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BUPHTHALMOS WITH FACIAL NAEVUS AND ALLIED CONDITIONS

BY

A. J. BALLANTYNE

GLASGOW

THE association of buphthalmos with facial naevus has received attention in ophthalmological literature from time to time over a period of many years, and a recent revival of interest in the subject has been stimulated by the appearance of articles by Cushing, Parkes Weber, Aynsley and others. About the time of the appearance of Aynsley's paper the following very early case came under my notice at the Glasgow Eye Infirmary.

Stanley C., aged three weeks, was brought to the out-patient department on January 3, 1930. His mother stated that the birth had been difficult—face presentation—but no instruments had been used. There had been no maternal injury during pregnancy. Two of the family of four are dead, but the family history throws no light on the present case. The father and mother have no blood-relationship. After birth it was noticed that there was swelling and red staining of the left side of the face. The eyelids were swollen and the eye bloodshot. It was thought that the redness was already fading and had disappeared from some parts, *e.g.*, beneath the chin. The right eye was found to be normal. The left cornea was relatively large (12.5 mm. diameter, right cornea 10 mm.) It was faintly opalescent and its surface steamy. There were no linear opacities. The anterior chamber was deep and the pupil small (1.5 mm.), the iris, flat, dark and featureless. The sclera was china-blue with a few dilated vessels. The tension to the finger seemed normal in both. A light port-wine staining of the skin occupied the left side of the head and face, mapping out fairly exactly the area of distribution of the first and second divisions of the fifth cranial nerve. The naevus involved the gum of the left upper jaw and there was another small isolated naevus in the left lower occipital region. No other congenital defects were found, but there was slight asymmetry of the facial bones in the form of relative prominence of the left superior alveolar ridge. After a few days' use of pilocarpine and dionine the corneal lustre

improved, but opalescence persisted. Under chloroform the tonometer measurements were: R. 25 mm. of mercury, L. 41.5 mm. of mercury (Schiotz). No ophthalmoscopic view could be obtained in the left eye and the right disc seemed doubtfully paler than normal. Radiograms of the skull showed no abnormality. At the age of five weeks Elliot's trephining was performed in the left eye and thereafter the corneal opacity gradually cleared. The cornea is now quite transparent and the normal lustre completely restored. The Schiotz tonometer, about two weeks after operation, gave the tension of the left eye as 16 mm. of mercury. At the age of six weeks the child was operated on for hernia. He is thriving well and the naevus, though no less extensive, is of a slightly paler colour.

This case does not differ materially from others which have been published, but it is probably the youngest which has been put on record, other early cases being those of Elschnig (nine weeks) Marchesani (four months) Nakamura (four months) and Galezowski (nine months). These cases present the simple association of facial naevus with buphthalmos, but a glance at the literature shows that there are many other conditions of an angiomatous nature more or less linked up with these and with each other and offering interesting problems in pathology.

It might be worth while to attempt a more complete review of these cases than is at present available.

Bibliography—Naevus and Buphthalmos

Our search takes us back to 1860 when Schirmer¹ described a case of capillary naevus affecting the skin of the face and trunk and the mucous membranes of the eye, nose, mouth and pharynx, associated with buphthalmos of the left eye. He noted marked

dilatation and tortuosity of the retinal veins but no choroidal abnormality.

