Herpes zoster ophthalmicus is a painful condition which produces a rash on some of the skin supplied by the first division of the fifth cranial nerve. Ocular complications or sequelae arise in approximately one-half of the cases. The epidemic form is caused by an acute infection involving part of the Gasserian ganglion and fifth cranial nerve on one side, and is analogous to herpes zoster occurring elsewhere in the body. Symptomatic herpes zoster is usually unilateral, but, unlike the epidemic variety, may be bilateral. It is associated with toxic, inflammatory, or neoplastic damage implicating the fifth cranial nerve, the Gasserian ganglion, or any of those fibres that constitute the central connections of the nerve. Therefore it may occur at any age. This symptomatic form cannot definitely be diagnosed as such, unless the patient presents evidence of some causal lesion, e.g., syphilis of the basal meninges, or cerebral tumour. In most cases the evidence is sooner or later available, but may remain latent until several months after the herpetic eruption has subsided. The following description is intended to refer chiefly to the epidemic form of the disease.

Most of the sufferers are middle-aged or elderly. The literature does indeed contain instances of the disease occurring in early
childhood, but some of these cases were probably examples of the symptomatic variety, wherein the essential cause of the trouble had not yet become manifest. Preponderance on the part of either sex does not appear to have been proved. One observer will quote a long series of cases in which females are easily outnumbered. Another will find that his experience has been in this sense directly opposite. It seems clear that epidemic herpes zoster ophthalmicus is almost equally common among males and females. The epidemic nature of the disease is shown by the occurrence of a number of cases simultaneously, although it must be far less infectious than most of the zymotic diseases. I do not know any example of ophthalmic zoster visiting two people in the same household. Trousseau, however, saw thoracic zoster in an old woman living with her son, on whose chest a similar eruption arose during his mother’s convalescence. Second attacks are extremely rare. Further support for the use of the term epidemic is provided by the sudden onset, accompanied by fever and prostration.

Clinical Course.—These are the three principal features:

(1) Pain along the course of distribution of the first division of the fifth cranial nerve.

(2) A skin rash appearing about three days later on a portion of the corresponding area of the face or head.

(3) Limitation of the rash to one side.

At the time of onset the characteristic distribution of the neuralgic pain may be masked by symptoms of acute discomfort all over the body. Thus there may be nausea, rigors, generalised headache, and abdominal pain culminating in vomiting. The temperature is nearly always raised. Within a few hours all these accessory symptoms are overshadowed by the distinctive zoster neuralgia. Mild cases are seldom seen, in which sensations merely of numbness and tingling are felt in the areas concerned. More often there is severe burning and throbbing pain shooting up from the forehead towards the back of the scalp, and associated with exquisite tenderness of the skin in those regions. This pain, enduring without intermission, as it often does, for two weeks or more, seriously interferes with sleep, and has been vividly described by numerous writers. Thus an editorial note in the British Medical Journal, 1866, Vol. I, p. 470, says: “... A man need wish his worst enemy no worse week’s or fourteen day’s excitement than an attack of it [Herpes zoster of the head and face] ...” Many of the older patients become dangerously exhausted after long, successive days of uninterrupted agony. I have seen one instance of fatal collapse attributable to this cause.
Jeffries reported the death of an old lady at the end of six weeks' herpetic neuralgia of the head and face.

The skin eruption, which appears several days later, is associated with intense redness and swelling of the affected area, so that it has often been mistaken for erysipelas, a disease whose favourite site is the upper part of the face. The fact that both conditions produce vesicles helps further to explain their confusion with each other. Nevertheless, such an error in diagnosis would be unlikely to be committed by anybody to whom a genuine case of herpes zoster ophthalmicus had once been demonstrated. The extent of the rash is usually proportional to the severity of the attack. Of the three main branches—lacrimal, frontal, and naso-ciliary—into which the first division of the fifth cranial nerve divides, the frontal never escapes, so that some spots always appear over the upper orbital margin, forehead, or scalp. When the forehead eruption has been remarkably severe, I have twice seen it transgress the middle line by more than an inch. This phenomenon presumably depends on overlapping of the fibres from the two different sides, and need imply no essential contradiction of the rule that epidemic herpes zoster ophthalmicus is a unilateral disease.

