

## **The pathology of ophthalmoplegia / by W.J. Collins and L. Wilde.**

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*with the authors' comments*

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*The Pathology of Ophthalmoplegia.*

BY

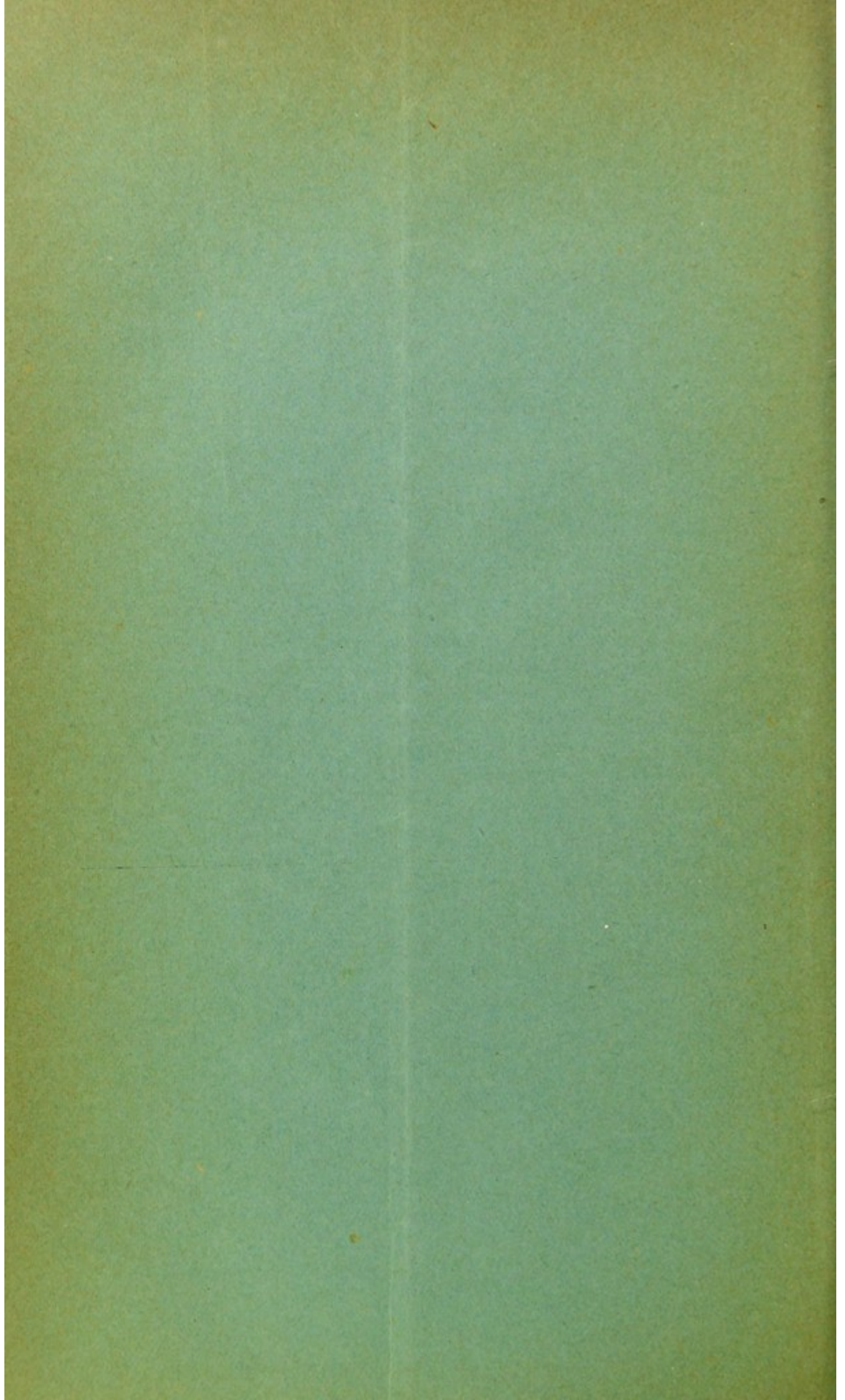
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## THE PATHOLOGY OF OPHTHALMOPLEGIA.