After Schirmer's publication some nineteen years seem to have elapsed before the subject was referred to again. In 1879 Allan Sturge² presented to the Clinical Society a patient with a congenital port-wine mark on one side of the face and affected with epileptiform convulsions on the opposite side of the body, attributed by Sturge to a naevoid condition of the vessels of the brain. The eye on the same side as the facial naevus was described as having a large cornea and very myopic refraction. The choroid was darker than that of the opposite eye and the retinal vessels were tortuous. A few years later Horrocks³ showed to the Ophthalmological Society a girl, 9 years of age, with naevus of the right side of the face including the eyelids, dilatation of the anterior ciliary veins, tortuous retinal veins and enlargement of the cornea in the same eye. Clonic convulsions and spastic hemiplegia were present on the opposite side of the body. The description of the eye condition in the cases of Sturge and Horrocks was incomplete, and leaves some doubt as to whether they are cases of true buphthalmos. The state of the ocular tension is not mentioned, but the abnormally large corneal diameter is at least suggestive of buphthalmos. These two cases were quoted by Stephen Mackenzie in the discussion on a case described before the Ophthalmological Society by Milles⁴, in which an angioma of the choroid, demonstrated in the excised eye, had led to retinal detachment and blindness, and was accompanied by a naevus of the temporal and orbital regions on the same side. In Milles' case the tension of the eye was reported normal, but in other respects it closely resembles the case of Lawford⁵, where, with a naevus of the left side of the face, there was a naevus of the choroid, sub-retinal haemorrhage, detachment of the retina and glaucoma, presumably secondary, in the left eye. Galezowski's case⁶, published thirty-eight years after Schirmer's, was a typical congenital naevus of the face, with buphthalmos of the corresponding eye, and many other examples of the same combination have been recorded by Cushing⁷, Elschmig^{8,9}, Marchesani¹⁰ and others. Including my own case, described above, I find records of some thirty-one cases which should probably be placed in this category. These cases differ widely in their characters, *e.g.*, in Beltmann's¹¹, the naevus, though mainly in the distribution of the fifth nerve, affected both sides of the face and involved the mucous membranes of the nose, mouth and pharynx. The buphthalmos was bilateral. In Cabannes'¹² the naevus was cavernous rather than capillary and there was marked hypertrophy of the neighbouring bones and orbit. In Kaiser's¹³ and in Marchesani's, the naevus, though predominating

on the side of the buphthalmic eye, affected the neck, limbs and trunk. Röttl's case¹⁴ had homonymous hemianopia on the side opposite to the buphthalmos.

Naevus and Simple Glaucoma

Duschnitz's contribution in 1923 introduces a somewhat new aspect of the subject in that the eye condition in his case, although the patient was young, was no buphthalmos but simple glaucoma. In the same year further cases of naevus with simple glaucoma were reported by Salus¹⁶, Safar¹⁷ and Löwenstein¹⁸, and others were published in more or less detail by Ginsburg¹⁹, Derby²⁰, Hudelo²², Suglian²³ and Krause²⁴—some ten cases in all.

Naevus and Secondary Glaucoma

Although in some of these cases (Hudelo and Ginzburg) there were teleangiectases of the conjunctiva bulbi and other periocular structures, there was no intra-ocular angioma which could be held responsible for the rise of intra-ocular pressure. Such cases are sharply demarcated from a further group in which cutaneous naevus is associated with secondary glaucoma, in the more characteristic members of which there was a massive angioma of the choroid, with, or without, retinal detachment or haemorrhage, and the glaucoma could fairly be looked upon as an end result of these gross intra-ocular changes. Such were the cases of Lawford, already referred to, Snell²⁵, Steffens²⁶, de Haas²⁷ and Wagenmann²⁸. Somewhat different was that of Bär²⁹ in which ophthalmoscopic examination showed, in addition to glaucomatous cupping of the disc, dark tortuous retinal veins, anastomosis of veins and a grey sharply-defined patch in the retina associated with fine venous twigs. Bär conceived that this fundus patch represented an old haemorrhage. Krause's first case had varicose vessels in the iris and conjunctiva bulbi and enormous enlargement of the choroidal vessels in the periphery of the fundus. In Knapp's case³⁰ a number of grey nodules were seen scattered over the iris which, on microscopic examination, showed thickening of the iris stroma with enlarged thin-walled vessels. In Knapp's view the glaucoma here was explained by the presence of these changes in the peripheral zone of the iris, leading to obstruction at the angle of the anterior chamber.

More nearly approaching to the simple glaucoma group is the case of Yamanaka³¹ in which the secondary character of the glaucoma was suggested only by the presence of wide and tortuous retinal veins round the optic disc. A somewhat similar state of the retinal veins, without any visible evidence of involvement of

the choroidal vessels, was referred to in the buphthalmos cases of Schirmer, Beltmann and Aynsley³² and in the pseudo-glaucoma case of Voegele³³. The presence of these abnormalities of the retinal vessels has led Elschnig and others to assume the existence of a corresponding abnormality of the choroidal vessels and to seek an explanation of the glaucoma in the vascular dilatation and "plethora" in the choroid.

