HERPES ZOSTER OPHTHALMICUS: REPORT OF CASES AND A REVIEW OF THE LITERATURE*

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Herpes zoster ophthalmicus presents an interesting problem. Although the disease was known to physicians of antiquity, their ideas concerning the affection were obscure. They described, in considerable detail, the characteristics of the disease, but their interpretations were brief. To the Greeks, the disease was known as zoster, and Pliny, a Roman, is said to have been the first to apply to the eruption the denomination of zona. From these ancient times to the early nineteenth century, the literature on the subject is scant. Mehlis, in 1818, suggested that the eruption followed the distribution of nerves, and Parrot, in 1856, noted that the eruption, like pain, developed along the course of branches of nerves most frequently superficial, and that it was here that the neuralgias ordinarily manifested themselves. This was proved in 1861 by von Barensprung. Hutchinson, in 1866, and Bowman, in 1867, were the first to describe herpes zoster ophthalmicus in detail, and each reported several cases.

An enormous amount of work has been done in recent years in the investigation of the pathology and treatment, and upon various manifestations of zoster and other herpetic diseases. Although the affection is comparatively rare, the literature on this subject is large, a great many cases having been reported.

In degree of frequency, herpes zoster has been noted to occur in the proportion of 1 to 2 per cent. of all skin diseases.

* Condensed version, made by the author from the candidate's thesis for membership accepted by the Committee on Theses.

Max Joseph found 163 subjects in 15,603 skin cases; Knowles saw 286 subjects in 21,337 skin cases, and Greenough found 235 subjects of zoster in 17,741 skin cases. De Fonesca, in 1882, saw four cases of ophthalmic zoster among 13,000 eye diseases, and Galezowski encountered 19 among 36,000 patients. Fouchard, in 1898, found 57 cases of ophthalmic zoster in 5,000 eye cases, and Head and Campbell saw 18 cases in 416 cases of herpes zoster. Only five cases were seen at the Will's Eye Hospital in 1913–1914 out of a total of 30,000 eye cases.

There are several varieties of herpes zoster, distinguished mainly by the region that is involved. In 1924, Achard stated that the ophthalmic type represented about 7 per cent. of all types of the disease. Ophthalmic zoster is, after thoracic zoster, the most frequent type, and, like other localizations of the disease, it is usually unilateral and non-relapsing in character. At times it is so frequent as to amount to an epidemic, and at other times it is seen seldom.

The disease may be of long duration, ranging from two weeks to several months, and it occurs with greatest frequency and with most severity in the latter half of life. It displays no predilection for age, color, or sex. It may be confined to certain branches of the fifth nerve, and is observed most frequently upon the inner half of the upper lid, the adjacent side of the nose, over the eyebrow, and in the region of distribution of the supratrochlear, infratrochlear, supra-orbital, and oculonasal nerves. The area most often affected is that of the supra-orbital nerve, the supratrochlear being next in frequency. The frontal may be affected alone, and some observers believe that this nerve is always involved. Rossander, in 1877, described a case, however, in which only the infratrochlear nerve was affected. The most serious complications occur when the lacrimal and nasociliary branches are involved. The entire region of the ophthalmic nerve may be implicated, namely, the upper lid, which is swollen and covers the globe; the internal frontal region, upon which are

distributed the vertical rows of vesicles arranged in the form of a fan; the anterior third of the scalp, and the root of the nose. At times a single branch is affected, for example, the frontal, causing involvement of a large triangular territory with a superior base; or the nasal branch, resulting in the internal third of the upper lid and the ala nasi becoming affected; or the lacrimal branch, with consequent implication of the external third of the eyelid. Bar, in 1925, reported a case from which he drew interesting deductions. In addition to cutaneous anesthesia in the right frontal region, upper lid, conjunctiva, and cornea, there was involvement of the ophthalmic division of the nerve, with the exception of the terminal branches of the nasociliary and anterior ethmoidal, resulting in diminution of sensation in the lower lid and upper half of the side of the nose. From this derangement of sensibility Bar concluded that some twigs of the first division of the fifth nerve supply the lower lid, as well as fibers from the second branch.

Herpes zoster ophthalmicus may be associated with zoster of the superior maxillary branch, with vesicles upon the lower lid; the superior maxillary region as far as the upper lid and malar bone, tonsils and velum palati; with the inferior axillary branch, with vesicles upon the chin and lower lip; with geniculate zoster, with vesicles in the external auditory canal, and frequently with facial paralysis, and with zoster of the glossopharyngeal nerve. Sometimes all nerves of the first branch or several of these branches are affected simultaneously with the second branch. Involvement of all nerves of both branches is seen less often, and implication of all three branches together is quite rare. Zoster without eruption is exceptional, although Lederer, in 1900, reported such cases.

ANATOMY

The physiologic makeup of the fifth nerve is a complicated one. This nerve resembles a spinal nerve, being made up of a compressed group of afferent posterior roots. Its ganglion,

the Gasserian, is a fusion of posterior root ganglia of all the posterior sensory roots, corresponding to all motor nerves from the brain stem. The nerve enters the pons midway between its lower and upper borders, and sends an ascending root upward to the brain stem and a descending root to the tissues, as far down as the second cervical level. Mainly, it is sensory, provided by the Gasserian ganglion, but it is linked up with fibers from the cervical sympathetic, which carry vasoconstrictor impulses and motor fibers to the levator palpebrae and to Müller's muscle and to the dilator pupillae fibers.

The ganglion lies in the middle fossa of the skull, and from its upper portion arises the ophthalmic division of the fifth nerve, which passes into the cavernous sinus and runs along its lateral wall. It gives off a branch to the tentorium, the recurrent nerve of Arnold, and sends off filaments to the third and sixth nerves and sometimes to the fourth.

The ophthalmic division of the fifth nerve is a flat nerve, about one inch in length, the smallest of the three divisions of the fifth nerve. It is joined by sympathetic fibers from the superior cervical ganglion, and just before it enters the sphenoidal fissure it divides into the frontal, lacrimal, and nasociliary nerves.

The eye receives its sensory innervation from the ophthalmic division of the fifth nerve. Afferent impulses pass through this route to the Gasserian ganglion, and thence to the pons. Some fibers end in the chief sensory nucleus, and other fibers descend through the pons and medulla to the upper segments of the spinal cord. These form the spinal root of the fifth nerve and connect with the substantia gelatinosa of Rolando, which extends from the pons to the upper cervical cord. From the sensory nuclei, a second afferent neuron decussates to form the trigeminal fillet, and then runs to the optic thalamus, where a third afferent neuron passes by way of the internal capsule and corona radiata to the cortex.

The first branch, the ophthalmic, with the ciliary ganglion, supplies sensation to the upper lid, conjunctiva, eyeball, lacrimal gland, forehead, anterior part of the scalp, frontal sinus, root and anterior portion of the nose, and caruncle, and a branch from the ciliary ganglion enters the optic nerve with the central artery of the retina.

The second branch, the superior maxillary, with the sphenoidal ganglion, furnishes sensation to the cheeks, anterior temporal region, lower lid, side of the nose, nasopharynx, antrum, ethmoids, soft palate, tonsils, and roof of the mouth.

The third branch, the inferior maxillary, with the otic and submaxillary ganglia, is motor and sensory, and is distributed to the skin of the side of the head, part of the auricle and the external auditory meatus, lower part of the face, lower lip, mucous membrane of the mouth, tongue, mastoid cells, lower teeth, gums, salivary glands, dura mater, and skull.

The frontal is the longest branch of the ophthalmic division. It enters the orbit through the superior orbital fissure and divides into two branches, the supratrochlear and the supra-orbital. The supratrochlear branch escapes from the orbit between the trochlea and superior orbital foramen, passing up to the forehead, and gives off branches to the conjunctiva and skin of the upper lid. The supra-orbital branch passes through the supra-orbital foramen, giving off branches to the upper lid, and ends in two cutaneous branches to the scalp.

The lacrimal nerve is the smallest branch of the ophthalmic division. It anastomoses with the facial (pars intermedia of Wrisberg), and enters the orbit through the superior orbital fissure, enters the lacrimal gland, giving off branches to the gland, conjunctiva, and skin of the upper lid. It is often difficult to determine whether or not this nerve is involved in herpes zoster if the conjunctiva and upper lid are affected, because they receive filaments also from the superior trochlear, from the frontal, and from the inferior trochlear. The

temporal branch of the superior maxillary nerve, in its course through the orbit, receives a filament from the lacrimal nerve, and at times the zygoma may exhibit vesicles, although the superior maxillary nerve itself may not be involved.

The nasociliary nerve becomes the main sensory nerve to the eyeball. This nerve crosses the optic, and at the inner wall of the orbit it divides into two terminal branches, the infratrochlear and the nasal nerve proper, supplying the iris, ciliary body, and choroid. The infratrochlear emerges from the orbit above the internal tarsal ligament. Its branches supply the lacrimal sac, conjunctiva, skin of the lids, and root of the nose. The nasal nerve proper leaves the orbit by the anterior ethmoidal foramen to the anterior part of the cranium, at the inner margin of the cribriform plate. Here it turns forward under the dura and passes through a narrow opening at the side of the crista galli, to reach the nasal cavity below the nasal bone, and gives off branches to the skin; it connects with the facial nerve. In its course it sends a branch to the ophthalmic ganglion, a small filament that runs alongside the optic nerve. It gives off the long root of the ciliary ganglion, from which short ciliary nerves pass to the iris, and then sends long ciliary branches to the ciliary muscle and iris; subsequently it divides into the external and internal nasal nerves, which supply the middle and tip of the nose.

