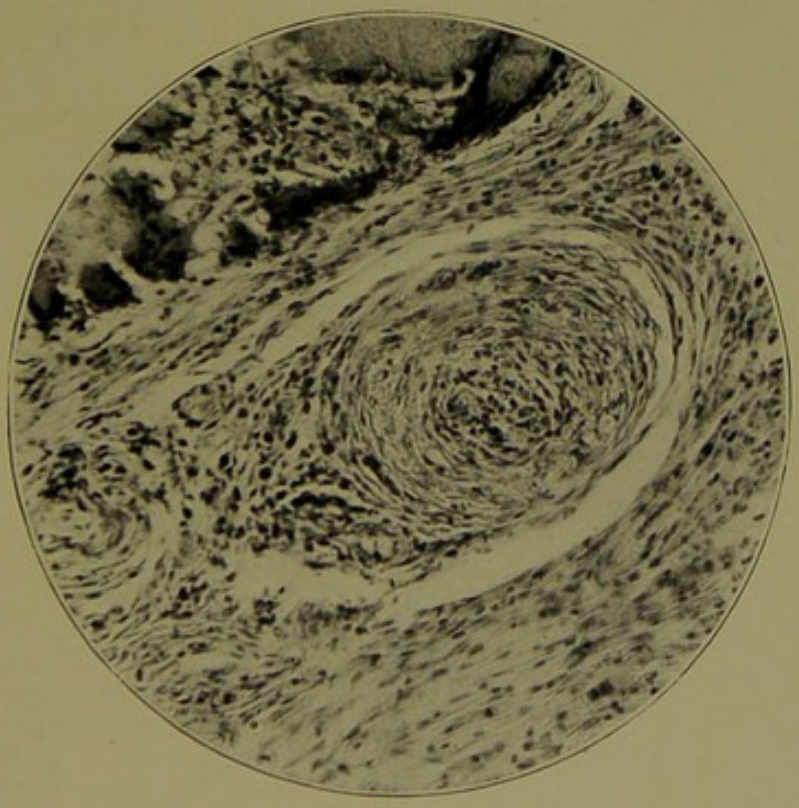


Fig. 2.

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PLATE XIX.

Illustrates Mr. E. Treacher Collins' and Dr. R. D. Batten's paper on Neuro-fibroma of the Eyeball.

For the photographs reproduced on the plate the writers are indebted to Mr. E. Collier Green.

Fig. 1.—Shows a section of the choroid. It is much thicker, denser in structure, and more highly pigmented than normal. Scattered throughout it are seen numerous small, oval, light-coloured bodies; they are the hypertrophied nerve-end organs.

Fig. 2.—Shows some of the hypertrophied nerve-end organs in the choroid under a higher power. Some have shrunken away slightly from the surrounding tissue. A convoluted delicate fibre is faintly shown in the centre of each of them. An enlarged nerve is seen to be attached like a stalk to the largest of the bodies.

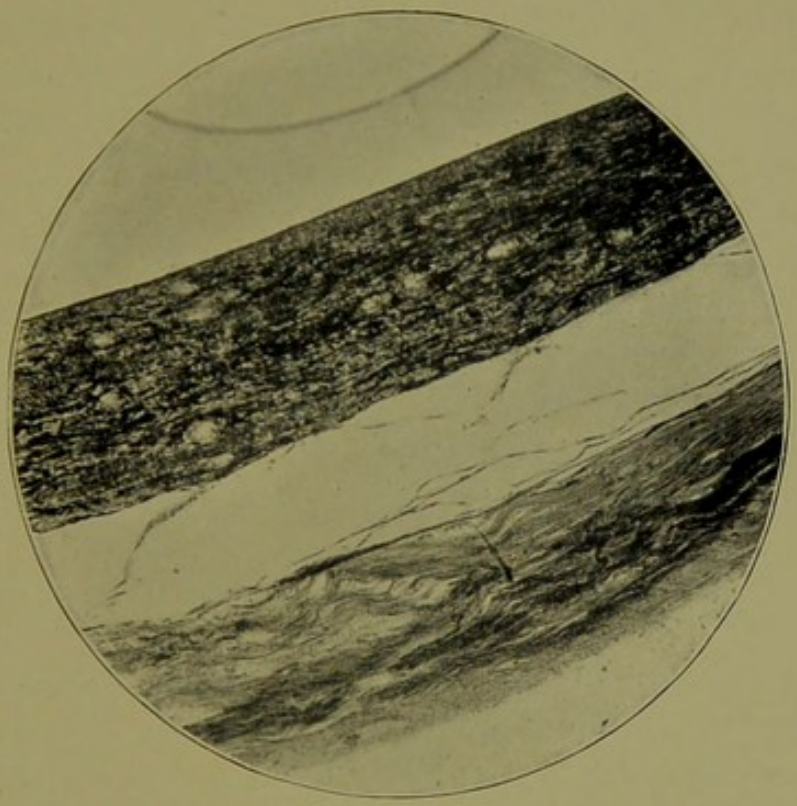

Fig. 3.