Those cases in which we find varying degrees of abnormality of the retinal arteries, and especially the case of Bär, may be related to the condition known as v. Hippel's disease, or angiomatosis retinae, many cases of which are now on record, and an excellent illustration of which is given by G. H. Pooley³⁴ in the *Transactions of the Ophthalmological Society*. Interest in this condition has been increased by the more recent work of Lindau³⁵, who has found the characteristic retinal vascular changes associated with capillary angiomata and hemangiomatous cysts in the brain, spinal cord, liver, pancreas and kidney. The initial lesions here are supposed to be congenital. Thus Lindau's cases are linked up, on the one hand through angiomatosis retinae and on the other through congenital vascular disease of the central nervous system, with the cases with which we are here concerned, and this association is further strengthened by the case, mentioned by Collins³⁶, of angiomatosis retinae associated with small angiomata in the skin of the eyelid. It is to be noted also that eyes affected with v. Hippel's disease frequently succumb to secondary glaucoma.

Naevus and Pseudo-glaucoma

In 1925 Voegele³³ described a case of a man, aged 62 years, with a capillary naevus of the right side of the face; with excessive vascularity of the conjunctiva, sclera and episclera of the right eye, glaucomatous excavation of the papilla, slight varicosity of the retinal veins and a very slightly increased corneal diameter; while the anterior chamber, the tension, field of vision and visual acuity were all normal. We are probably justified in describing this as a case of "pseudo-glaucoma," and thus grouping it with the cases reported by Macrae³⁷ and Thomson³⁸ in this journal some four years later. It is true that these three cases were not similar in their clinical characters, but they had as a common feature the absence from the affected eye of hypertension and other characters necessary for the diagnosis of glaucoma or buphthalmos. The condition of the optic disc in these cases was probably a congenital deformity, and Voegele's case was unique in that the visual acuity and field of vision were unaffected. In the patient described by Thomson the affected eye was myopic while the normal eye was slightly hypermetropic. In this

connection I might refer to a further case which recently came under my notice.

The patient was a man, aged 29 years, with a patchy capillary naevus of the left lower eyelid, cheek, nose and upper lip, the left eye having myopia of 5D. with myopic astigmatism of 1.5D. and a Fuchs coloboma of the lower segment of the disc. The corneal diameter, the colour of the iris, size of the pupil and depth of the anterior chamber were the same as those of the right eye and there was no glaucomatous cupping. The bones of the left side of the face were slightly larger than those of the right side.

In this case the myopia and the coloboma of the disc are probably congenital anomalies analagous to the myopia and the deformity of the disc in Thomson's case.

Naevus and Cerebral Disease

In Macrae's case the arm and hand on the side opposite to the affected eye were abnormally small, and in Thomson's case there was a history of paralytic attacks affecting the arm and leg on the side opposite to the affected eye. This brings us to the consideration of a very important group of cases which present, in addition to naevus of the skin and glaucomatous or other allied changes in the eye, signs and symptoms of intracranial disease, generally of the nature of a meningeal angioma. The earliest example of this combination to which I can find any reference is the case of Sturge², which was afterwards quoted by Mackenzie³⁹ and is frequently referred to as Mackenzie's case. This patient had a port-wine stain on one side of the face, tortuous retinal vessels and choroidal changes on the same side, and the affected eye was very myopic and had a large cornea. Epileptiform seizures had occurred on the opposite side of the body, and Sturge attributed these to a naevoid condition of the vessels of the brain similar to that of the face and eye. Mackenzie, in the same connection, quoted the case of Horrocks³ which presented a naevoid condition of the face and eyelids, dilated anterior ciliary and retinal veins and a large cornea, and suffered from spastic hemiplegia on the opposite side of the body. Horrocks pointed out that the affected vessels belonged to parts derived from epiblast and suggested that the vessels of the pia mater might be similarly affected. These shrewd suggestions of Sturge and Horrocks were justified and confirmed in two of the three cases reported by Cushing more than twenty years later, in one of which, at necropsy, and in the other, in the course of operation, the suspected naevoid condition of the meninges was found. The clinical diagnosis of this group of cases was carried a stage further by Parkes Weber⁴⁰. His case was first reported in 1922—a female, aged 28 years, with widespread congenital naevus of the face, chest, arms, back, etc., right sided spastic hemiplegia, relatively poor development of the right face and limbs, and left sided buphthalmos. In addition, there was a condition of dystrophia adiposo-genitalis. A diagnosis of

vascular naevus of the meninges on the left side was made, and in 1928 it was possible to demonstrate, by radiograms of the skull, the presence of a calcified meningeal angioma in that situation.

