THE JOURNAL OF NEUROLOGY AND PSYCHOPATHOLOGY.

VOL. II.

MAY, 1921.

No. 5.

Original Papers.

SOME PROBLEMS IN NEUROLOGY.

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I.—THE ARGYLL ROBERTSON PUPIL.

CONTRIBUTIONS to the study of the Argyll Robertson phenomenon have been so frequently introduced by allusions to its prominent rank as one of the vexed questions of neurology that omission of such preliminary matter may be not unwelcome. If, none the less, the problem still awaits full solution, the lines of approach have been laid down, and clinico-pathological as well as experimental data, whose import is not to be mistaken, have been steadily accumulating. In this paper fresh evidence is furnished pointing to the central origin of the disorder, and a new and simple explanation is proffered for its common occurrence in neurosyphilis.

Strangely enough, doubt still exists as to what actually constitutes the Argyll Robertson pupil, and unless unanimity is reached such horrid expressions as 'a pseudo-Argyll' will continue to blot the pages of what is euphemistically called medical literature. The point is simply whether myosis is or is not to be taken as an integral part of the symptom-complex. Under the title "Four cases of spinal myosis, with remarks on the action of light on the pupil", Argyll Robertson¹ published in 1869 a series of cases, chiefly of tabes dorsalis, in which he observed the phenomenon since associated with his name. Present-day opinion, however, with few exceptions, holds myosis to be facultative and not obligatory, so that the sign may be defined as consisting in absence (or obvious diminution) of the direct reflex to

light, the consensual reflex being either absent or present, with preservation of the pupillary reaction on convergence-accommodation. That this is the soundest view to take is substantiated by the fact that myosis may occur without the dissociated-reflex* phenomenon of the A.R. pupil, and vice versa, and since two different mechanisms are involved they should be considered separately. Why some 30 per cent or more of A.R. pupils should also be myotic is a point of legitimate importance, discussed below. Vision is assumed more or less tacitly to be unimpaired in the A.R. phenomenon, but there seems no good reason to exclude cases of relative blindness which exhibit the dissociated reflex, though in this paper such are omitted. A frequent but not perhaps constant correlated feature of the A.R. phenomenon is absence of dilatation of the affected pupil on painful stimuli from the trigeminal area or elsewhere. Irregularity or inequality of the pupils in the condition is incidental.

CLINICAL CONDITIONS IN WHICH THE A.R. SIGN IS FOUND.

1. The A.R. pupil thus defined, our first concern is with its clinical incidence. As all the world knows, the A.R. phenomenon is encountered in a high percentage of cases of neurosyphilis, of whatever variety, though it cannot be taken as pathognomonic of that morbid condition, or as an infallible index to preceding syphilis. Recall of the prime neurological principle that symptoms depend less on the nature of the pathological process in the nervous system than on its site and the mechanisms involved should have led to hesitation in assuming a unipathological basis for the phenomenon. For the moment, however, the point is that, neurosyphilis being essentially a diffuse toxi-infective state, the peculiarly specific and local action of the spirochæte or its toxin on a particular mechanism will require an explanation which is both simple (for the A.R. pupil is very common in neurosyphilis) and in harmony with the occurrence of the sign in non-syphilitic cases.

By way of illustration only a single example need be given, selected because of the combination of unilateral myosis and bilateral A.R. pupil.

Case 1.—S. S., female, age 40, has a strongly positive Wassermann reaction in the blood, but no signs whatever in the nervous system except a double A.R. phenomenon. The right pupil is in a state of myosis and measures $1\frac{1}{2}$ mm. in diameter; the left, on the contrary, is rather large, in diameter 5 mm.; yet both show the typical dissociated reflex, and from neither is a consensual light reaction obtained in the other.

* I use the expression 'dissociated reflex' only for convenience of description; the reaction of the pupil on accommodation-convergence is not a 'reflex' but rather an 'associated movement'.

This case illustrates the impracticability of attempting to restrict the A.R. sign to the myotic eye, for in all other respects the phenomenon is identical in the two.

2. Of no less importance, if of minor frequency, is the occurrence of the sign in cases of nervous disease altogether independent of syphilis. Still confining our attention to the toxi-infective group, we must emphasize its occasional appearance in the course of epidemic encephalitis. In a recent monograph Tilney and Howe² state that manifestations due to interference with the oculomotor apparatus have been present in 53 per cent of the reported cases, and specify the occurrence of unilateral or bilateral paralysis of pupil-movement on accommodation, dissociated from light-reflex involvement—i.e., the reverse of the A.R. phenomenon, in a sense, for they do not, apparently, point out that the former may be merely the sequel to a paralysis of convergence. The true reversed A.R. pupil consists in absence of reaction on actual convergence of the globes, with presence of the pupillomotor reflex to light. I have, however, seen at least one case of A.R. pupil in the disease.

Case 2.—In a paper³ on epidemic encephalitis a case was detailed, of the mild recovering type, in which bilateral ophthalmoplegia externa was an early and marked symptom. The pupils, rather large and slightly unequal, reacted to light very sluggishly indeed; convergence was impossible, nor was there any pupil movement in the attempt. At a later stage, however, uninterrupted improvement resulted in the complete disappearance of the external ophthalmoplegia, but the light reaction remained greatly impaired. After the paper was written I saw the patient on several occasions, and was able to satisfy myself that the response on convergence had become normal while the reflex to light was still (December, 1918) very imperfect. That is to say, the condition approximated closely to the ordinary A.R. phenomenon. Both in blood and spinal fluid, syphilitic tests always proved negative.

It is known, of course, that reaction of the pupil may take place in an eye paralyzed for convergence, on an attempt at the latter being made. Thus Guillain⁴ has reported an interesting case of unilateral A.R. sign in a patient with a typical syndrome of Weber (non-syphilitic); the left eye showed the A.R. phenomenon, and was also the one paralyzed by the oculomotor lesion. When the patient converged, the right eye moved in and its pupil contracted, and simultaneously the left pupil contracted strongly though that eyeball did not move at all.

3. Again, the sign has been observed occasionally in unmistakable cases of disseminated sclerosis. It was found by Uhthoff⁵ only once in one hundred cases, but it has been seen also by Probst,⁶ Pini,⁷ Marburg,⁸ Rad,⁹ Liwschütz,¹⁰ and others. Rad's two cases, in particular, do not appear to leave any room for doubt. I have myself seen one typical example in the disease.

Case 3.—The patient was a young girl of 22, who came to the National Hospital complaining of paræsthesiæ in the limbs and of dimness of vision of subacute onset. On examination, the abdominal reflexes were absent and the plantars were in extension. Nystagmoid jerking was noted on lateral deviation. Investigation of the blood for syphilis proved negative.

Both pupils were rather dilated (diameter 5 mm.) and completely inactive to strong light, direct or consensual, but they reacted quickly on convergence. The optic discs were normal. I showed the patient to my colleague, Dr. James Collier, who corroborated the A.R. finding, and agreed that the case was one of early disseminated sclerosis.

As the patient disappeared from observation not long afterwards, further survey of the case became impossible.