Fig. 4.

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double its normal thickness (Plate XIX, fig. 3). Its blood-vessels are few and inconspicuous. It is mainly composed of layers of fibrous tissue which is highly nucleated. There are an unusual number of densely pigmented branching cells. The membrane of Bruch and the pigment epithelium lining it present their normal appearance over the thickened choroid. In some areas of the thickened parts there are numerous small oval bodies (Plate XIX, fig. 3). The tissue immediately surrounding them is densely pigmented. In some of them a capsule composed of a single layer of flattened nucleated cells can be seen. In one or two instances this capsule has become slightly separated away from the surrounding tissue. The core of these oval bodies within the capsule stains with eosine; it is composed of delicate convoluted fibres, which have been cut in various directions in different sections. In some of the bodies, between the fibres, the elongated nuclei of cells are seen. These oval bodies present the appearances of nerve end organs. In one or two instances they are seen to be prolonged out on one side into a stalk-like projection which is evidently the nerve-fibre passing into the end organ (Plate XIX, fig. 4).

Sections through the atrophic area, above referred to, show the retina and choroid there firmly united and both coats reduced to strands of nucleated cells, a few fibres, and patches of deep pigmentation.

Sclerotic.—Appears normal in structure though thinner than usual. In it, sections passing through the ciliary nerves are seen, and they appear slightly but not very strikingly larger than normal.

Remarks by E. Treacher Collins.—The multiple soft fibromata of the skin known as "molluscum fibrosum" were in 1882 demonstrated by von Recklinghausen to be of nerve origin, and due to a fibromatosis of the terminal filaments of the cutaneous nerves. Certain hypertrophies of the skin in a particular region or segment of the body, often accompanied by pigmentation, and described clinically as "congenital elephantiasis" are likewise of nerve

origin, there being, in addition to a diffuse hyperplasia of the skin and subcutaneous tissue, a marked overgrowth of the fibrous tissue elements of the cutaneous nerves.

Associated frequently with these two conditions is some thickening of the nerve-trunks, or a group of nerves supplying the part may be converted into a mass of convoluted cords with nodular and fusiform swellings. To this latter condition Verneuil gave the name of "plexiform neuroma." The enlargement of the nerves is seen microscopically to be due to overgrowth of the peri- and endoneurium. The convenient term "neuro-fibromatosis" has been introduced to comprise the above different conditions essentially of the same pathological type. A most useful monograph on neuroma and neuro-fibromatosis was published by Alexis Thomson (1) in 1900.

Eyelids.—Several cases of congenital elephantiasis of the eyelids due to neuro-fibromatosis have been recorded. Mr. Snell (3) at a meeting of this Society in 1903 brought forward three excellent examples. In two of his cases I had the opportunity of making a microscopical examination of the hypertrophied tissue, and found, in addition to the general hyperplasia of the skin, a plexiform condition of the nerves. In Mr. Rayner Batten's case above described a similar condition of the lid was present. The microscopical appearances in his case were, however, complicated by there being in addition to the neuro-fibromatosis a periadenitis around the Meibomian glands. These glands were much enlarged and distended, whilst in the surrounding tissue there were numerous giant-cells and groups of inflammatory leucocytes.

Orbit.—In one of Mr. Snell's cases, in a case recorded by Sachsalber (2), and in one recorded by Rockliffe and Parsons (4), besides elephantiasis of the eyelids due to neuro-fibromatosis there was a plexiform condition of the nerves of the orbit, in the last mentioned case causing considerable proptosis of the globe.

Conjunctiva.—In cases where an eyelid is the seat of this affection the palpebral conjunctiva becomes involved

in the general hyperplasia. In the discussion on Mr. Snell's paper before this Society Mr. Verhoeff, of Boston, mentioned how he had met with a case of plexiform neuroma of the eyelid in which on the surface of the eyeball four or five tortuous, worm-like bodies could also be seen clinically.

Buphthalmic condition of eyeball.—In this case of Verhoeff's, in Sachsalber's case, in Mr. Snell's second case, and in Mr. Rayner Batten's case here recorded, besides the neuro-fibromatosis of the eyelid there was a buphthalmic condition of the eyeball. In Mr. Snell's and Mr. Rayner Batten's cases the buphthalmic eyeball was excised and I am much indebted to those two gentlemen for kindly handing me the specimens for pathological examination. In connection with these buphthalmic eyes the question arises as to whether the enlargement of the globe is in some way directly connected with the neuro-fibromatosis or whether it is brought about, as is usual in other cases of congenital buphthalmos, by increase of tension due to some mal-development of the channels of exit for the intra-ocular fluid. In both the eyes I have examined I find considerable malformation about the angle of the anterior chamber. The spaces of Fontana do not seem to have been developed. In each eye there was a broad adhesion of the iris to the posterior surface of the cornea at its periphery, those structures never apparently having become properly separated during fœtal life. I think there can be no doubt that the enlargement of the eyeball in these two cases was secondary to an increase of tension. Though the buphthalmic condition of the eyeballs is accounted for in this way, there is evidence that individual parts of the eye do become affected by this condition of neuro-fibromatosis.