This nasociliary nerve exhibits a complex distribution. Through its ciliary ramifications it furnishes sensibility to the globe; through its external course it innervates the internal part of the two eyelids, the lacrimal sac, and the nose. Its internal distribution is partly to the nasal mucosa and partly to the skin of the lobe of the nose. The ciliary or lenticulate ganglion lies in the orbital fat between the optic nerve and the external muscles. It is made up from a filament from the nasal branch of the ophthalmic (sensory), fibers from the motor oculi (motor), and a branch from the cavernous plexus of the sympathetic. Its branches are the short ciliary nerves

that accompany the long ciliary nerves and pierce the sclera near the entrance of the optic nerve. They are distributed to the cornea, iris, and ciliary body.

Anomalous ramifications and unconventional distribution of branches of the fifth nerve have been reported in some cases, and this should be taken into consideration in any unusual case of herpes zoster ophthalmicus.

AGE

Apparently neither age nor sex assumes a decisive role in herpes zoster. It is clear that observers are not agreed as to the time in life when the disease is most prevalent. It may occur at any age, but is seen more commonly among elderly persons. From an analysis of 2,250 cases of herpes zoster ophthalmicus reported in the literature, the writer found the average age to be forty-four. Numerous cases have been reported in young children and infants less than one year old. Kalb, in 1909, described a case in a new-born infant in which there were multiple grouped scars symmetrically arranged in the area of the first and second divisions of the fifth nerve, which he concluded were the remains of a bilateral intrauterine herpes zoster ophthalmicus.

SEX

Some authors report a preponderance of zoster in males; others assert that a greater number of females are attacked, and some believe that the disease occurs with equal frequency in males and females. The present writer found that 54 per cent. of males were affected in 2,250 cases of ophthalmic zoster. The right eye was involved in 54 per cent. of all cases.

SEASONAL OCCURRENCE

The seasonal occurrence of herpes zoster ophthalmicus varies. Many believe that it is associated with the cooler months of the year, but epidemics have occurred in the

summer months as well. Recent investigators believe that the disease is most frequent during October and November.

EXPOSURE

Many observers believe that herpes zoster has developed as the result of chilling of the body, due to exposure to wind, cold, and dampness. Paget, in 1866, reported such a case in a male aged twenty-five years. Jefferies, in 1870, described three more cases. Other cases having a similar history have been described by Eyer, Hinde, Moore, Lagarde, DeFonesca, Hybord, Horstmann, Martini, and others.

PRODROMAL SYMPTOMS

The general prodromal symptoms of malaise, headache, nausea, chills, fever, and anorexia usually precede the eruption by several days. The temperature generally recedes with the onset of the skin eruption. Preliminary gastric disturbances are sometimes present, and are due to existent relations between the trigeminal and vagus nerves. The skin temperature is higher on the affected side, with anesthesia of the skin surface. In some cases all these symptoms are absent, the patient complaining merely of local pains, neuralgic in type.

PAIN

As a rule, the disease is accompanied by subjective symptoms, especially pain of neuralgic type along the entire branch of the trigeminal nerve, at times radiating to other branches as far distant as the occiput; it precedes the eruption, as a rule, by hours or several days. The neuralgic pains manifest themselves in all degrees of intensity, and the greatest pain often is experienced when the skin lesion is but mild. The severity of the pain and the extent of the lesion bear no relation to each other.

The whole cycle lasts several weeks. Pain continues throughout, and in the graver forms of the disease may last for years. Occasionally exacerbations occur following the dis-

appearance of the zoster, and react markedly upon the general health of the patient. In elderly persons the distress may end only with the termination of life. The continued after-symptoms have sometimes led to suicide. All writers on this subject agree that after the eruption, pain is undoubtedly the most important symptom of the disease. In most cases, after the subsidence of the main symptoms, there is reduced sensitivity over the affected areas for a long time after the disease subsides. In some cases, even years after an attack, exposure to cold, wind, or rain produces a tingling sensation in the skin, and at times the most intractable postzosterian pains are observed. In children the pain is less severe, rarely continuing beyond the period of eruption.

VESICLES

Herpes zoster ophthalmicus is an infectious disease of the nervous system, characterized by the appearance of erythematous red plaques on an edematous skin surface, and followed later by the formation of yellow vesicles which are discrete or occur in groups, along the terminal ramifications of the fifth nerve. The vesicles vary in size, are irregular, may occur in small or large groups, be scattered or confluent, and display a tendency to group or coalesce. They may appear immediately or at different times. At first the vesicles contain a clear yellow fluid which, in a few days, becomes cloudy. The erythema of the skin gradually disappears, and the vesicles soon become modified in character. They may become purulent, even gangrenous at times, and in some cases may result in extensive loss of skin.

As a rule, after a few weeks, the vesicles dry up and leave a characteristic black crust which gradually falls off, leaving the skin in an anesthetic state and very tender. Scarring usually follows, a characteristic, slightly depressed, pale, white cicatrix of the skin remaining, and, with their typical distribution, they may often render possible a retrospective diagnosis of previous herpes zoster.

The vesicles in ophthalmic zoster are usually smaller and more numerous than when the affection is localized on other parts of the body. In some cases, papules, bullae, and pustules may appear in place of vesicles. The inflammatory period lasts from eight to twelve days, although the skin ulceration takes a long time to heal. The extent of the eruption varies, and it is always confined to one side of the face, except in cases of bilateral herpes zoster, which may or may not occur simultaneously. Overlapping of the midline has been reported in several cases, but this was probably due to an erythema of the skin with edema, and was not vesicular in type; or it may have been due to overlapping of nerve elements from the opposite side, and because of the distribution of the fifth nerve, it is often different on the opposite side.

LYMPHATIC GLANDS

The lymph glands adjacent to the affected areas are practically always enlarged and such enlargement may appear at times before the eruption. It is almost always unilateral, is independent of all secondary infection, and may be associated with the slightest eruption. The skin over the swelling never undergoes any change in color unless the gland becomes infected from the vesicles. In herpes zoster ophthalmicus the preauricular gland is enlarged, and sometimes there is subangulomaxillary adenopathy. This primary adenitis gradually disappears about the tenth day. It never suppurates and has a favorable prognosis. However, every adenopathy in the course of the disease is not always of zosterian nature, and every herpes accompanied by adenitis is not always herpes zoster.

EYELIDS

In practically all cases the lids are swollen, and there are redness, edema, and induration. Early in the disease a ptosis is often present, which may be due to mechanical edema or paresis of the sympathetic fibers to the levator muscle or paralysis of the internal rectus or other third nerve palsy.

Zoster of the upper lid may be serious, and the older the patient, the more are its complications to be feared. Tacke, Clarke, Phillips, Barre, and others have described several cases in which destruction of the upper lid resulted.

CONJUNCTIVA

When the eruption is at its height, a conjunctival injection is usually seen, with increased secretion. Simultaneously with the appearance of the initial eruptive elements, vesicles may form in the conjunctiva. At times small pustules may be seen, which run the same necrotic course with scarring, or the vesicles may resemble a phlyctenular conjunctivitis, with severe pain, photophobia, and lacrimation. Occasionally the conjunctival injection may precede the formation of the skin vesicles, and it often persists long after the recovery of a keratitis.

OCULAR COMPLICATIONS

Ocular complications, if any, may be observed in different phases of herpes zoster from the first day of onset to a remote date—even months after the healing of all skin lesions. The affection extends to the globe in about 50 per cent. of cases, causing complications in the transparent media, iris, sclera, cornea, and ocular muscles. Involvement of the cornea is observed in practically one-third of all cases. The writer found 39 per cent. in 2,250 cases examined.

CORNEAL ANESTHESIA

The corneal eruption is usually preceded by a period of insensitiveness. The anesthesia may occur simultaneously with the eruption, or corneal anesthesia may supervene with the subsidence of herpes zoster. In certain instances anesthesia of the cornea appearing without a lesion of that membrane constitutes the only symptom of corneal zoster. However, it is usually transitory in nature and the cornea recovers its sensibility after a period of months or even years.

CORNEA

The eye is often affected with keratitis during the course of the zoster, and is then the seat of the most serious ocular manifestations. Many forms of keratitis present themselves. They may be ulcerative, superficial or deep, non-ulcerative, superficial or deep, or a combination of these. Some cases have been observed where the initial lesion was a keratitis.

It is customary to consider two forms of keratitis occurring in the course of this disease. One form is characterized by the occurrence of groups of minute transparent vesicles, usually multiple, which rupture, resulting in small shallow areas of ulceration which tend to coalesce and leave crenated borders. These small ulcers, as a rule, heal rapidly and may be followed by fresh crops of vesicles, or the ulcers may enlarge and fuse, leaving a large cloudy area of denuded epithelium. Corneal denudations have a variable result. A simple ulceration may leave a leukoma or numerous nebulae. Some opacities always remain and pannus may develop, or the ulcers may become infected secondarily and may result in perforation. In some cases the vesicles may be accompanied by deep corneal infiltrates without ulceration. The corneal infiltration may precede the vesicular eruption in the cornea and in the skin and may heal with it, leaving as a sequela, a more or less dense zone of anesthesia. Precipitates on Descemet's membrane and striae at different corneal levels have appeared quite frequently, but are difficult to discern without the aid of the slit-lamp.

The other form of keratitis is characterized chiefly by the invasion of the deeper parts of the parenchyma or interstitial tissue, without vesicular eruption or effect on the deep epithelium. Corneal infiltrates may appear, which may or may not leave a permanent scar, and deep infiltrates may form which do not undergo purulent disintegration. Paresis of nerves may remain, and a neuroparalytic keratitis may occur. These infiltrates are similar in clinical appearance and course to disciform keratitis. Some writers believe that

parenchymatous keratitis is the form customarily and most frequently found in herpes zoster ophthalmicus. Corneal relapses are common, because the damaged epithelium is unable to resist exposure and the vitality of the cornea is lowered. Hypopyon and sloughing of the cornea, resulting in perforation and necessitating enucleation, have been reported in many cases.