From the foregoing it is apparent that a characteristic A.R. phenomenon is an occasional occurrence in diffuse toxi-infective states other than neurosyphilis, and surprise might be justifiably expressed if this were not so, for diffuse morbid processes must sometimes light on the same area and disturb the same mechanisms as are implicated in the A.R. pupil of syphilis.

4. The not infrequent development of the dissociated reflex, as a stage towards, or without going as far as, complete fixity of the pupil, has long been recognized to accompany certain cases of cerebral tumour in the vicinity of the third ventricle, aqueduct, or anterior corpora quadrigemina; but this knowledge does not appear to be widely diffused outside neurological circles. Yet these are the cases which furnish the most valuable clue to the general, i.e. commonest, site of the lesion underlying the A.R. sign, and are of significance out of all proportion to their comparative rarity. Two or three illustrative instances from personal observation may be given in some detail.

Case 4.—A. B., male, age 19, came to hospital complaining of headache, lassitude, inclination to sleep, vomiting, diplopia, and an uncertainty of gait. On examination, intense double optic neuritis was found (highest point +6D); there was no ptosis or nystagmus, but conjugate upward movement was defective, and there appeared to be some very slight general weakness of the right limbs; cutaneous and deep reflexes alike, however, showed no deviation from the normal.

The pupils were of medium size; the left was quite inactive to light, and the right responded with great sluggishness, while both reacted briskly on convergence, i.e., there was a double A.R. pupil.

From the defect of upward movement the lesion was with some certainty attributed to the region of the anterior corpora quadrigemina, and it was held that the double A.R. pupil supported this localization. Improving somewhat under general treatment, the patient left without operation after a stay of some ten weeks.

He was seen again almost exactly four years later, and reported himself as quite well and at work. The optic discs were entirely normal, with normal physiological pits. Conjugate upward movement was greatly impaired, in fact almost lost, the eyes tending instead to converge with the effort. No other symptom was present, except that both pupils were

slightly but definitely irregular, medium in size, and exhibited a typical dissociated A.R. reaction on both sides, being immobile to bright light, direct and consensual, but responding actively with accommodation-convergence. On this occasion opportunity was taken to examine the blood for the Wassermann reaction, which was found to be negative.

No doubt can be entertained, I consider, that the case was one of cerebral tumour in the neighbourhood of the superior colliculi, the paralysis of conjugate upward movement being highly characteristic of lesions involving the tectum opticum, and the accompanying typical A.R. sign must similarly be attributed to involvement of some structure or structures in the same part of the mesencephalon.

Case 5.—C. D., male, age 42, was admitted to hospital with a six months' history of headache, giddiness, diplopia, staggering gait and a tendency to deviate to the left, and increasing drowsiness and apathy. On examination the patient was found to have advancing optic neuritis in both eyes, highest point +5 D. There was gross defect of upward movement, the effort always leading to slight divergence merely, with closure of the eyes. Convergence was fair on both sides, though less on the left than on the right. The pupils were equal in size, diameter $2\frac{1}{2}$ mm., and entirely immobile to light, consensual or direct; but both reacted through a fair range, though not briskly, on convergence. No dilatation of either pupil was obtained on painful stimulation of the skin of neck or cheek. A decompression operation was undertaken without any resultant improvement, and some weeks later death ensued.

At the autopsy a tumour was found involving both anterior corpora quadrigemina and the vicinity of the aqueduct generally, which proved on microscopical examination to be a glioma.

In this case the same combination of double A.R. pupil and paralysis of upward conjugate movement of the eyeballs occurred, and the diagnosis of tumour of the superior colliculi was amply confirmed by subsequent pathological investigation.

*Case 6.**—E. F., male, age 24, was admitted to hospital with a history that for three months he had suffered from headache, and that during the last week or two his vision had begun to fail. Examination revealed intense double optic neuritis, and pupils which were rather large ($5\frac{1}{2}$ mm.) and immobile to light. There was no ocular paralysis at this stage, and though convergence was good the accompanying pupillary contraction was almost nil. A fortnight later associated upward movement of the eyes became very imperfect, and the pupils had come down to a diameter of $3\frac{1}{2}$ mm., the light reflex still being absent. Six weeks later upward movement was completely paralyzed, and while the light reflex was lost both on direct and consensual stimulation, the reaction on convergence was brisk, i.e., a double characteristic A.R. sign was obtained.

Operation was offered, but, the patient's friends refusing consent, he was removed from hospital.

* For permission to refer to this case I am indebted to my senior colleague at Queen Square, Dr. James Taylor, whose house physician I was when the patient was under his care.

The importance of this case, apart from its identity with the preceding two as far as the combination of the A.R. pupil with tumours of the superior colliculi is concerned, resides in the proof it furnishes of variability under observation of the phenomenon itself and of the accompanying pupil changes. Thus the original stage of dilated and almost fixed pupils was followed by one of reduction in size coupled with the appearance of a typical A.R. sign, the former being associated with normal eye movements and the latter with complete paralysis of conjugate upward deviation. Since there is a common idea that in neurosyphilis the A.R. phenomenon, once developed, is a fixture, special attention must be drawn to the fluctuating nature of the dissociation in certain cases of mesencephalic lesion, a variability which is only to be expected, but which, at the same time, is of considerable pathogenic significance.

The occurrence, then, of the A.R. pupil in connection with non-syphilitic lesions in the vicinity of the aqueduct and anterior corpora quadrigemina is amply proved, and renders pointless the *ex cathedra* criticisms of Dunn,¹¹ who declares that "it is impossible for me to understand how a tumour in the region of the third ventricle can produce a typical Argyll Robertson pupil. Every fact of the history of the growth of brain tumours and every fact of the history of the Argyll Robertson pupil pleads against such a possibility" (*sic*). His dogmatic assertions, however, are somewhat discounted by his admission that he has never seen a case of mesencephalic tumour and by his uncompromising adherence to the view which assigns myosis an integral share in the syndrome.

Analogous instances from the literature are rather few and far between, but an excellent case is the old one of Moeli's¹² (1887); in it a typical bilateral A.R. sign (pupils 5 mm. in diameter) resulted from a tumour of the third ventricle in a man of 57, vision being unaffected. From Weisenburg's¹³ useful paper on tumours of the third ventricle it would appear that 'impaired pupil reactions' have been often observed, though the A.R. sign is not specifically mentioned. In this respect, however, many of the cases quoted by Weisenburg from the literature have been very imperfectly examined. The reader may also be referred to *Case 2* in a paper¹⁴ on ectopia pupillæ in mesencephalic lesions, where the pupils were unequal, with sluggish reaction to light and brisk response on accommodation, and where the lesion was a colloid tumour of the third ventricle. Jelliffe and White¹⁵ state that the A.R. pupil has been found in cases both of third-ventricle and of pineal tumour, but do not give references. Farquhar Buzzard¹⁶ has also stated that he has seen the phenomenon in non-syphilitic cases of mesencephalic tumour, those he briefly describes being for all practical purposes identical with my own in

the combination of the A.R. sign with paralysis of vertical movement of the eyes. To the objection of Cestan and Dupuy-Dutemps¹⁷ that the sluggishness or fixity of the pupillary reflex to light in tumour cases is due to concomitant amaurosis the result of the optic neuritis, that such pupils are always dilated, and therefore that the condition is a 'pseudo-Argyll Robertson sign', there is a ready answer; many cases of optic neuritis are not accompanied by any defect of vision. Vision was perfectly normal in *Case 4* (A. B.) above, and but little diminished in *Case 5* (C. D.), while in *Case 6* (E. F.) the pupils were large and immobile to light at first and actually became smaller as the disease progressed and as vision became impaired. Moeli's case, too, disproves the contention.