Sclerotic and cornea.—In the buphthalmic eye from Mr. Snell's case I was able to demonstrate the ciliary nerves in the anterior part of the sclera thickened by overgrowth of their peri- and endoneurium. I also demonstrated how tracts of elongated cells could be traced from these

thickened nerves into the substantia propria of the cornea, showing that there was some thickening of the terminal filaments of the ciliary nerves supplying that structure. In Mr. Rayner Batten's case, in the cornea both before and after removal of the eye, several thin grey lines could be seen passing from its periphery towards the centre. Sections of the front of this eye examined microscopically showed these streaks to be due to tracks of elongated cells, similar to those met with in Mr. Snell's case. Unlike Mr. Snell's case, however, the ciliary nerves in the anterior part of the sclera did not show any conspicuous overgrowths of fibrous tissue.

Iris.—In Sachsalber's case microscopical examination of the eyeball showed an increase of the peri- and endoneurium of the nerves of the iris. In Mr. Snell's second case, in which the eyeball on the side affected was small and shrunken, he describes the iris as being purplish-brown in colour, with course, irregular, yellowish markings near its pupillary margin. In neither of the two buphthalmic eyes which I have examined microscopically was there any neuro-fibromatosis of the iris or ciliary body.

Choroid.—The choroid was, however, in both markedly affected. In both it was considerably thickened and denser than usual, due to an abnormal overgrowth of its fibrous tissue elements. The fibrous tissue was arranged in layers and highly nucleated. Scattered throughout the thickened tissue were an abnormal number of deeply-pigmented cells. The blood-vessels seemed few in number and formed a very much less conspicuous constituent than they do in normal choroid. In Rayner Batten's case numerous sections were seen, in the hypertrophied tissue, of small oval bodies with a nucleated cellular capsule and a convoluted fibre forming the core. I think there can be little doubt that these oval bodies are nerve-end organs. Bodies of a similar character were found by Parsons in the orbital growth in Rockliffe's case.

Ciliary nerve, at posterior pole of eyeball.—In Snell's case the ciliary nerves external to the sclerotic at the pos-

terior pole of the globe were seen, with the naked eye, to be enlarged and present a plexiform appearance. Microscopical sections showed a marked increase of their peri- and endoneurium. In Mr. Rayner Batten's case the ciliary nerves in this position were much less markedly affected; they were, however, slightly enlarged and tortuous.

It will be seen from the foregoing that all portions of the ciliary nerves supplying the eye may be affected by this congenital fibromatosis, and that in the uveal tract, as in the skin, associated with the neuro-fibromatosis there may be a general hyperplasia of the fibrous tissue of the part. The extent of the affection varies, however, in its distribution, sometimes being confined to one set of ciliary nerves, and the part supplied by them, and sometimes to another. In some cases only the terminal filaments and end organs of the nerves are involved, and in others the larger trunks are also affected.

Optic nerve.—The optic nerve besides the ciliary nerves is liable to a diffuse overgrowth of its fibrous-tissue elements. Many neoplasms of the optic nerve have been found, not to be localised tumours, but a general diffuse hyperplasia of the fibrous tissue. This hyperplasia may involve the intercranial portion of the nerve as well as the orbital. The non-removal of the entire growth in some cases has not been followed by any ill results, showing that the neoplasm was not of a malignant character. In some tumours of the optic nerve the fibromatosis involves the pial sheath, or perineurium, the trabeculæ extending from it into the nerve and the so-called neuroglia, or endoneurium; in others it has been confined to one of these divisions, or has affected one more extensively than another (5).

Retina.—I know no condition of the retina to which the term "neuro-fibromatosis" would be applicable. So far as I know no case of fibromatosis of the optic nerve has been recorded which has been accompanied by a new growth in the retina. Mr. Bland-Sutton in his book on *Tumours* says that ever since he became acquainted with

the changes in nerves of the so-called plexiform neuroma, it seemed to him that they were akin to the localised neuroglia overgrowths in the brain known as glioma. There is, however, nothing akin between neuro-fibromatosis and the exceedingly malignant small round-celled growth which is termed "glioma of the retina." The reason the retina is never the seat of this affection is probably because it is entirely derived, with the exception of its blood-vessels, from neural epiblast, neuro-fibromatosis being essentially a hyperplasia of tissue of mesoblastic origin.

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(2) Sachsalber.—*Beiträge z. Augenheilkunde*, xxvii, 1897, Heft 27, p. 523.

(3) Snell and Treacher Collins.—*Trans. Ophth. Soc.*, xxiii, 1903, p. 137.

(4) Rockliffe and Parsons.—*Trans. Path. Soc.*, lv, 1904, p. 27.

(5) Treacher Collins and Marshall.—*Trans. Ophth. Soc.*, vol. xx, p. 156. (*Read February 9th*, 1905.)

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