TENSION

Ocular tension may be divided into two groups. In the first form the rise in tension is probably associated with iridocyclitis of zosterian origin, whether or not the cornea is affected. Many such cases have been benefited by atropine. The second type of tension, involving acute or chronic glaucoma without iritis, may be due to zoster as a specific etiologic agent, precipitating a rise in tension in a predisposed eye. The increased tension is generally unilateral on the same side as the zoster, and usually supervenes in from fifteen to twenty days after the appearance of the eruption. Weeks stated that this condition following herpes zoster ophthalmicus was no doubt due to changes in the composition of the aqueous, which renders it less diffusible and prevents proper filtration through the lymph channels at the angle, as lymph spaces do not easily tolerate foreign products.

At times the tension is high early in the disease and later it is lowered. It is often low while the inflammation is subsiding. When the ocular tension is taken throughout all the different periods of the disease, many variations are seen which are transitory and invariably oscillate with a wide amplitude around normal tension. Many cases of herpes zoster ophthalmicus have been ushered in with an acute glaucoma.

IRIS

Secondary to corneal involvement, the anterior uveal tract is most frequently affected in herpes zoster. In most cases in which the cornea is affected some iritis will usually be present, with contracted pupil and photophobia. At other

times a true iridic inflammation may develop, with intense pain, leading in some cases to hypertension. The iritis may not appear until late in the disease, or it may begin simultaneously with the keratitis, or it may occur when the corneal complications are subsiding. In some cases the iritis may appear before the skin eruption. Iritis without a preceding keratitis is exceedingly rare, but many cases were reported in the literature.

SCLERA

Scleritis is a rare complication, and usually occurs late, in association with keratitis or iridocyclitis. The scleral nodules are small, circumscribed, red, painful areas with translucent centers. The conjunctiva over them is smooth, congested, and may be adherent. After many weeks the nodules become smaller in size, without ulceration, leaving a slate-blue discoloration of the sclera. The iris often becomes atrophic nearest to the nodules in the sclera. The pupil may be inactive or dilated. Relapses are common, and fresh nodules arise in areas of the sclera hitherto unaffected. Terrien, in 1900, reported a case in which episcleritis was the primary symptom. This again emphasizes the occurrence of primary ocular manifestations as an initial symptom of herpes zoster several days before the cutaneous eruption.

NASAL NERVE

The worst eye affections complicating herpes zoster ophthalmicus are generally associated with vesicles along the nasal nerve. While it is generally assumed that affections of the nasal branch entail the hazard of ocular complications, numerous observations have shown that iritis and corneal scars may occur when the nose is free from eruption and, conversely, may fail to appear when zoster has attacked the root of the nose and the side of the nose all the way to the tip. Instances in which eruption covers the entire side of the nose without affecting the eye are explained by an involvement of the ramifications of the second branch of the nasal nerve.

Wadsworth attributed a case in which the tip of the nose was affected but the cornea remained clear to an anatomic anomaly described by Turner, in which a small supratrochlear branch of the frontal nerve joined the infratrochlear branch of the nasociliary nerve. In such a case the zoster confined to the region of the frontal nerve will include the nose, but not the eye. Disease of the globe, with absence of eruption upon the nose, is attributed to alteration of the single ocular portion of the oculonasal nerve, whose course is endonasal, but becomes external only in the inferior portion of the nose. As a general rule, the eye rarely suffers when the nose is not affected, and the severity of the eruption of the nose is usually in direct relation to the severity of the eye symptoms. It does not follow that the eye is exempt if only the forehead exhibits an eruption of vesicles.

LACRIMAL NERVE

In many cases the lacrimal nerve is involved, and vesicles may appear in the skin of the lids, the conjunctiva, and the side of the nose. It is often difficult to determine whether or not the lacrimal nerve is affected, unless there is marked upper lid eruption, with edema and injection of the conjunctiva.

FACIAL NERVE

Trigeminofacial zoster includes in the course of the disease involvement of the fifth and seventh nerves. Most authors believe that a double lesion of two adjacent ganglia are involved, the Gasserian and the geniculate. The clinical picture is that of a facial paralysis, with vesicles on the ear and vesicles along the ramifications of one or several branches of the fifth nerve.

The anatomic relations between the fifth and seventh nerves render possible the comprehension of some unusual types of ophthalmic zoster. The facial nerve manifests itself almost entirely through its motor root. Its sensory root is

formed by the intermediary nerve of Wrisberg, which, by way of its intrapetrous course, enters the geniculate ganglion. Some sensory fibers extend beyond the last peripheral segment of the aqueduct and become involved with motor fibers of the trunk of the facial nerve.

Involvement of the facial nerve is usually unilateral, and is situated on the same side as the zoster. However, Caspar and Murphy each reported a case in which the facial nerve was affected on the opposite side. Association of facial paralysis with ophthalmic zoster is of relatively infrequent occurrence, although 110 cases were found in the literature. The paralysis usually appears during the first days of the eruption. Occasionally the paralysis is total, but more often it is partial. Recovery is the rule.

SYMPATHETIC DISTURBANCES

In ophthalmic zoster, sympathetic disturbances may assume the particular form of a Claude-Bernard-Horner syndrome, and has been reported in some cases with enophthalmos, contraction of the palpebral fissure, and miosis. Typical cases were described by Aubaret and Morenon in 1927. Anatomic investigations conducted upon the spine and cord of patients affected with herpes zoster have revealed lesions of the anterior horns of the cord, and others involving radicular ganglia and fibers of the posterior funiculi. As the sympathetic nerve bears a very close relation to the spinal cord, it is conceivable that it may be affected in some degree in the form of a paresis of the sympathetic nerve.

ARGYLL ROBERTSON PUPIL

Pupillary disturbances of purely nervous origin, without resultant iritis, may occur in conjunction with herpes zoster ophthalmicus, and the Argyll Robertson pupil has been observed in several cases. This sign appears late, often months after the eruption, is unilateral, and occurs on the same side on which the zoster appeared. The consensus of opinion is

that this phenomenon is due to a lesion of the ciliary nerves and of the ganglionic cells attached thereto.

SYMPATHETIC OPHTHALMIA

Occasionally cases of iridocyclitis due to zoster may cause blindness and atrophy of the diseased eye, and may threaten the sound eye with sympathetic ophthalmia. Numerous cases displaying this complication were recorded in the literature.

EXOPHTHALMOS

There sometimes occurs in herpes zoster a transitory exophthalmos, with or without hypertension, which accords closely with the theory of sympathetic excitation. Exophthalmos as a complication has been reported by several writers. Some investigators believe that the proptosis is due to inflammation of the retrobulbar tissue.

MUSCLE PARALYSES

Ocular muscle paralyses are not rare in herpes zoster, and are not dependent upon the severity of the pain or on the degree of the affection. They appear with greater frequency the closer the zoster is situated to the cephalic extremity, and they are encountered most often in cephalic zoster, especially in herpes zoster ophthalmicus. Such paralyses which develop in the course of the disease are commonly observed when the infection involves the ophthalmic nerve. The motor complications usually disappear after a few weeks or months, but may persist for a long time after the cutaneous symptoms have disappeared. These paralyses generally appear later than the skin eruption. However, cases were found in the literature in which the paralysis appeared simultaneously with the skin eruption, and several instances, also, in which the paralytic phenomena appeared before the skin eruption, and others were found that occurred after the zoster had disappeared.

Sometimes the paralysis involves several pairs of nerves simultaneously, each of which may be individually implicated, either partially or totally. The question has sometimes been raised whether these paralyses are actually complications or whether they are merely concurrent affections. Paralyses of ocular muscles occur presumably from encroachment of inflammation of the fifth nerve to the motor nerves as they traverse the cavernous sinus and superior orbital fissure. Some authors believe that it is due to an associated meningitis or occurs by extension of the infectious process to the neuraxis, with production of a nuclear lesion or an involvement of the motor nerves on the anterior horns of the cord, with resultant paresis of the muscles affected.

THIRD NERVE

The most common complication of diseases of the ocular muscles is a total or partial paralysis of the muscles supplied by the third nerve, with or without participation of the pupil. The writer found 96 cases of third nerve paralysis in the literature. Isolated paralysis of the pupils is frequently encountered and may be the only symptom. The pupil is dilated, and does not react to light or to distance. In some cases involvement of the entire internal musculature is observed, and patients present, in addition to paralysis of the pupil, a paralysis of accommodation that impairs close vision. These cases of paralysis of accommodation and paralytic mydriasis may persist for a long time. Only one branch of the third nerve may be involved—that which supplies the levator palpebrae—and ptosis may result. Usually all cases recover.

THIRD, FOURTH, AND SIXTH NERVES

Numerous cases have been recorded of paralysis of the third, fourth, and sixth nerves simultaneously. The writer found total ocular muscle paralysis to have occurred 40 times in reported cases.

Fourth Nerve

Isolated transitory paralysis of the trochlear nerve represents an exceptional and rare complication in the course of herpes zoster ophthalmicus. A total of 21 cases of fourth nerve paralysis was found in the literature.

Sixth Nerve

Abducens paralyses are intermediate in frequency and usually appear shortly after the cutaneous eruption. The writer noted sixth nerve paralysis in 47 cases.

First and Second Branches

Up to the present time there have been reported in the literature 72 cases of involvement of the first and second branches of the fifth nerve. Many of these cases gave a history of complications involving the globe and ocular muscles. When the eruption is limited to two branches, the adjacent branch is the one that is always involved. No case has been observed where two remote nerve trunks, such as the ophthalmic and the inferior maxillary division, have been affected.

First, Second, and Third Branches

Involvement of all three branches of the ganglion is occasionally reported. There were 25 such cases described in the literature.

BILATERAL CASES

Jefferies, in 1876, was the first to report a case of bilateral herpes zoster ophthalmicus. This occurred in a female, aged sixty-four years. Both corneae were affected, and perforation of the cornea resulted on each side. The writer found 44 cases in the literature.