5. Reflex iridoplegia, again, has been described in syringomyelia or syringobulbia (Lévi and Sauvinau,¹⁸ Dejerine and Mirallié,¹⁹ Sicard and Galezowski,²⁰ Rose and Lemaitre,²¹ and others). In Dejerine and Mirallié's case the A.R. phenomenon was unilateral, as in the case of Sicard and Galezowski, and in one of two published by Rose and Lemaitre. Interesting though these records are, their value would be increased were information as to the pathological lesions forthcoming.

The occurrence of the A.R. pupil in chronic alcoholism has been reported, among others, by Nonne,²² whose case certainly appears entirely free from criticism; in it the Wassermann tests were repeatedly negative. One such case has come under my personal observation.

Case 7.—J. S., male, age 58, was under my care at the National Hospital for nervous symptoms associated with chronic alcoholism. He had long been known to be a chronic tippler. I was called to see him at his own home one day, the history given me being that he had fallen in the street and had remained unconscious for almost twenty-four hours. On regaining consciousness he was confused and disoriented, and complained of his vision being 'funny'. When I examined him I found the optic discs quite clear. The pupils were rather small and absolutely immobile to bright light—on previous occasions their reactions had always been normal—both direct and consensual, whereas they reacted slightly but definitely on convergence. This movement of convergence, it should be said, was poor, and ocular movements generally were poor in range and not particularly well sustained in any direction. A diagnosis of polio-encephalitis hæmorrhagica superior was made. After about six weeks, when the patient visited hospital again, both the light and the convergence movements of the pupils had much improved.

It is true that in this case a Wassermann test was not made, but apart from this regrettable omission I submit that the known facts in connection with the case substantiate the clinical diagnosis.

Biermann²³ has put on record a good case of the A.R. pupil in diabetes mellitus, Wassermann tests being repeatedly negative. Mention may also be made of the development of the sign in the chronic

hypertrophic interstitial neuritis of Dejerine-Sottas, and in some reported cases²⁴ of progressive muscular atrophy or amyotrophic lateral sclerosis. But no such cases can now be accepted as genuinely non-syphilitic unless they have run the gauntlet of serological and spinal-fluid tests.

6. Of considerable interest and importance are the examples of the phenomenon of traumatic origin; in fact, a surprising number have now been put on record, many of which are beyond cavil genuine A.R. cases.

Two groups may be distinguished: (a) cases in which the lesion is in or behind the eye itself; and (b) cases in which the lesion is in the central nervous system. To the first of these belong the cases of Axenfeld,²⁵ in one of which the eye itself was injured by a splinter of wood; with vision $\frac{2}{25}$, and a large pupil immobile to light, a prompt reaction on convergence was nevertheless obtained. Analogous examples of A.R. pupil from direct unilateral lesion of globe or orbit have been published by Cosmettatos,²⁶ Ohm,²⁷ Velter,²⁸ Abelsdorf,²⁹ and others. In Ohm's case a splinter of iron entering the eye was followed by a mydriasis traumatica and fixity both for light and convergence; several months later the reaction on convergence returned, thus leaving a pure A.R. pupil, with good sight. Velter's case was that of an attempted suicide, with an orbital smash from a revolver bullet; a complete unilateral A.R. pupil resulted. Other examples of the condition have followed fractures of the base (Axenfeld). In the second group are the bilateral cases resulting from central traumatic lesions. Finkelnburg³⁰ has reported a case in an old man on whose head fell an iron instrument weighing some 150 lb., unconsciousness immediately resulting. In addition to general intracranial symptoms of concussion or contusion, the patient developed a bilateral A.R. phenomenon within a week or two of the accident, and the suggestion is that they were due to minute hæmorrhages in the peri-aqueductal grey matter and consequent degeneration. A particularly interesting case is that recorded by Bergl.³¹ The patient was a soldier concussed by the explosion of a shell twenty feet away; in addition to familiar symptoms of intracranial commotio, within a few days a typical double A.R. pupil was found, the pupils being rather large, and yet after some three weeks of continuous observation the phenomenon disappeared entirely and pupillary reactions became normal. Of other traumatic central cases that of Guillain, Rochon-Duvigneaud, and Troisier⁴ may be briefly mentioned.

The patient was a young man of 26 who had attempted suicide with a revolver, the bullet entering on the right side of the neck just at the level of the hyoid, and being found by *x*-ray examination to have lodged in the

position of the right cerebral peduncle. A complete left hemiplegia ensued, with left hemianopia, some ptosis, weakness of some ocular muscles on the right, and a classical A.R. sign on the right and incomplete on the left (this pupil reacting sluggishly to light). Repeated examination of the spinal fluid for evidence of syphilis proved negative. It should be stated that the A.R. pupil developed under observation, for it was not present in typical form when the patient was admitted to hospital shortly after the injury.

Further reference to these traumatic cases is made in a later paragraph.

From a consideration of the clinical material, personal and otherwise, at our disposal, pathological multiplicity for the A.R. phenomenon must be accepted, in which case questions as to its diagnostic and prognostic import assume a subsidiary position. Recourse to serological and spinal-fluid tests has taken the place of unsatisfactory speculations on the A.R. pupil as a criterion of active syphilis. It may undoubtedly remain as a neurosyphilitic 'scar' long after active mischief has ceased, and cannot be held to be prognostic of anything. Its localizing importance, on the other hand, is fundamental, and is intimately bound up with the difficult question of its pathological physiology.

THE ANATOMO-PHYSIOLOGICAL ARC FOR THE LIGHT REFLEX.

When light falls on the eye the physical stimulus sets in action two physiological mechanisms, one concerned with vision (the 'sight' mechanism) and the other with reflex contraction of the pupil (the 'light' mechanism). That these are physiologically distinct can admit of no doubt, though whether they are also anatomically separable is possibly not so certain, Magitot's³² contention being that the reflex-activating fibres are no more than collaterals of the visual fibres, leaving the tract at a point near the external geniculate body. The following considerations, however, must be borne in mind.

1. The presence of both thick and thin fibres in the optic nerve and tract, the former of which were traced by Monakow to the superior colliculi, but none of the latter, suggests a difference of function (substantiated also by Reichardt's³³ case), to which, further, the existence, according to Cajal,³⁴ of single and multiple combinations in the retina of ganglion cells with bipolar cells and rods or cones lends support; his plausible hypothesis is that the single combinations subserve vision and the multiple the light reflex.