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WHETHER we regard the complexity of the structures concerned, or the rarity of opportunity for post-mortem examination, or the indirectness and consequently secondary character of the evidence on which we accordingly have to rely, the difficulty of the explanation of the pathology of ophthalmoplegia is obvious. Bearing in mind the destination of the third, fourth and sixth nerves, with the second and parts of the fifth and seventh, together with the sympathetic, to the eye and orbital contents, the eyelids and appurtenances; the long and varied course which several of these pursue from their nuclei to their termination in the orbit; the more complicated connections of their centres with the nerve-tracts proceeding from the spinal cord, medulla, and pons, and those proceeding to the cortex of the brain, the varied and extended ocular symptoms which may result from even a small intra-cranial lesion are self-evident. Probably nowhere has post-mortem examination been of less service to pathology than here. We are constrained to rely upon clinical observations, judicious analogy, and certain experiments upon animals, for a rational explanation of the symptoms with which we are dealing. This field of research, common to the physician and the oculist, it is not surprising to find, was permitted to remain fallow until within the last twenty-five or thirty years. The term ophthalmoplegia had been employed by Brunner as early as 1850, and was first brought to the notice of Continental oculists by Von Graefe, who reported a case in 1856, and exhibited a typical example of this disease to the Berlin Medical Society on January 29, 1868. The more modern (1878) division into ophthalmoplegia externa and ophthalmoplegia interna may prove, on further investigation, to be of as little value pathologically as, according to Mauthner, it is perhaps incorrect etymologically.

The site and nature of the lesion to which the group of oculo-motor palsies (for which we employ the term ophthalmoplegia as an equivalent) is due, have been the chief points upon which discussion has taken

place. It is obvious that disease affecting the nucleus of origin or the nerve in its continuity or termination, whether such disease be intrinsic or extrinsic, may be productive of results difficult to separate. Disease of the second nerve alone of all cranial nerves is recognizable by other means than those having reference to disturbance of function. The magnified image of the optic disc exhibiting, in the case of optic neuritis, increased vascularity, lymphatic engorgement, intra-neural hemorrhage, proliferation of fibres, gives us an insight into what may be going on in other nerves during life when they are the seats of neuritis, whose evidence is only rendered visible by the less precise method of post-mortem examination, or inferred by reason of disordered function. It is now well recognized that what is called sclerosis, or some other equally precise, more acute, and more truly inflammatory process, is liable to overrun on definite lines, both centripetally and centrifugally, the cerebro-spinal system, and that the same may be scattered sparsely over the brain and cord, or localized in certain parts. It follows that the symptoms may be as diversified as the sites of this degeneration are various, and it is impossible to understand aright the effects resulting from a lesion affecting the deep origin of any one nerve, or group of nerves, without taking a survey sufficiently broad to cover similar lesions affecting neighboring areas. It was at one time argued that a group of oculo-motor paralyses occurred which was sufficiently distinct from the previously recognized single-nerve palsies or single-muscle palsies, on the one hand, and from symptoms indicating invasion of the spinal cord or brain on the other, to warrant their collection into a separate category, and their being dignified with the exclusive application of the term ophthalmoplegia. This appears to have been the view of Hutchinson when he communicated his paper on "Ophthalmoplegia Externa, or Symmetrical Immobility (partial) of the Eyes with Ptosis" to the Medico-Chirurgical Society in 1879.

He therein states that cases of single muscle paralysis, occurring in syphilis and in locomotor ataxia, are to be distinguished from the class for which he "ventured to propose the name of ophthalmoplegia externa" upon the three following grounds:

1. By the fact of non-symmetry of the former.
2. By the early completeness of the paralysis.
3. By the ease with which very frequently they are cured.

He, however, admits that symmetry is not invariable; indeed, one of his fifteen cases was unilateral, and several others exhibited less symmetry than mere bilaterality.

As to the absence of early completeness of the symptoms, it may be true that the affection of the various muscles may be progressive, but the invasion may be sometimes sudden, as in his eighth case; and it is difficult to understand why the cause which he suggests of the unilateral

and partial category of cases, viz., a gumma in the nerve-trunk, should manifest itself by suddenness of onset.

As to the comparative facility of cure in the two sets of cases, it is difficult to see why he should regard as more unfavorable those he calls ophthalmoplégia, since he says: "The effects of remedies in several cases were very remarkable, the patient having been rescued from a very dangerous condition." And again: "Often it is distinctly influenced for good by treatment."

As showing that the group of palsies which Hutchinson had in view was less capable of sharp separation from the recognized results of similar affections of the neighboring parts, it is important to note that among his fifteen cases, "in six the lower extremities were more or less weak and liable to pain, the condition approaching more or less closely to locomotor ataxia," and several cases exhibited affection of other cranial nerves—*e. g.*, first, fifth, seventh, and eighth—and in two cases there was insanity; and he finally admits that "there can, however, be no doubt that ophthalmoplégia externa is sometimes a part of the general malady known as progressive locomotor ataxia."