RECURRENT CASES

As a rule, the disease occurs once in a lifetime, but in some cases it has reappeared in the same person. Charcot, in 1859,

published an account of the first case with recurring herpes zoster ophthalmicus. Forty-two such cases were discovered in the literature.

OPTIC NERVE INVOLVEMENT

The disease sometimes affects the deep membranes of the eye, and many observers described cases with retinal hemorrhage and degenerative retinitis, choroiditis, optic neuritis, papillitis, optic atrophy, and retrobulbar neuritis. Inflammation of the optic nerve may complicate herpes zoster ophthalmicus, and may manifest itself when the eruption appears or as an end result. It is post-neuritic in type and may or may not heal without resulting atrophy.

The insidious character of herpes zoster ophthalmicus is apparent at times in optic neuritis, which develops with the characteristics of a papillitis and may terminate in blindness. This complication may be the only one observed in the course of the disease. The neuritis is more often localized in the eye on the side of the eruption, although both eyes may be affected. The pathogenesis of nerve involvement is still a matter of dispute.

Hebra, in 1870, was the first to report a case of bilateral optic atrophy following herpes zoster. Since that date the writer discovered 36 cases reported by numerous writers.

OTHER NERVE INVOLVEMENT

Just as there are paralyses of certain parts at a distance from the eruption in herpes zoster, so motor nerves of the eye may be affected in the course of zoster with remote localization. These cases, in which wide separation exists between areas involved, are most unusual. It is probable that two ganglia are affected at the same time. Cases are reported in which ophthalmic zoster followed or preceded zoster in other regions.

Hemiplegia of peduncular or alternate types is likewise encountered. Sulzer, in 1907, reported a case with paralysis of

all the external ocular muscles. A few weeks later the patient developed a hemiplegia over the right side. The muscular paralysis soon disappeared, but paralysis of the sphincter irides remained. Numerous other cases complicated by hemiplegia have been reported. Perrin and others believed that the co-existence of ophthalmic zoster and hemiplegia was due to an exclusive radiculoganglionic lesion, and that this has warranted the establishment of the theory of zosterian neuraxitis. The latter concluded that in certain subjects who presented vascular fragility the virus of zoster might induce the occurrence of hemiplegia.

In some cases zoster is distributed over several adjoining segments, while only one spinal ganglion is involved, due, no doubt, to the occurrence of communicating fibers. Cases of ophthalmic zoster with involvement of the third, sixth, seventh, and eighth cranial nerves have been described. The extension from sensory to motor nuclei occurs through the spread of a basilar infection by way of the subarachnoid space, a meningitic process being demonstrated by spinal fluid leukocytosis. Disastrous consequences sometimes ensue in ophthalmic zoster, not only to the extent of complete destruction of the eye, but even death may follow this usually mild infection. Many observers have reported fatal cases.

TYPES—EPIDEMIC AND SYMPTOMATIC

Two main types can be differentiated. The epidemic type, sometimes called primary, specific, idiopathic, or true zoster, and the symptomatic type, often called secondary, nonspecific, or zosteriform eruption. The true variety is contagious and bears a resemblance to varicella, encephalitis, and anterior poliomyelitis. One attack usually confers immunity. It presents many symptoms commonly observed in eruptive febrile diseases, runs a definite course, and is not related to other diseases.

The symptomatic types are associated with various diseases or supervene after trauma or intoxications. They are

attributed to the most diverse etiologic factors, ranging from acute infection to various kinds of trauma, errors of refraction, and even to severe mental strain and emotion. They are associated with toxic, inflammatory, or neoplastic damage involving the fifth nerve, the ganglion, or fibers that constitute the central connections of the nerve. Other etiologic factors are syphilis, tuberculosis, acute or chronic infections, metabolic diseases, chronic poisonings, multiple sclerosis, malaria, leukemia, degenerative processes, atmospheric conditions, subarachnoid hemorrhage, and trauma. Numerous cases have been reported following lesions of the orbit, pontine tumors, basal or spinal fracture, extraction of teeth, after cataract operations, a retrogasserian neurotomy, as well as following various kinds of wounds. The eruption is not due to a virus, but to secondary involvement of the nerve or posterior root ganglion in the course of other diseases. These eruptions are unaccompanied by fever, run a chronic course, subside, and may recur, depending on the cause. The eruption clears rapidly without deep scarring or pigmentation, and is preceded by severe pain for several days or even weeks. Its evaluation and termination are variable.

CHICKEN-POX

Much clinical evidence has been presented to associate herpes zoster with chicken-pox. The histologic characteristics of the vesicle are the same, and the fixation reaction is the same in both antigens. Animal experimentation to prove the similarity of the virus in both diseases, however, has not been successful.

The relationship of the two diseases is strengthened by the transmission of zoster by varicella cases and the production of chicken-pox by zoster inoculation. In view of the number of cases of herpes zoster following varicella, and of varicella following zoster, either may be the starting point for an epidemic of either type of disease. Many observers believe that the virus causing varicella and zoster has two phases

which are transmutable or are modified strains of the same parent virus. However, varicella is inoculable, whereas zoster is not. The hematologic formula is not the same, and neither is the spinal fluid changed in varicella, as it is in zoster.

Some writers believe that the virus which causes herpes zoster in the adult may cause varicella in the child. Numerous investigators have described such cases, and Netter collected 174 examples of varicella following exposure to zoster.

It is less rare for zoster to follow exposure to varicella, but many cases were found in the literature. Thus, zoster may be followed by zoster in one person and varicella in others and the same is true of varicella, or a person may manifest both diseases at the same time. Numerous cases have been reported.

Some authors believe that varicella is a blood infection, whereas in zoster the virus reaches the posterior root from the spinal fluid, to which it gains access through the nose.

HERPES SIMPLEX

Herpes zoster is believed by some investigators to be related to other affections caused by a neurodermotrophic virus, such as herpes simplex, although the latter does not immunize, is inoculable, shows no nervous topography, and fails to show the fixation reaction of zoster.

Two diverse views are entertained concerning the identity of the viruses of herpes zoster and herpes simplex. One is to the effect that herpes zoster neuralgias represent the form of herpes with an especially marked nervous component. The proponents of this theory affirm an etiologic relationship between both pathologic agents, which, although they differ morphologically, nevertheless produce the same specific injuries to the nerves. Adherents to the other opinion, although admitting the alleged identity, insist that these pathologic agents are essentially quite distinct. This latter hypothesis is now accepted by the majority of investigators, who con-

clude that zoster is produced by a specific pathologic agent and that the virus is not identical with the virus of herpes simplex, although the pathologic picture agrees in some details.

PATHOLOGY

Von Barensprung, in 1861, attributed the disease to lesions of the posterior root ganglion, and was the first to report pathologic investigations. In 1865, Charcot and Catard found injection of the capillaries and nerves in the ganglion. Wagner and Weidner, in 1870, reported changes in the ganglia and nerves, and one year later Wyss found small hemorrhages and round-cell infiltration in the ganglion. In 1874, Jaclard published an account showing intense cellular infiltration of the connective tissue. Sattler, in 1875, found changes in the ophthalmic division of the nerve, and Kaposi, one year later, described areas showing destruction of ganglion cells. Similar findings were reported by Chaudelux, in 1879, Lesser, in 1881, and Leudet, in 1887. In 1883, Pitres and Vaillard found changes in the peripheral nerves, which was confirmed, in 1884, by Dubler. In 1900, Head and Campbell reported detailed findings in the ganglia of the posterior root, in the posterior root itself, in the peripheral nerves, and in the spinal cord. If the patient died at the time of the eruption, the ganglion was in a state of severe inflammation. The interstitial tissue was crowded with small round cells, especially in the central ganglion tissues around areas of extravasated blood. In the surrounding zone of small round cells the remains of ganglion cells were usually seen. The nuclei of ganglion cells were swollen, and the substance of the bodies of these cells was devoid of definite structure. Over the inflamed ganglia the sheaths were invaded by small round cells. The vessels were engorged, and extravasated blood was often seen. In some cases the inflammation subsided and left no changes in the ganglion, but the severer the eruption, the more certainly would permanent changes be found. As the inflammation subsided, absorption began.

Ultimately the focus of inflammation became converted into fibrous tissue, and the extent of this depended upon the severity of the inflammation. In this scar tissue the ganglion cells and nerve fibers were destroyed. The sheath over the scar tissue was thickened and altered in appearance. Secondary degeneration also occurred in the posterior nerve roots, similar to changes in the ganglion. Sometimes the degeneration extended into the posterior column of the cord and down the sensory nerve and its branches to the skin. The peripheral nerves also showed changes that could be traced back to the fine twigs which passed into the skin.

In symptomatic zoster, Head and Campbell found that the blood supply to the ganglia was definitely disturbed, and they believed that the process was one of acute destruction of ganglion cells due to vascular changes, rather than damage by poison leading to degeneration and death of the nerve cells.

Lauber in 1903, Andre and others in 1912, Sunde in 1913, Rollet and Colrat in 1926, Hesser in 1924, and many others have confirmed the findings of Head and Campbell.

The point of origin of the disease, whether it is central, epidermal, or neuronal, is not known. Many investigators, as Lauber, Wyss, Weidner, Kaposi, and Head and Campbell, believed that the primary focus originated in the ganglion and that the neuritis and degeneration of nerve fibers were secondary developments. They explain the skin and corneal lesions solely on a neuritic basis. Some authors believe that a lowered trophic influence permits the entrance of the herpes virus. Meller considered that the epithelial changes were due to trophic disturbances produced by inflammation in the more proximal portion of the nerve. Gilbert, Friedrich, and Gardilic held similar opinions. Duke-Elder, von der Scheer, Aubaret and Margillan believed that ophthalmic zoster was dependent upon a trophic disturbance, associated with a radiculoganglional and sympathetic affection by an unknown virus, and that the essential cause of the neurotrophic disturbances is unknown. In contradistinction, we have the

views of Dubler, Curschmann, and Eisenlohr, who maintained that the chief emphasis must be placed on the peripheral neuritis. These observers hold that the pathologic processes in the ganglia are probable results of the peripheral changes or may be co-ordinate with them. Wilbrand and Saenger, Orr and Howe, Montgomery and Culver, also believed the affection to be an ascending process. Teague and Goodpasture were of the opinion that the virus, incubated at the site of the inoculation, passed along the afferent nerve to the ganglion, producing hemorrhagic inflammation, and then proceeded along branches of that ganglion to the skin, where the vesicles developed. Marianesco and Dragenesco believed that the infection was located in the sensitive nerve ends and involved the motor nerves secondarily, with dissemination by the veins and lymphatics. Wohlwill believed that the disease was due to an ascending infection, utilizing the lymphatics of the nerves. He assumed a reflex causation of the skin lesions by vasomotor disturbances, and believed that this phase might come to an end as soon as the reflex arc was interrupted, by the complete degeneration of some of the sensory components.