2. In spite of the general truth that vision and reflex activity to light diminish *pari passu*, so that in complete optic atrophies the pupils are often immobile, the exceptions are so numerous as to suggest an anatomical as well as the accepted physiological distinction between the two systems. In optic neuritis, optic atrophy, detachment of

the retina, quinine amaurosis, etc., vision may be lost yet the pupillo-motor reflex may persist; on the other hand, Axenfeld's and other peripheral traumatic cases show that with loss of the light reflex vision may persist. To assume an anatomical difference, represented also by the difference in susceptibility or vulnerability, does not appear unjustifiable, although the subject could do well with less speculation and more patient anatomical research. In this connection the case published by Reichardt³³ may be quoted, one of optic atrophy and amaurosis with conservation of the light reflex. Histological examination revealed persistence of a large number of undegenerated optic nerve fibres, whence it might be deduced that these were capable, during life, of mediating the light reflex but incapable of provoking a quantitative sensation of light (Magitot³²). But this interpretation (which is not Reichardt's, be it noted) is at least doubtful, since the excellent researches of Léri³⁵ on tabetic optic atrophy have shown how few need be the persisting fibres in the optic nerve to allow of the appreciation of light stimuli.

However this may be, a physiological differentiation for reflex impulses as opposed to visual impulses must be fully admitted; the physiological results both of stimulation and of destruction of the external geniculate body are quite different from those relating to the superior colliculi, and prove the pupillary and visual paths are not identical.

Omitting in this place the question of the exact retinal origin of the light-reflex fibres, and leaving the visual route aside, we may proceed along the reflex pupillomotor path. It undergoes a partial crossing in the chiasma (analogous to the visual crossing), as is shown by the researches of Cajal and of van Gehuchten. Parsons³⁶ states that this partial decussation is also "proved by the hemiopic pupil reaction of Wernicke"; but less reliance can be placed on that reaction since the studies of Walker³⁷ have demonstrated its occurrence in some cases of posterior hemianopia, i.e., due to lesions behind the level of the external geniculate body, and an equally convincing case has been published by Dejerine and Jumentié,³⁸ the lesion being a hæmorrhagic softening which had destroyed, *inter alia*, the optic radiations posterior to the basal nuclei.

In the optic tract the pupillomotor reflex fibres can be followed to a point just before the external geniculate body is reached. The best method of physiological demonstration in this respect, that of constriction of the pupil by electrical stimulation of the optic nerve, has been utilized by Karplus and Kreidl,³⁹ who have found that all along the optic tract, except where it enters the lateral geniculate, electrical excitation contracts the pupil, and these pupil-controlling fibres can be followed, millimetre by millimetre, along the superior

brachium (or 'arm' of the corpus quadrigeminum anterius) and the anterolateral edge of the superior colliculus. At this point the electrical effect is again lost. From these important experimental results it may be taken that the pupillomotor reflex path avoids the external geniculate body and passes to the grey matter of the superior colliculus by the brachium. After bilateral section of the superior brachium the reaction of the pupils to light is absent; in this fashion Karplus and Kreidl have, in the ape, produced a bilateral A.R. sign which remained unchanged for eight months after the operation. They do not assert that in the A.R. phenomenon in man the lesion is of necessity at the same spot where they have been able to produce it experimentally, but their results are obviously of the first importance.

At this stage, however, it is desirable to deal with the arguments denying to the superior colliculus and its brachium a place in the linked chain from retina to iris. Omitting the early experiments of Knoll (1869) and Bechterew (1884) we may consider the researches of Ferrier and Turner (1901).⁴⁰ These investigators destroyed with a cautery the region of the superior and inferior colliculi in seven monkeys; in all the experiments, with one exception, the pupils after the operation were contracted to the size of pin-points, but only temporarily, for after two days they returned to their natural size. In the author's own words: "As regards the pupillary light reaction, *in the cases in which it was tested it appeared to be present (so far as reliance may be placed on this reaction when tested in animals, where it is so difficult to eliminate the complication of convergence and accommodation)*" (italics mine). To the evident hesitation of the authors themselves in the matter, further doubt is added when it is remarked that a perusal of their protocols shows apparently that only one animal is recorded as having had its pupil reactions tested, and in it (see their *Fig. 1*) "the anterior border of the nates on the left side, and the posterior margin of the testes" remained. Thus their work can *not* be taken to prove that the whole anterior colliculus may be destroyed without preventing the light reflex, both because of the limited number of animals in which the pupillary reflexes were investigated and the admitted difficulties in the way of testing, and because in view of the uncertain path of the light reflex fibres from brachium to oculomotor nucleus no adequate proof is forthcoming from the experiments that these fibres could not have escaped. In fact, the complexity of cells and fibres in and beneath the superior colliculus is such that cases of incomplete lesion of that structure without apparent pupillary disorder cannot be taken to invalidate the views here advanced.

Special stress is laid on this matter, because Ferrier and Turner's experiments have been cited over and over again as supposedly proving that the superior colliculi have nothing to do with the light

reflex (Lhermitte,⁴¹ for example, states that these observers "n'ont pu obtenir chez le chat ou le singe aucune modification de la réflexivité pupillaire par l'ablation de la paire antérieure des tubercules quadrijumeaux").

The experimental work of Levinsohn⁴² must also be noticed. This observer destroyed *one* superior colliculus only in each of three apes, and after a few days found normal light reflexes in both eyes in them all. From the photographs accompanying the paper it is not very clear precisely how much of the colliculus was destroyed; in one, at least, much of the peri-aqueductal grey matter seems to have been left intact. Nor is there mention of microscopical investigation of a sufficiently detailed character. Levinsohn does not state whether direct or consensual testing was made, and since only one colliculus was injured the experiments are open to some indefiniteness of interpretation.

Undoubtedly the crux of the whole question lies in the fact that the exact anatomical pathway from the anterior colliculus to the sympathetic nucleus in the oculomotor nuclear system has not yet been definitely traced, yet the difficulty resides not in poverty but in plenitude of neuronal connections. As Edinger⁴³ says, "Fasernetze und Züge, durch welche die Verbindung stattfinden *könnte*, sind in dieser Gegend mehrfach vorhanden. Das beweisende Experiment oder die beweisende klinische Beobachtung mit nachträglich erhobenem Befunde steht noch aus". It may be assumed with a considerable degree of certainty that the light-reflex neurones whose origin is retinal end at the level of the brachium or superior colliculus—for after enucleation of the eyeball Probst⁴⁴ has not been able to trace degeneration beyond the latter structure—and that there they enter into connection with a new set. Of the various more or less alternating layers of grey and white matter in the superior colliculi, certain cells and arciform fibres therefrom derived, belonging to the deepest layer, engage our attention. They constitute the colliculonuclear tract, which takes origin especially in the large cells of the fourth layer and has both a direct and a crossed connection with the mid-brain; the latter is made via the "fountain-like" decussation of Meynert, whereby collaterals and terminal branches reach the oculomotor nucleus (and also the other ocular nuclei), while the uncrossed fibres descend to terminate in the homolateral third-nerve nucleus and in the others also (Tilney and Riley⁴⁵). According to this description the crossed fibres skirt the aqueduct below to reach the opposite oculomotor cell-groups, but of no less importance is the dorsal crossing above the aqueduct, with subsequent connection to the opposite nuclei, as already mentioned. This lamina commissuralis mesencephali (Edinger) is to be distin-

guished from the posterior commissure which lies in front of it, and with which it has been erroneously confused.