In most cases of this group the clinical evidence of intracranial involvement takes the form of unilateral spastic hemiplegia or epileptiform convulsions, and a degree of mental defect is common. In some cases (Parkes Weber, Macrae) the limbs on the side opposite to the affected eye were smaller. Aynsley's paper³² gave special attention to this association of cerebral lesions with naevus and with buphthalmos and other eye conditions. He refers to 13 such cases; and to these I am able to add the cases of Sturge and Horrocks, already referred to, and the cases of Hudelo, Voegelé, Ginsburg and Röttl. Hudelo's and Ginsburg's patients suffered from simple glaucoma, but in all the other cases the eye condition was buphthalmos. In eight of the 19 cases in this list radiograms demonstrated the presence of a naevus of the cerebral meninges, while in two this was proved by operation or at necropsy. It may be presumed that in some, at least, of the others a meningeal angioma was present, in which calcification had not yet occurred and therefore gave no evidence in the radiograms. A case which has special interest for the ophthalmic surgeon was that in which the association of facial naevus with a contralateral homonymous hemianopia enabled Foster Moore⁴¹ to suggest that the latter might be caused by a meningeal angioma, and the diagnosis was subsequently justified by the radiograms. This case is, however, not unique, as in an earlier case of Röttl's, which presented facial naevus, buphthalmos and homonymous hemianopia, there was X-ray evidence of an angioma of the meninges in the occipital region. In Foster Moore's case buphthalmos was not present, but there were congenital abnormalities in the form of slight dislocation of the lenses and a small coloboma of the left disc.

I have included in this group two cases which differ materially from the others in that the intracranial disease is apparently not vascular in its nature. These are the cases of Voegelé, combining facial naevus and pseudo-glaucoma with dystrophia adiposogenitalis, and of Ginsburg, with facial naevus, glaucoma simplex and acromegaly. In Parkes Weber's case, too, while facial naevus and buphthalmos were associated with spastic hemiplegia due to meningeal angioma there was evidence of pituitary disease in the form of obesity, defective sexual development and a small pituitary fossa. The significance of the pituitary disease in these cases is obscure and in the absence of any record of post-mortem investigation one can only speculate as to the nature of the intracranial lesion. The number of cases is so small that the association of pituitary involvement with naevus and glaucoma

might be purely accidental, but, as we shall see, radiological evidence of enlarged sella turcica has been found in cases of buphthalmos associated with neuro-fibromatosis, and in one such case (Vogt) there was acromegaly affecting the face and limbs on one side. It is difficult to resist the belief that in such cases there exists a vascular or nervous lesion which is interfering with the pituitary body.

Detachment of the retina has formed a feature of some naevus cases in which angioma of the choroid led to secondary glaucoma (Lawford, Snell, Steffens, Paton and Collins⁴²), but it has also been found in some cases without glaucoma. Thus Onken⁴³ reports a case of unilateral naevus of the face with double detachment of the retina. There was no ophthalmoscopic evidence of choroidal angioma, but he quotes a case of Salus with angioma of the choroid, retinal detachment and no glaucoma, and a similar case was reported by Milles. A case which has recently come under my notice may belong to this group. This young woman has a capillary naevus of the face and eyelids, varicosities of epibulbar vessels, complete cataract and divergent squint, all affecting the right side. The light projection tests make it probable that a detachment of the retina is present, and one might almost assume the presence of a vascular choroidal lesion.

Other cases which have some affinity with these we are considering are those of facial naevus with retinal vessel changes, but not buphthalmos or glaucoma (Hartridge⁴⁴ and Work Dodd⁴⁵) and others with angioma of the choroid leading to glaucoma, but without facial naevus.

Buphthalmos with Neuro-fibroma

This sketch of the groups of cases relating themselves to facial naevus and buphthalmos would be incomplete without reference to another large group in which buphthalmos or glaucoma has been found associated with neuro-fibroma or plexiform neuroma of the face, eyelids or orbit on the same side. The first case of this kind seems to have been reported by Schiess-Gemuseus⁴⁶ in 1884. In 1903 Snell⁴⁷ reported three cases of plexiform neuroma involving the eyelids and orbit of one side, and in one of these cases buphthalmos was present on the same side. Histological examination by E. T. Collins demonstrated the presence of the neuro-fibromatous change in the ciliary nerves. Discussing this case Verhoeff⁴⁸ of Boston referred to a similar case in his own experience. Snell did not see any causal connection between the two conditions and thought that the buphthalmos was explained by abnormality of the angle of the anterior chamber, but Verhoeff pointed to the involvement of the nerves and the eye on the same side and thought the abnormality of the ciliary nerves might have