Some authors believe the disease to be due to irritation of vasodilators and not to an extension of inflammation to the terminal filaments of nerves in the skin, and they are of the opinion that the eruption is due to an inflammation of the sympathetic fibers distributed through the arteries, which causes distention and possible rupture of the capillaries. The exponents of this vasomotor theory are von Recklinghausen, Ebstein, Abadie, Wohlwill, Aubineau, Nobl, Kreibich, and others.

Rosenow and Oftedal reported a complete study of their experimental work in which they endeavored to prove that herpes zoster was a streptococcus-infection, gaining entrance to the circulation through diseased tonsils or pyorrhea pockets, and possessing an elective affinity for the posterior root ganglion.

Gruter claims to have produced an eruption of zoster by injecting brain substances from animals that were infected with herpes zoster. Flexner, Teague and Goodpasture, Kuchner, and Kundratitz asserted that they demonstrated the presence of the virus in the intervertebral ganglion as well as in the vesicles.

However, it has proved impossible for most investigators to reproduce the disease experimentally, or at least to obtain transmission in series. Accordingly, the nature of zoster virus is unknown, but it is assumed that herpes zoster is a specific infectious disease, due to a non-filtrable neurotrophic virus.

SKIN

Head showed that in an unruptured skin vesicle the vesicle was split by small septa, extending from the roof to the floor, and that masses of round cells were in the floor. The external covering of the vesicle consisted of the non-nucleated cells which made up the epidermis. Head believed that the septa were due to partially raised epithelial cells that retained their attachment to the roof and floor.

When a vesicle is changing to a pustule, the cells in the septa increase and push apart the epithelial cells on the floor of the vesicle. The cells are often so greatly enlarged as to contain several nuclei and surround the nerve trunks and press on the nerve covering. This causes the fine nerve twigs in the deeper layers of the corium to show swelling of the neurilemma, with degenerated myelinated sheath, and causes the white substance of Schwann to disappear, leaving the axis-cylinder swollen and alone.

The changes in the skin are usually found in the rete layer of the epidermis. The epithelial cells, from traction, assume various shapes, which are degenerated epithelial cells. In these cells, in and around the vesicles, are found inclusion bodies resembling protozoa, believed at first to represent parasitic cell inclusions, but which are now considered merely degenerative changes.

OPTIC NERVE, RETINA, CHOROID

In some cases the optic nerve has been involved during the inflammatory process, and this may be due to the fact that the organism may spread locally from the posterior ganglion to adjoining structures. The optic nerve and the Gasserian ganglion are very close together, and this may account for the blindness that has been observed in some cases, either by the toxin or by the specific virus involving nearby structures. Meller found small foci of round cells around the choroidal vessels. Head and Campbell, in some cases, found the optic papillae to be edematous, and the optic nerve showed destruction of the medullary sheaths of the nerve fibers. Gilbert, Gardilic, and Kreibig found similar changes.

Bruce carried out a series of experiments to show that these sensory fibers must bifurcate at their extremities at the periphery of the body, one limb ending in the sensory end organs in the skin and the other limb ending in the vessels. The former branch carries sensory impulses centralward, and the latter carries vasodilator impulses to the periphery. The common stem carries impulses in an ascending and descending direction. If the cells of the posterior root ganglion are irritated, they will be capable of originating impulses that pass in two directions—one centralward, causing the pain and peripheral impulses along fibers to the bifurcation, which ends in a vessel and produces dilatation. Teague and Goodpasture believed that the virus followed the nerves and penetrated into intervertebral ganglia, and that it must have traversed the same route in an opposite direction in order to produce a herpes zoster in the corresponding cutaneous region. This assumption they proved experimentally.

GLAUCOMA

Disturbances of ocular tension in herpes zoster have for several years been the object of investigators, whose results have served to add to our knowledge of the physiopathology

of the sympathetic nervous system. While the action of the sympathetic in ocular tension is not as yet clearly understood, the glaucoma which supervenes in ophthalmic zoster is related apparently to sympathetic excitation. However, it appears that regulation of ocular tension is not controlled by the sympathetic nerves exclusively, and it is possible, as many believe, that the zoster virus may act upon tension of the eye by way of other nerve elements. Experimental retrogasserian neurotomy is accompanied by diminution of ocular tension. Excitation of the root of the trigeminus immediately beyond the protuberance raises the ocular tension, whereas section of the trigeminus lowers it. This indicates that zoster should be accompanied by a diminution of tension.

Adjoining Ganglia

Although the specific inflammation attacks chiefly one sensory ganglion, the adjacent ganglia may not always escape involvement. This explains those cases in which the eruption is in the zone of one ganglion, and complications occur which can be attributed to involvement of other ganglia. Multiple involvement of these ganglia is not infrequent, thus producing a variety of clinical combinations. From a consideration of many cases, the symptoms of herpes zoster ophthalmicus of face, neck, ear, mouth, eye, and nose may occur grouped together in almost every possible combination.

Spinal Fluid and Blood

In herpes zoster ophthalmicus the cerebrospinal fluid is modified, and it is not surprising to find, after inflammatory changes have occurred, that degeneration in the posterior roots and posterior column of the cord has taken place. The pia-arachnoid culdesacs bathe the Gasserian ganglion, and the inflammatory ganglionic process may, according to its intensity, provoke reaction in the spinal fluid, causing lymphocytic hypercytosis and hyperalbuminosis. Brown and Dujardin reported on the cellular elements in 42 cases, with

inconstant results. The majority of cases showed a lymphocytosis which bore no relation to the intensity of the eruption. Numerous investigators found similar results. Some reported an increase of tension in the spinal fluid, and others described a reduction of tension.

Glaubarson and Rabinovicz found, in most cases, a slight decrease in neutrophils and a marked increase in lymphocytes. They found leukocytosis from the first to the fifth day, a normal white count from the fifth to the eighth day, and from the eighth to the twelfth day; during the stage of drying of the vesicles, a leukocytosis was present.

PROGNOSIS

In consideration of the ocular complications that may develop during the eruption or afterward, the prognosis with respect to vision is reserved. If the eye becomes inflamed when the skin eruption appears, the cornea is usually severely affected, giving rise to various eye pictures, but, as a rule, if the cornea does not become inflamed until the termination of the attack, the symptoms are less severe. Corneal ulcerations may become infected secondarily, terminating in iridocyclitis, glaucoma, or perforation. When iritis develops the prognosis is grave, for the eye may continue irritable and subject to high tension, with ensuing glaucoma. Severe neuralgic pains with anesthesia may persist, and the exhaustion subsequent to continual pain may be a serious factor. Violent delirium has been known to occur.

Apart from the serious risks which optic neuritis may offer for function of the eye, the prognosis for the future is also unfavorable. Only rarely does visual function recover even a fraction of its normal integrity.

When ophthalmoplegic symptoms which do not recede completely are observed during the course of the eruption, the prognosis must be reserved. Muscle complications may be divided into two distinct categories, those which tend toward complete recovery and others which are followed by

more or less permanent disturbances after some improvement. In some cases a certain degree of paresis may become permanent.

DIAGNOSIS

The diagnosis of herpes zoster ophthalmicus is based upon the symptoms and upon the evolution of the affection. As a rule, there is no confusion in the diagnosis, provided a thorough examination of the functional state of the eye is conducted in every instance of a zoster eruption. A careful test of visual acuity should be instituted first, followed by tests for binocular vision and motility, whereupon the existence of a slight degree of diplopia or of a strabismic deviation will be readily recognized.

The disease has been mistaken for erysipelas, supra-orbital neuralgia, frontal sinus disease, migraine, eczema, cyclitis, dacryocystitis, impetigo, sinus thrombosis, brain tumor, meningitis, and herpes simplex. In erysipelas, there are large bullae and the skin is markedly swollen. The eruption is not limited to the midline, but affects both sides, and assumes the aspect of the wings of a butterfly. The temperature is higher and pain is absent. Ophthalmic herpes may be confused with herpes simplex because of the localization of the latter and the nervous disturbances that are associated with it. It is not, however, accompanied by neuralgic pains. Impetigo exhibits its characteristic crusts and may be situated in all parts of the face. In some cases, with an associated unilateral paralysis of the ocular muscles, an aseptic thrombosis in the cavernous sinus must be considered. In this type of case, there is marked chemosis, frequently exophthalmos, and the symptoms are often bilateral. Sinus disease can usually be eliminated by means of the x-rays. Slow hemorrhage from an aneurysm of the internal carotids, or circle of Willis, will give such a picture. Cerebral tumor can usually be eliminated by the history of sudden onset, negative x-rays, and the absence of signs of intracranial pressure. The fifth nerve sends a

branch to the meninges, and often a severe local meningitis may accompany the disease.