Rupture of the vesicles occurs soon after the outbreak of the rash. Their liquid contents gradually become dried up to form scabs which, on separating, leave permanent marks in the shape of small, pitted scars. Healing is usually established within three weeks of the original eruption, unless the issue is complicated by sepsis. In many cases the lacrimal and naso-ciliary nerves are involved, and spots may be seen on the skin of the eyelids, or on the side of the nose. Occasionally the conjunctival surface of the lids is attacked. Simultaneous partial involvement of the second division of the fifth nerve has been seen. One of Hutchinson's cases, an elderly man who displayed the rash on his forehead, nose, eyelids, and cheek as far down as the upper lip, disproved that observer's previous statement that the cheek always escapes. Another patient of Hutchinson's, suffering from rightsided zoster in the area of distribution of the fourth dorsal nerve, developed left ophthalmic zoster one day later.

Detailed examination of the eye during the eruptive stage is rendered difficult by tenderness and brawny swelling of the eyelids, more especially of the upper one. Some degree of conjunctivitis is invariably present, and is often aggravated by staphylococcal invasion from the adjacent skin-lesions. In such cases the homolateral preauricular lymph-gland is often enlarged. Whenever the state of the eyelids has allowed close inspection of the eye, I have been able to detect epithelial oedema over the whole surface of the cornea, whether or not the patients were
destined subsequently to develop zoster keratitis as ordinarily defined. I suspect that this sign would be constantly found if it were always possible to make a thorough examination. Corneal sensation is always impaired, if not abolished. The intra-ocular tension in an uncomplicated case is said to be reduced, but the swollen state of the eyelids commonly prevents the examining fingers from gaining any reliable information concerning this feature.

The forementioned eye conditions would appear to be essential elements in the clinical picture. The inconstant ocular complications will be considered afterwards. Hutchinson is often said to have believed that these complications never arise unless the eruption appears on the side of the tip of the nose; furthermore, that they can definitely be foretold whenever a spot appears in that situation. But this opinion, expressed in the first paper that he wrote on the subject, was modified by his later experience, which provided him with opportunities to observe exceptions to his rule. Bowman, Jessop, and others have also reported cases where the eye escaped in spite of spots being present on the tip of the nose, and cases in which severe ocular complications were unaccompanied by a nasal rash. Nevertheless, the so-called Hutchinson rule is a useful rough-and-ready guide, most observers being agreed that subsequent eye trouble is rendered more probable by involvement of the oculo-nasal twig. The true explanation may be as follows: Of the three main branches of the ophthalmic nerve, the frontal is the only one to be constantly implicated in herpes zoster of this region. Often it is the only branch to be so affected. Clinical experience tends to show that ocular complications are more to be feared in those cases where the eruption is most extensive, involving other branches in addition to the frontal one.

During the active stage of ophthalmic zoster the general principles of treatment are rest in bed, sedatives to relieve the pain, light diet, and a bland, oily dressing for the rash. Mr. C. B. Goulden's clinical experience has led him to believe that, under conditions of rest and skilled nursing, the patients are less likely to develop serious ocular complications; and that, if complications are not entirely warded-off, their severity will at least be tempered. Strong, irritant preparations applied to the skin can only do harm. A simple, oily dressing will suffice, and will lessen the liability to deep scarring. In some cases, however, the skin is so tender to the slightest pressure that no dressing will be tolerated. Routine measures of treatment for the conjunctivitis are usually contra-indicated by the condition of the eyelids, which are so swollen and tender that one is reluctant to force them apart for the purpose of irrigation. Moreover, the adjacent skin would
be still further damaged by the repeated soaking of its already excoriated surface. For these reasons it is better to neglect any conjunctival inflammation that exists at the height of the rash. The occasional instillation of oil will reduce the tendency of the lid margins to become stuck together by dried secretion.