brought about the buphthalmos by disturbing the nutrition of the eye. It would probably be more correct to assume, as in cases of buphthalmos with naevus of the skin, that some embryonic fault was the starting point, both of the neuro-fibroma and of the buphthalmos. It is noteworthy that in some of these cases (Snell) the eye presented other congenital abnormalities, such as absence of part of the zonule, malformation of the lens and coloboma of the iris. Other English references to cases of this group will be found in the *Transactions of the Ophthalmological Society* in contributions by Collins and Batten⁴⁹ and by Sutherland and Mayou⁵⁰. A further interesting parallelism between buphthalmos with neuro-fibromatosis and buphthalmos with capillary angioma is illustrated by cases reported by Vogt⁵¹ and Mintschewa⁵², in which there was radiological evidence of enlargement of the sella turcica, while in Vogt's case there was acromegaly affecting the arm and leg as well as the facial bones on the same side as that of the buphthalmos and neuro-fibroma. The appended list of cases of buphthalmos with neuro-fibroma is largely taken from Mintschewa's paper and is probably incomplete.

Discussion

Considerable interest attaches to the question of the aetiological connection, if any, between buphthalmos or glaucoma on the one hand, and on the other hand the vascular or nervous lesions shown to occur in the brain and meninges, in the mucous membranes, skin and subcutaneous tissues, bones of the skull, pituitary gland and even the viscera. When one considers the variety of associated lesions and the many different combinations in which they may occur, it is evident that a theory which might fit one or two cases may fail when it has to be applied to the whole group, and it cannot be pretended that any satisfactory explanation of the origin of these anomalies has been offered. Some authors have hoped to find in them a guide to the pathogenesis of glaucoma in general. In the examples of choroidal angioma with secondary glaucoma, such as that of Lawford, we may presume that mechanical factors, similar to those operative in any case of intra-ocular neoplasm, may have brought about the rise of tension; but the sequence of events is not so clear in the cases of buphthalmos and simple glaucoma. In some instances no vascular anomaly, extra- or intra-ocular, has been discovered; in some there has been no more than a minimal hyperaemia of the episcleral vessels, and in others, as in Schirmer's original case, merely some dilatation and tortuosity of the retinal veins. No one has suggested that these slight vascular changes are in themselves causes of buphthalmos

or glaucoma, but between these and cases like Lawford's, Snell's and Steffens' varying degrees of angiomatosis, both intra-ocular and epibulbar, have been observed. This has led to the advancement of two *vascular* theories to account for the glaucoma; one, accepted in more or less similar form by Beltmann, Elschmig, Ginzburg, Clausen⁵³, Nakamura⁵⁴, Yamanaka, Bär and Krause, which assumes an increased number and size of the choroidal veins leading, through "plethora" in the choroid, to increased transudation and diminished outflow of intra-ocular fluids, and thus to elevation of intra-ocular pressure; and the theory of Hudelo who postulates the existence of an angiomatous lesion impeding the evacuation of the cavernous sinuses, delaying venous circulation in the choroid and causing accumulation of CO₂ in the uveal blood stream. It is difficult to accept either of these explanations as valid for the cases of simple buphthalmos and still more so for cases of pseudo-glaucoma, like Thomson's and Macrae's. Ginzburg explains that the angiomatous conditions are congenital and in some cases operate early so as to produce buphthalmos, while in others the congenital disposition to glaucoma remains latent and only manifests itself later, owing to some senile vascular change or increase of intra-ocular teleangiectasis which upsets the balance and allows elevation of intra-ocular pressure. Hudelo also argues that the angiomatous lesion may take on growth in adult life and thus cause the development of glaucoma instead of buphthalmos, but these suggestions are not very helpful. Cabannes' case was somewhat peculiar, in that, in association with an extensive subcutaneous angioma in the temporal fossa and neighbouring region there was enormous hypertrophy of the same side of face, tongue, facial bones and orbit, while the enormous buphthalmic eye had neither high tension, glaucomatous cupping nor obstruction of the canal of Schlemm and spaces of Fontana. Discussing his case, Cabannes points out that hypertrophy of tissues and organs in the neighbourhood of angiomata is a well-known fact and argues that the buphthalmos is a congenital hypertrophy due to over-nutrition from the proximity of the naevus. It is true, that hypertrophy of soft tissues, and even of bones, in the neighbourhood of the angioma is illustrated in some of the cases under review, and the hypernutrition assumed by Cabannes, might be applicable in some of these; but in many cases there is no evidence of an angiomatous condition in the vascular system of the eye, and, in any case, hypertrophy due to hypernutrition would not explain the many other cases of buphthalmos with tension, glaucoma simplex and pseudo-glaucoma.