TREATMENT

In an attempt to determine what course of treatment should be followed in ophthalmic zoster, the results and types of treatment employed in past years have been analyzed. A specific treatment for herpes zoster is not available, and we must choose from a wide variety of therapeutic measures. A vast number of remedies has been suggested, but no one of them has been successful in all cases. The treatment of zoster has been largely symptomatic, and has been directed chiefly to the relief of pain. The general treatment consists of rest in bed, light diet, sedatives, and supportive measures. Salicylates, quinine, lactic acid, bromides, iodides, barbiturates, and arsenic have all been used as alteratives with beneficial effect.

Early protection of the cornea prevents superficial corneal involvement in many cases. The cornea can often be protected by the use of ointments, and atropine may be indicated. If ulcers develop and are deep, suturing of the lids may be necessary. Some advise bandaging the eye from the start for a period of weeks.

If hypertonia is present, miotics are indicated in some cases. Warm compresses are often advisable. Argyrol, neosilvol, dionin, optochin, holocaine, pontocain, have all been used with benefit in some cases. Pierron advises touching up the ulcers of the cornea with 1:1000 solution of methylene-blue or tincture of iodine, and applying ichthyol ointment, 1:200, between the lids. Ammoniated mercurial ointment and scarlet red ointment have also been recommended by some. Burwell, in 1912, used subconjunctival injections of normal saline and an occasional injection of 1 per cent. guaiacol and dionin, if corneal lesions were present.

Many types of treatment have been advised for the skin lesions. Some prefer various powders, such as zinc stearate,

talc, starch, and xeroform, whereas others use oils to prevent drying of the secretions. Painting of the vesicles with collodion has been advised, but this may increase the pain temporarily by contracting the skin in the vicinity. Fox, in 1922, advised a paraffin mixture. Others recommend the use of tincture of benzoin, hydrogen dioxid, sterile olive oil, pure alcohol, cocaine, calamine lotion, 2 per cent. gentian violet, lead-water and laudanum.

In 1938, Hollander introduced the treatment of anesthetizing cutaneous hyperesthetic areas for the relief of pain. These areas are located about the papules and vesicles of the herpetic rash. Hollander used 0.5 c.c. of a solution of benzyl alcohol, 5 per cent., benzocain, 3 per cent., phenol, 1 per cent., in expressed almond oil. This solution was injected into a square inch of skin, just under the corium. Some prefer the subcutaneous injection of 1 to 2 per cent. novocaine solution under the inflammatory tissue, with complete relief of pain in most cases.

The beneficial influences of vitamin B in neuritis, and its action in preventing certain degenerative changes, are acknowledged, and, as the prominent features in herpes zoster are a neuritis and degenerative changes, many investigators have used this vitamin with good results. Pain is quite often definitely relieved. Thiamin chloride, 5 to 10 mg., is often used subcutaneously daily for six days. Goodman reported excellent results from this type of treatment. Cevitamic acid has been used by some investigators. Its influence is assumed to be due to the fact that vitamin C acts directly upon the hypothetic virus of zoster.

Vendel, in 1926, was one of the first to enumerate the benefits of pituitrin (surgical) for herpes zoster. He advised daily injections of from one-half to one c.c. The effect of pituitrin is directed against the pain, but it has no effect on the course of the disease. This treatment would be contraindicated in hypertension, increased intracranial pressure, or pregnancy.

Radiotherapy, radium, *x*-ray, high-frequency currents, violet rays, short wave rays, the Hanau lamp, infra-red lamp, and diathermy have produced good results in many cases.

Some observers have had good results from the injection of arsphenamine, salvarsan, arsaminol, atophanyl, diphtheritic antitoxin, triple typhoid vaccine, sodium thiosulphate, iodobenzomethylformine, impletol, epinephrine, and antistaphylococcus vaccine.

Bryan relieved pain in the eye by cocainization of the nasal ganglion, and to relieve the pain in the distribution of the supra-orbital and frontal nerves, the ophthalmic division of the fifth nerve was reached with cocaine through the sphenoid ostium. Wood injected novocaine into the supra-orbital nerve, just back of the foramen, for severe neuralgia. In some cases gasserectomy, avulsion of the root of the nerve, and anesthesia of the sphenopalatine ganglion have been done for the relief of pain.

Friedenwald, in 1929, was the first to use convalescent serum for the severe neuralgias, with excellent results. Gunderson, in 1940, gave detailed findings, and reports 91 cases so treated. Autohemotherapy has been used successfully by many investigators.

In patients who suffer from persistent pain, accompanied by keratitis, it is often necessary to protect the cornea by a median tarsorrhaphy not only during the course of zoster, but even for many years following the attack. Long external blepharorrhaphy is successful in many cases. Cross, in 1918, performed pericorneal neurotomy in a patient for the relief of constant pain and corneal ulcer. Badot recommended removal of the central portion of the ophthalmic branch of the fifth nerve in severe cases. Peet, in 1929, sectioned the sensory root of the ganglion in two cases of post-herpetic trigeminal neuralgia.

The writer has used autohemotherapy with success in several cases. The method is simple and pain is quickly

relieved. The eruption responds to treatment, and few injections are necessary. This treatment consists in the withdrawal of 5 to 20 c.c. of blood and its injection into the patient's gluteal muscles. The amount of blood withdrawn varies. In children half the amount is withdrawn. There are no after-effects except a slight pain at the site of injection, and in some cases a mild febrile reaction ensues. As a rule, two or three injections suffice. Early treatment prevents severe pain and ocular complications. The method has no effect on well-established uveitis due to zoster, but it may prevent development of new uveal foci of infection.

During the eruptive period, when palpebral edema is present, local treatment should be restricted to the application of moist compresses to avoid the accumulation of secretions. Olive oil is often beneficial in cleansing the skin. At times a protective dressing is necessary. Cold air and drafts should be avoided.

As soon as the swelling of the lids subsides and the affected eye can be opened, it should be examined for corneal anesthesia, and afterward tests to ascertain the motility of the globe should be made. While corneal anesthesia persists, the eye should be covered by an occlusion bandage, and if anesthesia or corneal ulceration continues, tarsorrhaphy should be performed and maintained for several weeks.

Even after the disappearance of the zoster, patients should remain under observation, since corneal disturbance or increase of tension may manifest itself at a late date, and disturbance of sensibility may persist for a long time and perhaps indefinitely.

CONCLUSIONS

The severity and duration of the disease vary. Complete recovery may follow in a few weeks, or the condition may last for months in spite of treatment. In all cases of herpes zoster there is a morbid condition of the sensory nerves supplying the affected area, and the type and localiza-

tion of the changes are variable. Specific clinical manifestation appears to be the result of some form of irritative reaction to the ganglion or nerve, whether due to infection, trauma, or intoxication. It may be that predisposing factors, such as cold, injury, head colds, specific infections, sinus or dental disease, favor the establishment of herpes zoster. The process may start in various portions of the nerve, the ganglia, or in the peripheral branches, and even in the contiguous ganglia connected with the fifth nerve, such as the sphenopalatine ganglia.

A vast majority of cases of ophthalmic zoster are secondary or symptomatic. The causes and character of the basic disturbance vary. Different systemic diseases, even latent ones, may terminate in herpes zoster ophthalmicus. The basic disease may run its course, leaving only a predisposition toward nervous disturbance or nervous irritability. Levaditi believed that various causes were provocative agents, forming a point of least resistance upon which the latent virus of zoster might act.

In cases of herpes zoster which are coincident with other infectious diseases, it is not known whether these infections are actually produced by the same etiologic agent or whether they are produced by their own virus, the infection being facilitated by general lowering of bodily resistance..

According to some authorities, propagation of the virus occurs through the cerebrospinal fluid and thus it is explained how the more superficial fibers originating from specific sensory nerves or fibers destined for certain muscles are first affected in certain ganglia or nerve trunks. Proponents of this theory regard ophthalmic zoster as a manifestation of various infectious processes which are propagated by the spinal fluid and so account for its selective action upon particular sensory filaments and muscles, whose nerve fibers are superficially located in the nerve trunk. Goeckerman and Wilhelm believed that the same lesion might result from several causes, including trauma, hemorrhage, and focal in-

fection. These observers were not convinced that a single agent caused the disease.

There may be a form of zoster not induced by neuritis or affection of the nerve ganglia, but due to a disturbance in the higher sensory centers of the trigeminus in the medulla oblongata (bulbar affection), which has to date been described by Duhring and Huber in one case due to malaria. In this case these investigators concluded that the seat of the disturbance was a bulbar nuclear paralysis, probably located where the centers of the sensory trigeminus, the vagus, and the posterior horns of the second and third cervical segments lie close together. They believed this case was due to a vascular alteration after malaria, following endothelial proliferation and partial occlusion of vessels.

The traumatic origin of the disease has never been scientifically demonstrated, although it is possible that there is a connection between corneal trauma and corneal herpes zoster. In these cases it is questionable whether injury is the prime etiologic factor.

Ocular paralyses which supervene during zoster are not so rare as is generally assumed, although their frequency is variously estimated by different observers. Their occurrences are independent of intensity and distribution of eruption. They usually occur two or three weeks after the eruption. The third nerve is most frequently involved, and the involvement may be partial or total. It may be revealed by ptosis or mydriasis, although it must be remembered that these conditions may also be produced by inflammatory ptosis or by alteration of the pupil, due to lesions of the cornea, or by paralysis of the sympathetic. It has been demonstrated by Ingvar that the fibers corresponding to the levator palpebrae and the superior rectus occupy a superficial situation in the dorsal part of the nerve trunk of the fifth nerve, whereas those corresponding to the inferior oblique are also situated superficially, but in the ventral part. Therefore these muscles would be more readily affected by pathogenic agents attack-

ing the nerve trunks externally, as in instances of basal meningitis, or when the infectious agent is propagated by the spinal fluid.