The close similarity of these palsies to those spinal palsies common in children, and known as anterior poliomyelitis, has often been remarked, notably by Wernicke, and the term polio-encephalitis superior as opposed to polio-encephalitis inferior, or bulbar paralysis, has been suggested. This would appear to be the view entertained by Ludwig Mauthner in his valuable monograph on the subject, which reviews most of the previous literature and critically investigates the evidence at large.

We have hitherto made no mention specifically of so-called "ophthalmoplégia interna," which has been regarded in this country, in spite of accumulating evidence both physiological and pathological to the contrary, to belong to the category of orbital or peripheral lesions, rather than as of central origin. It is difficult to see *à priori* why, if a central control be allowed for the muscles of convergence, this should be denied to the muscles of accommodation, and, if allowed to the latter, why the same privilege should not of necessity be extended to the muscle of the iris.

In 1878 Hutchinson communicated to the Medico-Chirurgical Society his paper on "Paralysis of the Internal Muscles of the Eye"—ophthalmoplégia interna—a group of symptoms which probably indicates disease of the lenticular ganglion. He then held that if paralysis of the muscles of the iris and of the ciliary muscle alone coexisted the "seat of the disease can be in no other structure than the ganglion itself."

Curiously enough, out of the eight cases he relates, in five both of the eyes were affected. It will appear at the outset that such symmetry would be more easily explicable by a focal lesion in the neighborhood of the posterior part of the third ventricle where the third nerve takes



its origin, than by assuming that the widely separated lenticular ganglia should be similarly and synchronously affected. How such symmetry can be comparable to the symmetry of choroiditis, as Hutchinson suggests, is hard to understand. Indeed, it would appear from a footnote, which he added after the paper was read, that he was not well satisfied with the explanation he had volunteered. He says: "My only hesitation on this point is as to whether in some cases the same symptoms may be due to disease near the nucleus of the third nerve. It is not easy, however, in such cases to see why the vasomotor should be affected. I have, however, seen the pupil motionless and accommodation lost in some cases in which the disease was believed to be in this position; always, however, there were other complications."

This last observation appears to be most important and suggestive, and would seem to us to indicate at once the solidarity of so-called ophthalmoplegia interna, not only with ophthalmoplegia externa but also with bulbar and infantile spinal paralysis, so far as the nuclear nature of such lesions is concerned. Hulke, in the first volume of the *Ophthalmological Transactions* for 1880, traversed Hutchinson's lenticular ganglion theory, and suggested in its place disease of the "intra-ocular ganglionic plexuses in immediate relation with the muscular apparatus," as the approximate cause. Andamuk had demonstrated that after removal of the lenticular ganglion stimulation of the cervical sympathetic produces the usual dilatation of the pupil. This "appeared to be absolutely decisive" that there was a route from the sympathetic to the iris not *via* the lenticular ganglion. Hulke's preference for the ganglionic plexuses may be accounted for by his claim to have discovered these bodies coincidentally with Müller and Schweigger in 1858.

Hutchinson, in reply to Hulke, thinks, "so far as the choice lay between a central and a peripheral seat of change, Mr. Hulke and myself are in the same boat." Gowers, who followed, suggested that they might both be in the wrong one, and taking a broader view and following the researches of Hensen and Volkers, he regarded the probable seat of the lesion as being the anterior portion of the nucleus of the third nerve.

The researches here referred to, carried out in 1878, upon dogs, went to show that the most anterior portion of the nucleus of the third nerve at the posterior part of the third ventricle was the centre for accommodation; behind this came the centre for the iris, then that for the internal rectus, and posteriorly the other muscles of the eyeball. Kohler and Picks's clinical researches powerfully support the foregoing observations, while slightly varying the arrangement of the posterior portion of the nucleus, the internal part of which they would devote to the interior and inferior recti, the outer portion comprising the nuclei for the levator palpebræ, the rectus superior, and the obliquus inferior. Both sets of observers agree in regarding the centre for the fourth nerve as

practically part and parcel of that of the third, to the posterior extremity of which it is immediately adjacent. The nuclei of the sixth appear a little further back, close to the median fissure and the olivary fillet. There is reason to believe that a path of connection between the sixth nucleus of one side and the third nucleus on the other is provided by the posterior horizontal fibres, a nexus which appears at once to explain and to be supported by the facts in regard to what is known as conjugate deviation.