Above, below, and laterally these fibres of the colliculonuclear system skirt the central grey matter of the aqueduct, and would be the first to suffer from any peri-aqueductal toxic invasion. The significance of this statement is discussed more fully in a subsequent section.

In this fashion both the direct and the consensual reflex response of the pupil to light can be readily explained. If there is, as has been already stated, a partial decussation of pupillomotor reflex fibres in the chiasma, such a further semi-decussation on the afferent side of the oculomotor nuclei must be conceded; otherwise the consensual reaction from the temporal side of the retina of the affected eye in a case of unilateral A.R. sign could not be explained, as has been well pointed out by Harris.⁴⁶ The same author's study of the mechanism of the pupil reflex to light in animals and birds "proves the necessity for a posterior decussation of the pupil-reflex fibres between the corpus quadrigeminum or optic lobes and the third nuclei, total for those animals with total decussation of the optic nerves at the chiasma, and partial for those animals with semi-decussation of the optic nerves, in proportion to the size of the uncrossed bundle".

Though the experimental and clinical evidence now adduced argues strongly in favour of the passage of the light reflex by the superior colliculi, not a few writers have suggested a route which avoids these structures, viz., by the tractus peduncularis transversus, a fibre-system of uncertain origin and ending, which apparently leaves the optic tract at the outer side of the crus and skirts the latter mesialwards to enter the mid-brain at the side of the emerging fibres of the third nerve. Here it appears to end in, or reach, a small nucleus first described by Bechterew and by Marburg, which nucleus, according to Edinger,⁴³ represents a part of the ciliary ganglion that has not wandered out to the orbit. While further research may enlighten us as to the anatomy and physiology of this tract, our present knowledge is insufficient to justify any speculation as to its possible connection with the pupillomotor reflex.

Of other definite internuncial paths in the vicinity, reference may be made to the fasciculus longitudinalis dorsalis of Schütz, also known as the peri-ependymal longitudinal tract, consisting of a set of fine myelinated fibres immediately under, and above, the ependymal lining of the aqueduct, and therefore actually in the peri-aqueductal grey matter. Arising in a mesencephalic nucleus, the nucleus dorsalis tegmenti of Gudden, the tract seems to be of much less importance in man than in lower animals, since it represents a primitive motor pathway between the olfactory lobe and the ocular and lower

cranial musculature. For anatomical and comparative anatomical reasons, and notwithstanding its ocular connections, this tract cannot be supposed to mediate the nerve impulses from tectum opticum to oculomotor nuclei, disorder of which is responsible for the A.R. pupil. Similar statements may be made of the familiar posterior longitudinal bundle—another and more important (partially descending) mesencephalic pathway. Linking up, *inter alia*, vestibular and ocular apparatus, and extending as far forward, apparently, as the regio hypothalamica, the bundle nevertheless does not furnish clear anatomical proof of conveying impulses from intercalated collicular neurones to the intrinsic oculomotor nuclei. Finally, there remain the tectobulbar and tectospinal tracts, which arise in the grey matter of the superior colliculi and constitute the outer section of the arciform fibres alluded to above as originating in the deeper cell layers of the tectum. They cross below the aqueduct in the dorsal tegmental decussation of Meynert, between the twin red nuclei. The evidence suggests that these pathways serve to activate reflex movements in ocular, facial, neck, trunk, and arm musculatures in response to light stimuli via the anterior corpora quadrigemina, and, while the mechanisms are doubtless analogous to that responsible for the light reflex in the pupil, the latter is not carried out by these fibres [see below, however].

A further word of explanation is probably necessary. From what has been said already the student of the subject will gather that the arciform fibres of the tectum are divisible into colliculonuclear, tectobulbar, and tectospinal sets, distinguishable, to some extent at least, by the levels at which they effect a decussation. It is possibly somewhat impracticable thus to differentiate three groups; at any rate, what has been called the colliculonuclear tract is included by some authorities in the tectobulbar system. Van Gehuchten,⁴⁷ for example, states that the tectobulbar fibres, in descending and crossing below the aqueduct to apply themselves to, though remaining distinct from, the posterior longitudinal bundle, give off collaterals to the cells of the third-nerve nucleus of both sides. Cajal,³⁴ on the other hand, believes that the connection between tectum and oculomotor nucleus is effected by his nucleus interstitialis, the origin, or one of the origins, of the posterior longitudinal fasciculus, collaterals from which, as is known, reach the third nerve centres. We are, in fact, thus brought back to the view of Edinger, that the possible paths by which the junction can be brought about are abundant enough. It matters little, as a fact, what name is given to the innermost set of arciform fibres as long as we recognize that directly, or by the 'fountain' decussation of Meynert or the dorsal decussation above the aqueduct, those of the fibres which are nearest to the aque-

ductal grey matter reach the homolateral and heterolateral oculomotor nuclei.

Perhaps the point may be made clearer from another aspect. The tectum opticum (optic lobes, region of the anterior corpora quadrigemina, superior or anterior colliculi, nates) is a reflex station of much significance and of wide relationships in connection with light impressions, as is the region of the posterior corpora quadrigemina in connection with auditory impressions. Taking only the former, it stands in anatomo-physiological affinity with homo- and heterolateral mesencephalo-ponto-bulbo-spinal centres for eye, face, head, neck, trunk, and limb movements in response to the stimulus of light. These are effected via descending crossed and uncrossed connections represented by various tectofugal fibre-systems. Of these, the suggestion here advanced is that the most anterior is that concerned with the reflex contraction of the pupil to light, the next anterior with movements of the eyeballs in response to light, and so on. For the moment, the physiological actuality of the most anterior connection is of more importance for our purpose than the nomenclature we adopt for what appears to be the anatomical path for the reflex, viz., the fibres from the superior colliculi which skirt the aqueductal grey matter above and below on their way to the third-nerve centres.

Our next problem is to determine where in the latter is situated the iridoconstrictor centre, a problem, unfortunately, which is just as vexed as the other we have been discussing. To quote Parsons³⁶ again: "The number of reflex pupillary centres which have been described and localized by various writers, each with the utmost assurance, is bewildering in the extreme".