Combinations of paralysis of the trochlear and abducens sometimes occur. Only two cases of bilateral paralysis have been reported in the literature, one by de River in 1925, who reported a bilateral paralysis of the sixth nerve, and Gallois, in 1924, who described a bilateral paralysis of the third nerve. Paralysis of the motor nerves of the eye may be due to extension of the affection to the trigeminus, then to the motor nerves by way of the sensory ramifications, which the first branch of the fifth sends out to all motor nerves of the eye before entering the orbit. Vernon believed the muscle paralysis was due to the same influence as the herpes, and Wyss was inclined to refer the muscle paralysis to myositis. The writer found reports of 242 cases of ocular muscle paralysis in the literature.

The lacrimal gland reveals its participation in the affection by disturbances of nerves controlling the secretion of tears, which cause abundant transitory lacrimation. Terrien believed that the keratitis was favored by the abolition of continuous lacrimation, which he believed depended on the facial nerve, and stated that when the petrous bones were removed at the same time as the ganglia, the secretion of tears disappeared and the cornea was altered. If, however, the ganglion was sectioned without cutting out the petrous bone, the secretion of tears was preserved.

The epithelium of the cornea is soft, delicate, and loosely attached to Bowman's membrane. It is liable to injury, has a precarious nutrition, and retains its integrity mainly through its sensitiveness. The rich nerve supply protects the cornea by the sensation of pain and by the trophic influence, the influence which the healthy nerve has on corneal nutrition. This ease of epithelial denudation is an important factor in the development of corneal affections. In herpes zoster there is corneal anesthesia, and this invites secondary

infection and renders the cornea liable to injury. In addition, there may be an irritative influence passing down the nerve causing disturbed nutrition, or the normal influence that passes along the nerve may be disturbed. The small inflamed terminal nerve fibers set up an irritative process at the periphery in addition to the detached corneal epithelium. In cases of corneal ulceration the result is that of every infection of the cornea. Such ulcers may terminate in a scar and leave a marked diminution of vision.

The fifth nerve is similar, morphologically and physiologically, to a posterior radicle of a spinal cord nerve. According to Talkovskiy, it has a definite biologic arrangement in the ectodermal portion of the cornea, and appears neurotrophic for an ectodermal virus. This observer claimed that the development of the corneal process was explained by the morphologic character of the nerve apparatus of the cornea, the status of the nerve portions, and the anatomic communications with the nerve network of the cornea.

In zoster of the skin there is always anesthesia, and usually areas of anesthesia are found upon the cornea. The cornea may be hypoesthetic, and some authors believe that this underlies the corneal lesions. Experimental work has shown that, in section of the trigeminus in which sensibility was preserved, keratitis was rare, whereas keratitis was present in the majority of instances in which anesthesia was absolute. The impaired corneal sensation varies, due to the amount of damage sustained by the ganglion. Head and Campbell showed in their researches that the more severe cases exhibited complete destruction of nerve cells in the ganglion. Lesions of the cornea are present in 40 per cent. of cases.

Various hypotheses are advanced to account for the optic neuritis. Included among these are reflex disturbances and, particularly, the anastomotic union of a filament of the ciliary nerve into the optic nerve, with the central artery of the retina. According to this theory, infection proceeding from the ganglion descends along the nerve trunk of the ophthalmic nerve and thus reaches the optic nerve.

Iritis often manifests itself as an anterior uveitis or an iridochoroiditis, and is characterized by its torpidity and by the minute precipitate upon the posterior surface of the cornea. In some cases the classic form, with posterior synechiae, is seen. It may be associated with hypertonia, even though iritis is ordinarily associated with hypotonia. Iritis is present in about one-fifth of all cases of ophthalmic zoster.

No definite etiologic factor has been found. Some form of acute intoxication takes place, becoming localized in the ganglion and producing a toxic element that irritates the nerve ends of the part involved, causing herpes to develop. It is questionable whether the disease is due to any special etiologic factor, even though it appears contagious at times.

The skin lesions may be due to products of degenerated ganglion cells conveyed along the nerve to the skin termination, or caused by the exciting organism itself acting by nerve impulse on actual passage of the virus, or the products of degenerated nerve fibers in the skin might cause the eruption. There is selectivity, for at times the skin is not even reddened between the vesicles, as the vesicles do not appear in all parts of the skin supplied by the nerve.

Whether the disease is due to selective affinity of some virus or bacteria in a focal lesion, as claimed by Rosenow, or whether it is due to the selective action of their toxins, as suggested by Mackenzie, is questionable. If one virus is responsible for so many different lesions, it is certain that it is capable of different action at various times and places. It is quite possible that the virus is liable to a changing virulence, and may be inconstant in its affinity for the bipolar ganglion cells. An irritation of these cells causes the herpetic eruption, whether due to a virus or to some inflammatory process or growth. Whether it is exogenous, and extends to the ganglion by way of the nerve, or whether it is endogenous and attracted by the nerves and ganglion through increased neurotic irritation, is not known.

Age and sex are no factors. On the basis of blood findings in the disease and reports in the literature, the infection is of low virulence, and no definite conclusion can be drawn as to the severity of the disease by the blood examination.

It is often associated with dental and focal infection, but most adults have enough infection, local or general, in their systems, so that an attack could occur at any time and would not necessarily appear in epidemic form. There may be a special local or general susceptibility, for not every one contracts the disease.

The essential cause of the disturbance is unknown, whether due to destruction of trophic fibers, irritation of nerve elements, injury to insensitive structures, spread of the degeneration process from nerve terminals to cells in the ganglion, or due to a specific infection.

The pathology of ophthalmic zoster is an involvement, either in the gasserian ganglion or along the course of the branches of the fifth nerve, or both, affecting the skin, mucous membrane and tissues supplied by these nerves. These lesions may be the result of hemorrhage in the ganglia or sheath of the nerve, causing pressure on the nerve, or it may be due to senile degeneration or a localized inflammatory process in either the nerve or the ganglia, or to a tissue reaction to various types of irritant.

Secondary degeneration may be found in the posterior columns of the cord and in the fibers of the posterior roots central to the ganglia, and in the afferent fibers of peripheral nerves leading to the ganglia.

As a result of observation and experiments by many investigators, most writers conclude that an independent pathologic entity is involved, and that herpes zoster is now considered to be an infectious disease of one or more spinal ganglia.

It is possible that, instead of a virus, the real nature of the cause is due to changes in complex chemical protein molecules. Different strains or different arrangements of the

molecule may produce various types of disease. Under different degrees of body temperature the molecule may become weakened or strengthened to such an extent that it can then enter the body cells that have been altered, and the molecule is then capable of producing a different disease, as in herpes zoster or varicella. Investigators have shown that the molecule can grow when it touches the exact kind of living cell it selects for a home. These non-living molecules or enzymes merely exist, neither growing nor dying. They move about when they enter certain cells and then grow and probably reproduce. If their structure is unchanged, they are harmless, and depending on how they are put together determines whether or not they are dangerous. The molecule is at the mercy of its environment, but entering the right kind of cell, it reproduces itself and grows. As a result, rapid growth of molecules may cause immediate death of the cells. It was not until the development of the electron microscope that viruses could be photographed and their structure studied, and in all probability a virus is a chemical protein molecule.

After having made an exhaustive search of the literature, and with the aid of several translators, the writer finds that there are approximately 2,250 cases of ophthalmic zoster reported to date. Some investigators have made a very careful study of cases and of the pathology and picture presented. Others have made only brief reports, with short case histories. In many of the cases described no reference was made to sex or age or of the eye involved. The average age was found to be forty-three years; males were affected in 54 per cent. of the cases; the right eye was involved in 54 per cent. The cornea was disturbed in 39 per cent., and the globe was affected in 49 per cent. The ocular muscles were involved during the disease in 13 per cent. of cases, and the facial nerve in 7 per cent. An Argyll-Robertson pupil was described in 23 instances, and glaucoma appeared 65 times in the course of the disease. There were 35 cases of episcleritis

reported, 41 cases of recurrent ophthalmic zoster, and 52 bilateral cases. All the branches of the fifth nerve were involved in 25 cases, and the first and second branches were affected 67 times. Retrobulbar neuritis, optic neuritis, and optic atrophy appeared 40 times, and numerous cases resulted in perforation of the globe as a result of panophthalmitis. There were 68 cases of ophthalmic zoster under twenty years of age described, 44 were under thirteen years, 24 were under six years, and 14 were under one year old.

REPORT OF THE AUTHOR'S CASES

J. C., a male, aged seventy-five years, after being exposed to a cold wind and rain, complained of severe pain over the right eye and right side of the head. The neuralgic pain was of sudden onset in the area of distribution of the first branch of the fifth nerve, followed in two days by the eruption of vesicles.

When seen, two days after the eruption, which appeared on the right side of the forehead, sharply demarcated against the midline and extending to the scalp, eyebrow, and external palpebral commissure, there was associated edema of the conjunctiva, which partly covered the cornea, with increased lacrimation. Vision at this time was 20/100 in the right eye and 20/20 in the left. Temperature, 37.5° C.; respiration, 20; pulse, 90. The leukocyte count was 10,000. Urinary and Wassermann tests were negative. Personal history was non-contributory. The patient was a well-developed, well-nourished, healthy male. The heart was normal in size, rate, and rhythm. No murmurs were present. The blood-pressure was 160/80. The lungs were clear to percussion and auscultation, and no râles were present. The abdomen showed no tenderness or palpable masses. The reflexes were normal.

Four days later, sudden diplopia appeared, due to paralysis of the right sixth nerve. There was simultaneous increase in the periorbital edema, and the appearance of a new crop of vesicles at the nasal angle of the right eye and over the right half of the nose, in the area supplied by the infratrochlear nerve. The eyeball became intensely injected, with much lacrimation and mucopurulent discharge. The ocular tension was increased. A few erosions were noted on the cornea, which was somewhat edematous and hazy. The corneal infiltrate involved most of the nasal half of the cornea, with some vascularization. Hyperesthesia of the skin was present in the area supplied by the fifth nerve. The cornea was insensitive.

The abducens paralysis coincided with the appearance of the secondary crop of vesicles at the nasal angle of the right eye, probably due to the direct extension from the nasociliary to the sixth nerve in their passage through the supra-orbital foramen or deeper in the orbit.