It is well to note here that the recent researches of Gaskell led him to regard the lenticular ganglion as the vagrant motor ganglion of the third nerve akin to the sympathetic ganglion connected with the motor root of a spinal or segmental nerve, and composed almost entirely of third-nerve fibres. He does not regard the first division of the fifth nerve as their corresponding sensory nerve, but finds in the third and fourth trunks fibrillar tissue and cells which he considers to be the vestigial remains of long disused sensory roots and sensory (stationary) ganglia of these nerves. If this view be correct, it is doubtful whether reflex central functions can be attributed to the lenticular ganglion with any more assurance than they can be to the submaxillary ganglion. It would appear to be little more than a vestigial incident occurring in the course of distribution of the third nerve, and not to be regarded either as the primary or secondary seat of control of the intra-ocular muscles.

We have hitherto made no allusion to neural as distinguished from nuclear lesion as occasioning ocular palsy. In 1883, in *St. Bartholomew's Hospital Reports*, one of the present author's, in recording thirteen cases of oculo-motor paralysis exhibiting great variety of both unilateral and bilateral palsy, thus recorded his view of the pathology of these cases:

"In those cases where periostitis in the form of nodes or gummata was present, it is probable that the lesion was situated in the orbit or the sphenoidal fissure. In those cases of *bilateral paralysis*, especially when there is implication of the optic nerves, the base of the brain or the central ganglia are presumably the seat of disease."

In apportioning the effects of extrinsic (*e. g.*, tumor or aneurism exciting pressure), or intrinsic (*e. g.*, nucleitis or neuritis) causes it is important to bear in mind, as Mauthner insists, that we may speak of three categories of causation according to the proximity of the cause. Thus syphilis may cause tumor which may cause ophthalmoplegia. Here nerve-pressure is a cause of the first category, the cause of the proximate cause is the tumor, and the remote cause of this is syphilis. The relative irrelevance of the remote cause as compared to the proximate cause is obvious, yet its importance therapeutically is paramount.

In no other situation are there opportunities for a small lesion to affect so many cranial nerves in their continuity as in the cavernous

sinus. Putting aside the rather obscure ocular palsies of cortical origin the floor of the aqueduct of Sylvius and fourth ventricle and the walls of the cavernous sinus would be the most favorable site for small lesions to effect large results; in the former such lesions would be mostly nuclear, in the latter necessarily neural. We would here introduce the following scheme:

## OPHTHALMOPLÉGIA.

- |   |   |   |
|---|---|---|
| I. <i>Cerebral.</i>                         | (a) cortical                            | { conjugate deviation.<br>hemi-ptosis (?).<br>hysterical ophthalmoplegia (?). |
|   | (b) cortico-peduncular.                 |   |
|   | (c) nuclear                             | { 1. cycloplegia } "ophthalmoplegia interna."<br>2. iridoplegia               |
|   | 3d nerve                                | { 3. palsy of extra-ocular muscles.<br>ptosis.                                |
|   | 4th nerve                               | 4. palsy of superior oblique.   |
|   | 6th nerve                               | 5. palsy of external rectus.  |
|   | (d) radicular (and ? commissural).      |   |
| II. <i>Basal.</i>                           | (a) region of pons (vi.).               |   |
|   | (b) " " peduncles (vi. iv. iii.).       |   |
|   | (c) " " cavernous sinus (vi. iv. iii.). |   |
|   | (d) " " sphenoidal fissure.             |   |
| III. <i>Orbital</i> (including peripheral). |   |   |

Ophthalmoplegia of cortical or cortico-peduncular origin is usually conjugate, not unilateral; this is a corollary to the observation that movements, rather than muscles or nerves, are represented in the cortical colligation. The only exception to this rule apparently is that of ptosis occurring upon the opposite side exclusively to that of the cerebral lesion. (Landouzy.)

In order to complete the cerebral classification of intra-cranial sites of possible lesions resulting in ophthalmoplegia, it is necessary to add the "radicular," to include lesions intermediate between the superficial and deep origins of the various nerves concerned, and perhaps also commissural.

In addition to intra-cranial causes, there are those situate in the orbits, which logically should be made to include the so-called peripheral lesions, which some authors would place in a separate category. It is difficult to deny that in some cases of transient-ptosis, symmetrical cyclopareisis, convergent asthenopia may not be of peripheral neuromuscular causation; and it is certain that trauma may be productive of peripheral palsies, whether by extravasation or by more permanent sequelæ.

With a view to elucidate from a clinical standpoint some of the questions we have raised in what has preceded, we have been at some pains to collect and classify such available cases of ophthalmoplegia in English literature as would lend themselves to such treatment. We have

kept apart those cases in which paralysis of the intrinsic muscles of the eye only existed—twenty-one in number—and the heads of classification we have adopted have been the following :

1. Sex.
2. Age.
3. Alleged cause.
4. History, personal and family, with duration and cause of symptoms.
5. Seat of lesion as found, or presumed or inferred.
6. Symptoms, including the muscles paralyzed, vision, headache, condition of pupils, reflexes, optic discs, etc.
7. The treatment.
8. The result.
9. The autopsy in the rare instances in which such has been made.