The iris-constricting centre is usually taken to be located in the nucleus of Edinger-Westphal, a small-celled paired nucleus well to the anterior end of the oculomotor group and close to the mid-line. Edinger⁴³ himself believes from the cell-character of the nucleus (small, spindle-shaped or bipolar cells) that it is the visceromotor centre for the præganglionic fibres which, by a relay in the ciliary ganglion, are connected to post-ganglionic fibres running in the short ciliary nerves to the sphincter iridis; Westphal,⁴⁸ finding the nucleus unchanged in a case of complete ophthalmoplegia externa, argued for its visceromotor nature by exclusion. Many objections, however, have been raised to this localization in the Edinger-Westphal nucleus of pupillomotor function: (1) According to Magitot⁴⁹ the pupils react to light by the end of the fifth month of foetal development, but at that stage the cells of the Edinger-Westphal nuclei are completely undifferentiated, not being recognizable till the seventh month; only the ventral part of the principal lateral nucleus of the oculomotor

constellation is then found to be recognizable. (2) Magitot further states that the nucleus is not seen in any other animals than man and the ape; in fact, in the latter animal small-cell groups are scattered here and there in the oculomotor nucleus and central grey matter generally, "sicher sind sie aber nicht zu einem eigentlichen 'Kern' vereinigt" (Monakow)⁵⁰. (3) In several cases of fixity of the pupils to light, Majano⁵¹ found no pathological changes in the Edinger-Westphal nucleus, while in another case it showed outfall of cells though the pupillary reactions were normal. Other observers have reported analogous cases. (4) Experiments by Bach⁵² and by Biervliet,⁵³ and embryological researches by Tsuchida,⁵⁴ would appear to show that there is little specific localization either of individual external or internal muscles in definite parts of the oculomotor nucleus, but rather a diffuse or general localization. As far as the supply of the non-striped muscles of the eye is concerned, Monakow⁵⁰ concludes that their cells of origin are scattered mainly throughout the anterior (frontal) and mesial aspect of the principal lateral nuclei. Yet, if this were so, nuclear external ophthalmoplegias, the internal muscles unaffected, become more than ever difficult to explain.

Another by no means unattractive hypothesis may finally be mentioned. Is it possible that the light-reflex fibres from the superior colliculi, in the colliculofugal pathway already described, do not actually enter the oculomotor nuclei, but join the third-nerve trunks immediately below the nuclei and run with them to the ciliary ganglia, where they end in relation to post-ganglionic fibres to the iris? This is the contention supported by Majano⁵¹ with much carefully investigated clinico-pathological and experimental material. He has adduced evidence which goes to show that the fasciculus longitudinalis prædorsalis, as it is sometimes termed—i.e., the tectobulbar tract, distinct from the posterior longitudinal bundle, arising from the lateral nucleus of the superior colliculus and crossing in part in Meynert's dorsal decussation—contains fibres which run, homolaterally and heterolaterally, into the third-nerve trunks directly, and so to the ciliary ganglia. In this fashion he simplifies the reflex arc considerably, reducing it to three components: (1) from retina to superior colliculus; (2) from colliculus to ciliary ganglion, a path which joins the oculomotor nerves but avoids their nuclei; (3) from ciliary ganglion to sphincter iridis. Uncertain though the matter is, evidence placing a pupilloconstrictor centre somewhere in the general oculomotor group is not to be lightly set aside.

It is known that the visceromotor fibres of the third nerve are distinct from the somatic-motor fibres, for in incomplete lesions of

the third nerve they may be intact when the latter are involved, and an old experiment of Schiff would appear to show that they are to be found to the inner sides of the oculomotor trunk.

Of the last stage in the reflex arc, from ciliary ganglion to iris, little need be said. There can be no doubt that this ganglion is the actual peripheral sympathetic ganglion for the sphincter iridis, though the short ciliary nerves differ from other post-ganglionic fibres in that they are myelinated, i.e., they are 'white' rami, and not 'grey'. Excitation of the ganglion produces myosis; and paralysis, mydriasis to an all but maximum degree.

THE PATH FOR CONVERGENCE AND ACCOMMODATION.

The negative element in the A.R. sign being the failure of the pupil to respond to light, the positive element is its contraction with the effort of accommodation.

Ordinarily speaking, accommodation is a willed movement and therefore of cortical origin; in the act, three muscles take part—the internal rectus, the ciliary muscle, and the sphincter iridis. Now the fundamental principle of cortical motor activity is that, in the cortex, movements and not muscles are represented. The movement of closing the fist is cortical, and the cortex, as it were, knows nothing of the muscles by which this movement is actually effected, viz., the three sets of flexors of fingers and thumb, extensors of the carpus, and triceps, respectively. There is trustworthy evidence which goes to show that the link between these groups takes place in the spinal cord. Similarly, the movement of lateral deviation of the eyes has its cortical centre at a known spot in front of the precentral gyrus, but the linking of homolateral internal rectus and heterolateral external rectus is effected at the pontine level by association between their respective nuclei. By analogy, we must hold that accommodation, as a movement, has a cortical centre, whereas the linking of the muscular components is peripheral, and is mediated by peripheral internuncial paths.

Of the actual site of this cortical centre we are ignorant, though, since the physiological centre for the oculorotary system (anatomically, the corticonuclear tract) is situated approximately at the junction of the second frontal and precentral gyri, a twin accommodation centre, for convergence instead of lateral deviation, may conceivably lie in the same vicinity, corresponding areas in the two hemispheres being physiologically associated. Be this as it may, the anatomical pathway known as the corticonuclear tract proceeds by the internal capsule near the genu to the crus cerebri, whence the nuclear fibres pass dorsally by the pes lemnisci profundus, through the fillet, to the nuclei of the extrinsic ocular muscles; and it is no unwarranted speculation

to suppose that by this tract also the impulse to effect accommodation in the triad of muscles already mentioned reaches their peripheral centre in the oculomotor nucleus, from which, as far as the intrinsic muscles are concerned, the path must lie via the ciliary ganglion.

It is immaterial for the purpose of this paper what is the exact relationship of the contraction of the iris to the ciliary-muscle and the internal-rectus contractions respectively; suffice it to say that in the former we have an associated movement rather than a reflex in the strict sense, and that if this 'synkinesis' is unusual in that it is a combination of somatic-motor and visceromotor elements the fact that the sphincter iridis is phylogenetically a striate muscle should not be forgotten.

From this necessarily brief account of the anatomo-physiology of accommodation, the point of importance for the A.R. pupil that emerges is that distal to the oculomotor nucleus the pathways for iris-contraction in response to light and in association with convergence-accommodation are identical. Lesions of the oculomotor trunk never cause reflex iridoplegia: no claims for the existence of separate (sympathetic) fasciculi in the oculomotor trunk for the two visceromotor functions will stand investigation, though this is the contention made to explain some of the local traumatic cases (see below).

SITE OF THE LESION UNDERLYING THE A.R. SIGN.

From the above descriptions it will be apparent that a unique or single localization for the A.R. sign is not to be expected, except that clinical, experimental, and pathological evidence combine to place the lesion on the afferent side of the light-reflex arc, i.e., anywhere up to the synapse of pupillomotor reflex fibres with pupilloconstrictor centre in the third-nerve nucleus, or its vicinity.

1. In my view, by far the most common localization is in the neighbourhood of the aqueduct, where colliculonuclear fibres may be caught before they enter the oculomotor nucleus, and from which accommodation-fibres are far removed. Fresh evidence has been advanced in this paper of the association of the A.R. phenomenon with tumours of the superior colliculi and third ventricle, and on these cases I desire to lay the greatest stress. They prove beyond cavil the possibility of the development of the sign from non-syphilitic processes of mesencephalic origin on the afferent side of the third nuclear group. This view receives strong support from the researches of Karplus and Kreidl, which in reality provide that *experimentum crucis* hitherto wanting.