The frequency with which cutaneous naevus follows the distribution of the 5th cranial and other nerves has led to the

suggestion of its nervous origin, and attempts have also been made to explain glaucoma on nervous grounds, but no satisfactory *nervous* theory has been proposed to account for the simultaneous occurrence of these and the other abnormalities under discussion.

Endocrine disturbances have also been invoked to explain the origin of glaucoma, and Ginzburg draws attention to this in considering cases like his own in which glaucoma and naevus were associated with evidence of pituitary disease, and the case of Vogt of neuro-fibromatosis and acromegaly. Nothing, however, has been adduced to show how a primary pituitary fault could bring about the large variety of lesions found in the cases under consideration, and it seems at least equally probable that disturbance in the region of the sella turcica is the result, rather than the cause, of an angiomatous or neuro-fibromatous change.

At least a passing reference should be made to the possibility of a *traumatic* origin for some of these cases. In Macrae's case of naevus with pseudo-glaucoma there was a history of maternal injury in the seventh month of pregnancy. In Thomson's somewhat similar case there was a difficult instrumental delivery and the child was born with great swelling of the right side of the face and some bruising above the right eye, from which the naevus seemed to develop and spread. In a case of naevus and hemiplegia (Cockayne, quoted by Brushfield and Wyatt⁵⁵) the mother attributed the trouble to the fact that during the third month of pregnancy she had seen a cripple with a large birth-mark. In the case which I have described at the outset of this paper there was a history of facial presentation with difficult, but not instrumental, delivery, and the swelling and redness of the left side of the face and the abnormality of the left eye were all attributed to the abnormal delivery. Indeed the steamy opalescent appearance of the cornea when first seen was not unlike the first stage of a birth injury of the cornea. It must be admitted, however, that these cases are few and exceptional and their history scarcely justifies the serious suggestion that trauma played a part in their causation. Birth injury could not, for instance, account for a fully developed buphthalmos or congenital malformation of the disc.

Of the theories offered to explain the association of buphthalmos or glaucoma with the various angiomatous lesions described, the vascular theory has most to commend it, but it seems impossible to establish a causal relationship between the cutaneous or meningeal naevus and the ocular condition. At the most we can say that when angioma affects the choroid this leads to secondary glaucoma, and that a less obvious vascular lesion in the choroid may be present in cases described as glaucoma simplex, but an explanation which will embrace the cases of buphthalmos (with

widely differing clinical and microscopical characters) of pseudo-glaucomatous malformation of the disc and other congenital anomalies of the eye must assume a common initial lesion at a very early embryonic date.

Although vascular disturbances predominate we have to take account of congenital deformities, such as colobomata of the optic nerve, choroid, iris and zonule, polydactyly, cleft palate, hypotrophy and hypertrophy of bone and soft tissues, which may form part of the abnormal picture in different cases, and we cannot omit from consideration those cases in which buphthalmos and glaucoma are associated with neuro-fibromatosis rather than with vascular naevus.

Safar¹⁷ and Marchesani¹⁰ are among those who deny a causal connection between the associated lesions and see in them a group of co-existent congenital anomalies due to a defect in the germinal layers. When we consider the very wide diversity in the structures involved and in the extent and profundity of the changes produced it is necessary to assume an origin very early in embryonic life.

Whatever the cause may be which produces the cutaneous, meningeal or intra-ocular angiomas, or, it should be added, the neuro-fibromata found in other cases, the same cause affects the mesoblastic tissues of the eye, in some cases in such a way as to produce buphthalmos, in some, other congenital anomalies, in other cases giving rise to invisible structural changes which predispose to the occurrence of glaucoma in later life. A view somewhat similar to this is expressed by Aynsley, but this author, being impressed with the association of the intra-cranial and ocular lesions, suggests that when the initial cause "acts to produce naevi of the cerebral vessels *then* the mesoblastic structures of the developing eye may be affected" and "that it is probably in the cases where there is intracranial involvement that eye defects are likely to arise." But it must be remembered that many cases are on record (for bibliography see Parkes Weber⁴⁰) in which cutaneous and meningeal naevus co-existed without any ocular abnormality, and on the other hand cases have been reported in which there was buphthalmos, or other eye condition, with cutaneous naevus but no evidence of intracranial disease. It therefore seems unjustifiable to relate buphthalmos and meningeal angioma so closely to each other as Aynsley has done.