*Sex.* Of 120 cases of ophthalmoplegia 73 were males, 39 females, 8 unstated, giving 65 per cent. of the stated cases as males, showing a considerable preponderance in the male sex.

*Age.* Of the 120 cases, in 111 the age was stated. From 0 there were 8 cases ; from 10 there were 17 ; from 20 there were 26 ; from 30 there were 28 ; from 40 there were 19 ; from 50 there were 6 ; from 60 there were 4 ; from 70 there were 3 ; from 80 and upward there were 0 ; with 9 not stated = 120.

This summary, in the absence of the number of the population living at each decade, of course tells us nothing as to the actual age-incidence of the disease ; but, inasmuch as the population living at each ten years' period is less than that at any previous ten-year period, it proves that the increasing number of cases up to between 30 and 40 indicates a greatly increased liability to the disease up to that age. The fall to 19 in the next period—40 to 50, if viewed in relation to population living at such age—would not show any such considerably reduced liability to attack at that age as probably does occur at the ages beyond fifty.

*Syphilis as a cause.* In 40 cases out of the 120 there was some evidence or other of syphilis apart from the ophthalmoplegia, or in 33 per cent. of the whole. Of the 40 the result in 32 was stated. In 23 there was improvement under treatment, 11 recovered, and in 9 others the improvement was stated to be considerable and substantial ; in 7 there was no improvement, 1 was said to be progressive, and 1 was known to terminate fatally. On these facts we would remark that, while quite agreeing with Mr. Hutchinson that a more careful search for evidence of syphilis might most probably have revealed its presence in a larger number of cases, the disease, even in its central form, is probably not exclusively syphilitic ; but if syphilitic, and if unaccompanied by other more serious central disease, and especially if treated early, is apt to be very amenable to remedies.

*Eye affected.* Of 109 cases, 1 eye only was affected in 61 cases, both eyes in 48. In the 61 cases in which only one eye was affected, this was the right in 31, the left in 30; showing that the side affected is a matter of indifference. The above figures, of course, destroy the importance attached to the symmetry of the lesion. Our cases include many in which the affection was in the nerve-trunks, but in some of these the palsy was bilateral; and we think far too great importance has been attached to the question of symmetry as deciding the seat of the lesion.

*Distribution of the palsy as regards various portions of third nerve.* Of the 120 cases of ophthalmoplegia in which the external ocular muscles were affected, there was evidence of some affection of intra-ocular muscles in 65.

In 29 of the 65 both iris and ciliary muscle were involved.

We would, however, direct especial attention to the mode of linking of extra-ocular palsy with cycloplegia and indoplegia respectively as bearing upon the work of Hensen and Volker and of Kohler and Pick.

In the 34 cases in which only one of the two (viz., iris or ciliary) was affected, plus extra-ocular palsy, in no less than 31 it was the iris and not the ciliary, and in only 3 was it the ciliary and not the iris. If it be true that the centres for ciliary, iris, and extra-ocular muscles are arranged in that order—tandem fashion—on the floor of the aqueduct, we can understand why the linking of the palsies should be as above.

*Distribution of palsy as regards nerves involved.* Of the 116 cases in which the analysis could be made, in 47 the third nerve alone was affected (in 18 complete, in 29 incomplete); in 42 the third, fourth, and sixth were affected in company; in 11 the sixth alone was affected; in 8 the third and fourth failed together; in 4 the third and sixth are presumed to have been associated in palsy; in 2 the fourth and sixth, and in 2 the fourth alone.

The frequent bracketing of the third, fourth, and sixth might suggest the frequency of lesion in the course of the nerve-trunks; but the relative infrequency of attack of the sixth, in spite of its longer and more arduous extra-cerebral, intra-cranial course, would rather suggest an opposite reflection. The direct connections between the sixth nuclei and those of the third and fourth by the posterior horizontal fibres are to be borne in mind.

*Result.* Of the 92 cases out of the 120 in which the result is noted 53 improved under treatment, 26 completely recovering, and in 14 more the improvement was stated to be considerable; in 15 there was no improvement, in 2 the disease was progressive, and in 22 it was fatal.

*Age and fatality.* We have previously suggested that ophthalmoplegia of young children was probably more serious and fatal than that of adults. Of 6 cases under ten in which the result is recorded, 3 died, or 50 per cent.; of the 86 over ten in which the result is recorded, 19 died, or 23 per cent.