No originality whatever is claimed for this view, since it has been advanced many times before, but the support it receives from the tumour cases given in detail above is sufficient to place it beyond the

sphere of mere unverified hypothesis. Harris,⁴⁶ for example, in a closely argued paper, states that "although there is no positive evidence, I believe that the lesion of the Argyll Robertson pupil is a sclerosis of these fibres (fibres of Meynert's decussation), especially of their terminations in the neighbourhood of the third-nerve nuclei, a hypothesis which will account for all the phenomena of reflex iridoplegia".

There remains for some consideration the question of the frequency of the sign in neurosyphilis and its comparative rarity otherwise.

The neurologist is familiar with the peri-aqueductal degeneration often found in disseminated sclerosis; in fact, in that disease a subependymal sclerosis all round the ventricular system is common, and one of its possible explanations is a toxic lymphogenous invasion from an infected cerebrospinal fluid (though some have argued for a special vascular arrangement to explain this periventricular affection). Now in syphilis and other infective states an ependymitis or subependymitis is no uncommon condition—e.g., the granular ependymitis of parenchymatous neurosyphilis—and it appears to the writer a feasible speculation that there may be a special tendency for the syphilitic toxin to filter through to affect peri-aqueductal fibres, or terminal sensory arborizations, by lymphatic or possibly by vascular routes. A subependymal, peri-aqueductal, toxi-infective lymphatic spread will account for the frequency of the A.R. pupil in syphilis as readily as does a lymphogenous invasion via dorsal roots account for the absence of the knee-jerk. If it is asked why in such a postulated subependymal toxic spread the peri-aqueductal grey matter does not first suffer, one may legitimately point to the peculiar affinity of the syphilitic neurotoxin for afferent systems or for afferent terminal arborizations. In the search for a simple, uncomplicated, explanation of the *early* and *common* appearance of the A.R. pupil in neurosyphilis, at a time when the only other objective signs are likely to be toxic changes and evidence of meningeal reaction in the cerebrospinal fluid, I suggest that the theory now advanced, of an irregular spread of the toxin through subependymal tissues surrounding the aqueduct to susceptible afferent fibres or terminal dendrites, will be found more feasible than any other. The argument from the subependymal changes in disseminated sclerosis (peri-aqueductal, periventricular, under fourth ventricle floor, etc.) is topographically important though pathologically not to be stressed. By this theory the variations of the A.R. pupil in neurosyphilis—its uni- or bi-laterality, its absolute fixity or simple sluggishness, the presence or absence of consensual reflexes to light—can be readily understood. Jelliffe and White's¹⁵ view that "chronic meningeal exudates" in syphilis press upon the pupillomotor fibres in the brachium or anterolateral border of the

superior colliculus is, I submit, incapable of explaining the early appearance of, and variations in, the A.R. phenomenon as satisfactorily as the one now offered. Moreover, the first changes in the reflex arc being supposedly toxic, and not structural, one may in this way easily understand such observed facts as absolute A.R. pupils becoming relative, sluggish reactions becoming active, consensual reflexes returning, and so on.

2. In other and rarer cases, as we have seen, the site of the lesion is presumably nearer the back of the eye, in the course of the optic nerve or tract distal to the geniculate bodies. Axenfeld's unilateral traumatic cases can probably be elucidated on the supposition either that sufficient fibres were left to allow visual, but not pupillomotor, impulses to pass, or that there is a difference of vulnerability between thick and thin fibres. The observers of some of the other local (orbital) traumatic cases do not, however, thus explain the phenomenon. Abelsdorf,²⁹ for example, thinks a partial lesion of the third-nerve trunk in his case will account for the reflex iridoplegia; Ohm,²⁷ too, presupposes a double path in the nerve, one for the light-reflex and the other for the iris-reaction on convergence. These views are untenable, or at least unsupported by any pathological evidence. In cases of injury to the third-nerve trunk, Cushing⁵⁵ noted temporary paralysis of external muscles with intactness of internal muscles, but never a dissociated reflex in the latter.

3. Another theory assigns to lesions of the ciliary ganglion the phenomena of the A.R. pupil, a view urged notably by Marina,⁵⁶ and Lafon,⁵⁷ among others. Marina found degeneration and chromatolysis of cells in the ciliary ganglia in neurosyphilitic cases, and supposed the convergence-fibres run through the ganglion without interruption, only the light-reflex fibres being relayed. But the manifold objections to this theory far outweigh its possible attractiveness. The results of experimental paralysis of the ganglion (dilatation and complete immobility of the pupil for all stimuli) are utterly different from the clinical features of the A.R. sign; ganglionic lesions will not explain the myosis of many A.R. pupils, or the conservation of consensual reflexes in many instances; and not readily the absence of the dilatation-reflex following painful excitation. Pathologically, Thomas⁵⁸ found no degeneration in short ciliary nerves, ciliary ganglionic cells, or in proximal roots of the ciliary ganglion, in three cases of the A.R. phenomenon in tabes dorsalis. Lafon's attempt to override the manifest difficulties by supposing that syphilitic invasion of the ganglia causes 'perversion' and not 'paralysis' of function is, as it seems to me, almost a *petitio principii*.

In his Lumleian Lectures, Sir David Ferrier⁵⁹ has upheld the ciliary-ganglion theory nevertheless, although he apparently adopts it to

explain, not all cases of A.R. pupil, but only those of neurosyphilis. The endeavour is made to account for the dissociated reflex, not by Marina's view that the fibres for convergence-accommodation pass through the ganglion without interruption, but by supposing that "different nerve-fibres in the same trunk may be differently affected by destructive or toxic agencies"; the speculation is that syphilis may so affect the ciliary ganglion and ciliary nerves that though these "cannot transmit the reflex impulse of light to the sphincter pupillæ, they can readily allow the more powerful stimulus associated with accommodation to pass through". Why the assumption of a more powerful stimulus for accommodation should be made is not very clear, nor is the grave objection met that the theory fails to explain the preservation of the consensual light reflex in numerous A.R. cases. Besides, as already noted, the ciliary ganglion and short ciliaries have been found to be normal precisely in some cases of tabes with A.R. pupil—a serious blow to the theory.

It ought, perhaps, to be stated that changes in the ciliary ganglion in neurosyphilis are in no way excluded as an occasional or even a frequent occurrence, and with them the occasional or frequent irregularity of the syphilitic pupil may possibly be associated. But it must at the same time be pointed out that the argument (for the ciliary origin of the A.R. sign) which depends on a presumed association between pupil irregularity and the subsequent development of the A.R. phenomenon loses all force in view of the fact that a central (mesencephalic) origin for some pupil irregularities must be admitted¹⁴ (cf. *Case 4* above).

THE MYOSIS OF MANY A.R. PUPILS.