The distribution of the cutaneous naevus in the area of the 5th cranial nerve in many of these cases has naturally attracted some attention and has lent support to the view that some nervous factor accounts for the naevus and for the accompanying ocular lesion. As Cushing has pointed out also the meninges which may be involved in the angiomatous change are innervated largely by the

trigeminal nerve. Another interesting illustration of this association of the meninges and skin is provided by the case reported by Stanley Cobb⁵⁷ in which there was haemangioma of the spinal meninges and naevus of the skin of the same metamere. It is true that in some cases, as in my own case described at the beginning of this paper, the naevus and buphthalmos are unilateral and the naevus confined in a fairly exact manner to the area of distribution of the first two divisions of the 5th nerve, but in some cases we can only speak of a predominance of the naevus on the side of the buphthalmic eye, and in others the naevus has a very wide distribution on both sides of the face and even on the trunk and limbs. Here again, if we tried to bring all these cases into one category and to find the causal factor common to them all, we should be compelled to trace back the cutaneous, meningeal and ocular changes to a common origin, and to assume that while in some cases the initial disturbance may be more or less extensive, it may in others confine itself pretty strictly to one or more of the embryonic metameres.

The point of practical importance which emerges from a consideration of these cases, and to which attention has been directed by several authors, is that the presence of a cutaneous naevus, with or without buphthalmos or glaucoma, may give a valuable clue to the nature of a co-existent intracranial lesion. This was suggested by Allan Sturge as far back as 1879 and by Horrocks in 1883 and was confirmed by operation or by postmortem examination in Cushing's cases and by the radiological findings in the cases reported by Brushfield and Wyatt, Röttl, Foster Moore, Parkes Weber and Aynsley.

Cases of Naevus with Buphthalmos

Schirmer (1860), Sturge (1879), Horrocks (1883), Galezowski (1898), Beltmann (1904), Cushing, three cases (1906), Cuperus (1909), Cabannes (1909), Elschnig (1918), Freese (1920), Elschnig (1922), Nakamura (1922), Zaun (1924), Marchesani (1925), Kiranoff (1925), Vita (1925), Kaiser (1927), Brushfield and Wyatt, two cases (1927 and 1928), Röttl (1928), Aynsley, two cases (1928), Voegelé (1928), Clausen (1928), Parkes Weber (1929), Safar (1929), Krause (1929).

Cases of Naevus with Glaucoma Simplex

Duschnitz (1923), Salus, two cases (1923), Safar (1923), Löwenstein (1923), Ginzburg (1926), Derby, Waite and Kirke (1927), Hartmann (1929), Hudelo (1929), Suglian (1929), Krause (1929).

Cases of Naevus with Secondary Glaucoma

Lawford (1885), Snell (1886), Wagenmann (1900), Steffens (1902), Paton and Collins (1919), Bär (1925), Yamanaka (1927), Knapp (1927), de Haas (1928).

Cases of Naevus with Pseudo-glaucoma

Voegelé (1925), Macrae (1929), Thomson (1929).

Cases of Naevus, Buphthalmos (or Glaucoma) and Intracranial Disease

Sturge (1879), Horrocks (1883), Cushing three cases (1906), Voegelé (1925), Ginzburg (1926), Brushfield and Wyatt, two cases (1927 and 1928), Röttl (1928), Macrae (1929), Thomson (1929), Foster Moore (1929), Parkes Weber (1929), Aynsley, two cases (1929), Hudelo (1929), Krause (1929).

Cases of Buphthalmos (or Glaucoma) with Neurofibroma

Schiesß-Gemuseus (1884), Sachsälber (1889), Lezius (1889), Sachsälber (1898), Snell and Collins (1903), Verhoeff (1903), Collins and Batten (1905), Michaelson-Rabinowitsch (1906), Rosenmeyer (1906), Sutherland and Mayou (1907), Michael (1908), Komoto (1909), Murakmi (1913), Vogt (1924), Mintschewa (1926).

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