The skin eruption passed through the stages of vesiculation, the pustules drying, crusting, and terminating in pigmented scarring. The acute phase of the infection subsided in about eight weeks, and sixteen weeks later all symptoms had disappeared. Resulting vision was 20/60. The diplopia subsided in two weeks, and the tension returned to normal.

The pupil was kept dilated with 1 per cent. atropine sulphate, and 10 per cent. neosilvol was used in the eye three times daily. The eye was kept covered. Salicylates for the relief of pain were administered freely. Calamine lotion was used for the skin lesions. Thiamin chloride, 2,000 units, was given daily for six days.

E. R., male, aged forty years, after a few days of general malaise, headache, and left supra-orbital pain, developed a typical herpes zoster of the first branch of the left trigeminal nerve. When first seen, there was an eruption of vesicles, some dried and crusted, on the left upper lid, forehead, and nose, sharply limited to the midline. The lid was edematous and heavy, with chemosis of the bulbar conjunctiva. There was no proptosis or immobility of the globe. The cornea was hazy, with small areas of ulceration present and definite ciliary flush. The pupil was moderately dilated. The ocular tension was normal. No fundus details could be seen.

The temperature was 37.5° C.; white cell count was 9,500; the urinary and Wassermann tests were negative.

The patient's vision had always been good in each eye, and there was no history of any previous eye trouble. His general health was excellent. The heart and lung examination did not reveal any abnormality or evidence of disease. The abdomen showed no areas of tenderness.

Atropine was used to dilate the pupil, and local supportive measures were prescribed. Autohemotherapy, 10 c.c., was administered and repeated two days later. Immediate cessation of pain followed, and definite improvement in the skin eruption was observed.

Three weeks later the corneal involvement had disappeared, with no remaining leukoma. Vision was normal in each eye. The pupil was round and reacted normally to light, accommodation, and consensually. The fundus showed no abnormality. There was no

subjective or objective evidence of disturbed ocular muscle equilibrium. Vision was 20/30.

C. G., male, aged forty-five years, complained of severe pain and inflammation of the left eye. Neuralgia persisted, and soon there was swelling over the left temporal region, and the lids became swollen and then closed. The next day many small, yellow, raised, and irregular blisters appeared on the left side of the nose, the upper and lower lids, and upon the skin of the left frontal region as far as the hairline. These vesicles were not present on the remainder of the face, and were definitely delimited in the median line, so that they occupied the left side of the affected regions exclusively. The conjunctiva was decidedly hyperemic and chemotic. The cornea showed several small pinhead erosions. The pupil was dilated, and the iris was free. Ocular tension was not increased. The preauricular and posterior cervical glands were enlarged.

The temperature was 37° C. and the pulse, 78. The white cell count was 11,950, and the red cells were increased to 5,720,000. The urine showed an excess of albumin. The Wassermann test was normal. The general physical examination was essentially negative. The patient's health had always been good, and there was no history of any previous eye trouble.

On the sixteenth day diplopia developed, due to paralysis of the left sixth nerve, which disappeared in two weeks' time. At the end of the third week the corneal disturbances had also disappeared, with regeneration of corneal epithelium. Some superficial vessels were seen at the nasal limbus of the cornea. Vision was 20/40.

At this time the vesicles of the skin had dried and formed thick yellow-brown crusts, which fell off, leaving deep pits in the skin. Complete anesthesia persisted and extended to the scalp.

In this case the first and second branches of the left fifth nerve were affected. No specific special treatment was administered. Atropine was instilled in the left eye as soon as the corneal condition was discovered. Neosilvol, 10 per cent., was instilled in the eye three times daily, and the eye was kept closed. Calamine lotion was applied to the skin surface. Aspirin was given freely for the relief of pain.

P. F., male, aged sixty-two years, complained of severe pain over the right eye, which extended up and back over the frontal and over the parietal region. This pain lasted for forty-eight hours and was greatly increased during the night. The right upper lid was swollen and heavy, causing the eye to close. By lifting the lid,

however, the patient found that his vision was not affected. He described the pain as an "intermittent lightning pain" from which he was not free at any time. Later the neuralgia extended down the right side of his nose. At this time, on the fifth day, vesicles appeared over the painful region, to the right of the midline. The pain diminished, but did not disappear. The vesicles were clear, extending over the frontal region into the scalp and along the right side of the nose to the tip. On the right brow there was a large linear vesicle. Two vesicles appeared on the right upper lid. The eye was greatly engorged, and there were marked lacrimation and photophobia. Some conjunctival discharge was present. Several small vesicles appeared on the cornea, and the vision was greatly reduced. These vesicles occupied most of the pupillary area of the anesthetic cornea. Part of the iris could be seen and appeared to be swollen. The pupil was indistinct, but of medium size, and was not quite round. No fundus details could be made out. The preauricular glands were enlarged. The heart and lungs showed no evidence of disease. The blood-pressure was 140/75. The abdomen exhibited no areas of tenderness.

Atropine was used as soon as the cornea was found to be involved. Part of the iris remained fixed and swollen, and the iris vessels were easily discernible. The tension remained normal. Autohemotherapy, 10 c.c., was used, and repeated on two more alternate days. Calamine lotion was applied to the skin lesions. On the fifth day the pain had completely vanished, and the skin eruption was vastly improved. The skin crusts loosened and fell off, leaving deep scars corresponding to the confluent group of vesicles.

Slit-lamp examination showed small opacities in the deeper corneal layers, with deposits on Descemet's membrane. After staining with fluorescein, the minute corneal defects could be seen more clearly. The iris showed atrophy, and appeared of a duller tint than the opposite iris. It had lost its areolar structure, some crypts were effaced, and the fibrils were blurred. A few pigmentary spots were seen on the anterior capsule.

The white cell count was 8,100 and the red cell count was 4,850,000. The urinary and Wassermann tests were normal.

Six weeks later the eye was quiet, a central corneal leukoma remaining. At this time the patient suffered severe pain in the right eye, and two days later ciliary injection appeared and a hazy area was noted below the cornea. A small nodule of violet slate color developed, with marked injection of the vessels at this point, which became a small vesicle on one of the anterior ciliary nerves,

resembling an area of episcleritis. Atropine, 1 per cent., was again used in the eye, and the pupil was kept in a state of dilatation. The eye was kept covered. Sodium salicylate, 10 gr., was given three times daily, until all pain and discomfort had disappeared. Weeks later the conjunctiva recovered its normal condition and the nodule was less pronounced, assuming a grayish tint. Four weeks later, the nodule had disappeared, and in its place there was a small, darkened discoloration of the sclera. This nodule was beneath the conjunctiva and near the limbus, but did not reach the cornea. One year later vision was 20/30 with correction.

Mrs. T. T., aged seventy years, was first seen five days after the outbreak of herpes zoster. A number of vesicles were noted on the left upper lid, forehead, scalp, and the tip of nose. There was intense ocular congestion, with a central corneal ulcer. Severe neuralgic pain was present over the area involved, and from the left upper lid to the scalp the skin was red and tender, with swelling of the preauricular glands.

Vision was greatly reduced. The temperature was 38° C. The urinary and Wassermann tests were normal. The red cell count was 3,750,000 and the white cell count was 10,000. The differential cell count showed: polymorphonuclears, 41 per cent.; eosinophiles, 30 per cent.; small lymphocytes, 22 per cent.; large lymphocytes, 5 per cent., and basophiles, 1 per cent. Hemoglobin was 84 per cent. The general physical examination did not contribute anything pertinent to the case. There was a history of exposure to chicken-pox three weeks before the present illness.

Ten c.c. of blood was withdrawn from the arms and injected into the gluteal region (autohemotherapy). This was repeated two days later. After four days there was complete cessation of the pain, the skin condition was much improved, and the eruption had almost disappeared. This treatment, however, did not seem to have any effect on the corneal condition. Atropine was used to keep the pupil dilated. Codeine was prescribed for relief of the pain, and calamine lotion was applied over the skin of the forehead and scalp.

About four weeks after the onset the lid edema had subsided and the patient was able to keep her eye open. Throughout the illness the eyeball was considerably injected, with much lacrimation and mucopurulent discharge. The corneal ulcer had healed, but corneal sensation was still greatly diminished. At this time there were observed many minute gray papules in the cornea, and the patient complained of diplopia. Examination showed that this was due to paresis of the left trochlear nerve.

The pupil was round, and equalled 6 mm. in diameter. The fundus details were hazy. The slit-lamp revealed numerous minute gray spots situated in the epithelial layer of the cornea, in contact with Bowman's membrane. These spots were denser toward the center, and were scattered at the periphery. The superficial outline of the iris could easily be seen. The pupillary margin was pigmented, and in places particles of pigment had become separated from the iris. Two small holes were seen in the iris, which permitted light to pass through.

For several months a severe neuralgia in the left eye, left temple, and scalp persisted. Cutaneous anesthesia was present. The upper lid remained red and thickened, and the eyeball was injected for some time. The conjunctival injection gradually subsided, but the skin of the upper lid and forehead was extremely tender to the touch for a long time. The corneal involvement gradually became less apparent. The diplopia gradually diminished, and in one year's time had disappeared. Vision was 20/30.

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THE OCULAR PATHOLOGY OF METHYL ALCOHOL POISONING*

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INTRODUCTION

Methyl alcohol poisoning in relation to the eye is of interest not only because it is clinically important, but also because the resulting pathologic processes in the eye are not fully understood.

Any one who studies the literature on the subject is impressed with the lack of uniformity of opinion as to the effects of methyl alcohol upon the ocular structures, and opinions concerning the toxicologic process are also at variance. Most of these are based upon conclusions drawn from clinical observation, autopsy reports, and the results of experimental work in animals.

* Condensed version made by the author from the candidate's thesis for membership accepted by the Committee on Theses.