Though in numerous instances the A.R. phenomenon is observed in pupils of normal dimensions, the fact remains that in some 30 per cent, according to Uhthoff (quoted by Lutz⁶⁰), myosis accompanies it. Some of the proposed explanations of this concomitant myosis are rather vague. Higier,⁶¹ for example, says that it is due to "absence of sensory stimuli owing to disease of the posterior columns of the cord"; Argyll Robertson¹ himself stated that "for contraction of the pupil under light it is necessary that the ciliospinal nerves remain intact, and as in these cases of myosis the ciliospinal nerves are paralyzed, light does not influence the pupil". But the spinal explanation of myosis, possible enough though it be in some instances, will not serve for all by any means, least of all for myosis accompanying the A.R. sign.

The myosis of the A.R. pupil cannot be due to irritation or excitation, for it may continue for years, and, further, is unaccompanied by any spasm of accommodation (not that the latter point always

signifies). Ferrier's⁵⁹ opinion that it is caused by "degenerative changes of an irritative character in the sphincter itself" is open to the same objection; how irritation can be caused by degeneration in a minute muscle and continue indefinitely is difficult to conceive. The myosis must be the sequel, in large part at least, to paralysis of the pupillodilator mechanism, for which the descending sympathetic path to the so-called ciliospinal centre of Budge, thence via the superior cervical sympathetic ganglion to the carotid plexus, Gasserian ganglion, ophthalmic division, and long ciliary nerves to the iris, is well known. Some iridodilator fibres, however, probably pass from the carotid plexus to the sympathetic root of the ciliary ganglion and so possibly to the iris, for after gasserectomy the pupil never remains permanently contracted. A paralytic lesion of the descending pathway will occasion myosis without the A.R. phenomenon; for the combination, we must seek a solution at higher levels.

The descending iridodilator tract just described is known at the level of the medulla, where occluding lesions of the posterior inferior cerebellar artery cause softening of the lateral aspect of the medulla, one of the symptoms of which is homolateral myosis. Evidently, then, the pathway lies somewhere in the formatio reticularis—according to some, near the fasciculus solitarius. Higher up still, Spiller⁶² has in two cases of pontine lesion found evidence of involvement of the tract in the shape of homolateral myosis, deducing therefrom absence of decussation below that level. Here, however, clinico-pathological evidence comes to an end, but, fortunately, at the same point experimental work comes to our assistance. At a spot on the base, lateral to the infundibulum, near the exit of the third nerve, and just behind the optic tract, Karplus and Kreidl⁶³ have in a series of twenty cats obtained with constancy, on electrical stimulation, a maximum dilatation of both pupils; and have shown by suitable procedures that this stimulus is definitely transmitted by the homolateral peduncle, and crosses in part at a lower level, to descend to the cervical cord and so back to the eye by the familiar route. Further research by the same observers points to the sympathetic centre for this iridodilator path being located in the regio subthalamica, dorsomesial to the pes pedunculi, in the frontal part of the corpus Luysii.

Though this experimental work requires verification, we might be able to explain the frequent combination of A.R. pupil and myosis on the assumption that the iridodilating tract on its way through the mesencephalon passes near Meynert's dorsal tegmental decussation or near the aqueduct, but this is at present purely speculative. Lutz's⁶⁰ hypothesis is that the descending fibres run in the tectospinal tract,

and that lesions of the tectobulbar tract cause the light immobility, and of the tectospinal tract the myosis. The suggestion is interesting, but equally speculative, though by exclusion it is easy to demonstrate that the myosis of some A.R. pupils cannot result from involvement of the third-nerve sector and must be the outcome of a more centrally situated lesion. The problem, simply stated, is: Where do the light-reflex arc and the pupillodilator path come sufficiently close to each other to be simultaneously implicated in a common destructive lesion? In the present state of our knowledge the question is more easily posed than answered.

There is reason to believe that the effect of the pupillodilator mechanism is double; i.e., the iridodilator centre of the mesencephalon (or wherever exactly it be) exercises, in functional activity, both a stimulating action on the iris via the spinal route and an inhibiting action on the iridoconstrictor centre of the third-nerve nucleus by another—direct—route to the latter. Should, then, the dilating mechanism be at fault, or interfered with, the pupil contracts doubly, as it were, because of the loss of this inhibiting influence on the tonus of the constrictor centre.

Another interpretation of the myosis of the A.R. pupil is nevertheless possible, since the constrictor tonus of the centre in the third-nerve group is modifiable from another direction.

It is known, and has been experimentally demonstrated,³⁶ that dilatation of the pupils can occur when the usual dilator tract is out of action; the explanation offered, also supported by experimental evidence, is that the tonus of the pupilloconstrictor centre in the oculomotor group can be directly inhibited from the cortex. Though the paths by which this inhibitory influence is exercised are unknown, there is a very definite anatomical connection between cortex and corpora quadrigemina in the form of the palliotectal system of fibres, which end in large measure in the superior colliculus. From thence the assumption is warrantable, in fact probable, that the physiological influence passes by peri-aqueductal lines to the iris-constricting centre in the oculomotor group. Assuming that among these are the fibres stimulation of which inhibits the tonus of the latter centre, causing dilatation, then we must, conversely, consider that paralysis of these same fibres removes this cortical inhibitory action, hence overaction of the third-nerve constrictor effects, and consequent myosis.

Now it will be at once apparent that this hypothesis fits in with the view which assigns to destructive lesions in the neighbourhood of the aqueduct the usual appearance of the A.R. phenomenon, so that in this fashion the frequent myosis may find a simple explanation. Not only so; by such a postulated mechanism the common observation that the A.R. pupil does not respond to painful or

emotional stimuli by dilatation can be readily understood. Such suitable excitations as should lead, by this 'psycho-reflex' mechanism, to inhibition of the tonus of the third constrictor centre or centres, and consequent dilatation, fail to reach the latter owing to the assumed interruption of functional activity between the palliotectal terminations in the superior colliculi and the oculomotor group.

Other matters connected with the subject must be left over. It is scarcely an exaggeration to say that few problems in organic neurology will so well repay further minute anatomical and physiological research as the A.R. phenomenon, which has been a *Haupttummelplatz* of controversy for the last fifty years.

ADDENDUM.

While this paper was in the press, two communications have appeared which have a bearing on our subject.

Frank⁶⁴ has adduced fresh pathological evidence to negative any connection of the Edinger-Westphal nucleus with the irido-constrictor mechanism; on the contrary, he considers his researches point to its being the mesencephalic centre for convergence, and with it he associates functionally the anterior median nucleus of the oculomotor group. As for the centre for iris-contraction to light, he thinks it may be found in the central grey matter dorsal to the nucleus of the fourth nerve, in the nucleus of Boettiger-Westphal, and with this he links the nucleus rapheos posterior, but the positive evidence brought forward in support of this localization is less impressive than the negative evidence in regard to the former.

Of equal interest is a paper by Schuster⁶⁵ on paralysis of vertical eye-movement. His second case is that of an old man of 62, with double A.R. pupil and paralysis of upward movement of the eyes, and with no other neurological sign. Post mortem a small softening was found in the mesencephalon, skirting the aqueduct on the right side, in the deeper layers of the tectum. The author promises us a fuller examination of the case: in the meantime the combination of A.R. pupil and paralysis of vertical movement, on which stress is laid above in tumour cases, is here exemplified by a vascular lesion in approximately the same area.

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