Ocular Complications.—The ocular complications now to be considered may arise at any moment during the eruptive stage, but sometimes make their first appearance weeks or months after the rash has subsided, when they might be more correctly described as sequelae. Occasionally they precede the eruption. These are the possible complications:

1. Keratitis.
2. Iridocyclitis.
3. Ocular palsies.
4. Optic neuritis.

Keratitis affects the substantia propria in any of its layers, but hardly ever produces ulceration. Detailed examination is slightly impeded by the oedematous state of the epithelium mentioned above. A typical case shows irregularly shaped opacities situated at various depths in the substance, together with oedematous striae and generalised haziness. Folding of Descemet's membrane can often be detected in cases where the substantia propria is not sufficiently opaque to conceal the posterior layers of the cornea. Paton considers that this folding of Descemet's membrane is probably due to the hypotonia which has often been observed in ophthalmic zoster. In my opinion the existence of deep keratitis offers a far readier explanation thereof. Keratitis disciformis, interstitial keratitis, and other forms of deep keratitis commonly produce folds in this membrane, as a result of swelling and distortion of the hindmost lamellae of the corneal substance. Now, although the most characteristic residual opacity after zoster keratitis is situated in the anterior lamellae, yet it is not these layers that are solely, or even mainly affected during the active stage. Zoster keratitis is, in fact, a deep keratitis, and is therefore apt to produce folding of Descemet's membrane—a phenomenon whose absence may readily be noted in many soft eyes suffering from, e.g., simple detachment of the retina.

The severity and duration of zoster keratitis varies greatly among different patients. Under appropriate treatment by means of a mydriatic it may settle down within a fortnight, but more often drags on for weeks or months in spite of promptly applied remedies. In severe cases the cornea is not uncommonly invaded
by new vessels. Some opacities are always found after an attack. They may occupy any layer of the substantia propria, and may present no special features, but one type is characteristic—a round gray opacity situated in the anterior layers of the substance, and formed by the coalescence of numerous smaller dots. Several of these round gray areas may be found close together, and overlapping at their margins.

Probably the iris never remains perfectly normal throughout an attack of herpes zoster ophthalmicus. The pupil is usually small and sluggish as compared with that of the fellow eye. Spasm of the sphincter, together with vascular congestion and some infiltration of the iris stroma, may account for this condition of the pupil. Sometimes, on the other hand, the pupil of the affected eye is found to be dilated by reason of a partial third cranial nerve palsy. When keratitis supervenes, iridocyclitis is invariably found to some extent, as indeed it is in all forms of deep keratitis. Dots of keratic precipitates can be seen unless the corneal haze is too pronounced. Iridocyclitis may also arise as a complication or sequel in cases that have escaped keratitis. Often it is accompanied by a profuse plastic exudation in the anterior chamber, so that the pupil is prevented from responding to the action of atropine, and the patient is exposed to the risk of secondary glaucoma, either at the time of active inflammation, or in the future, when the exudate will have given rise to obstructive adhesions. The intraocular tension may, on the contrary, be lowered from atrophy of the ciliary processes. In some cases atrophy is sufficiently advanced to lead to phthisis bulbi. Since herpes zoster ophthalmicus exposes every patient to the risk of losing an eye from severe iridocyclitis, whether accompanied or not by keratitis, it would seem worth while to administer an occasional mydriatic drop for a few weeks after the beginning of an attack, especially when we consider that the pupil’s response to the action of atropine is defective, even in cases that have no iridocyclitis. This suggestion does not, however, imply that the worst cases could infallibly be saved by such prophylactic measures.

Ocular palsies not uncommonly occur, involving the third, fourth, or sixth cranial nerves. It is unusual for the whole of the third nerve to be affected at the same time. Often only one branch is involved, e.g., that which supplies the levator palpebrae superioris. During the eruptive stage there is always some ptosis from swelling of the upper lid, so that it is not always possible to diagnose paralysis of the levator with certainty until the rash has begun to decline. The prognosis with regard to these palsies is good, because most of them disappear in less than six weeks, but they do occasionally persist for a much longer time. Browne reports the interesting case of an elderly man who, at the end
of four days' thoracic neuralgia, developed a bilateral herpes zoster rash in the areas supplied by the dorsal nerves III - X. The left upper lid now began to suffer from anaesthesia dolorosa. Eight days later there ensued a partial palsy of the left third cranial nerve, resulting in ptosis and mydriasis. This palsy lasted for a little more than a week, and was not accompanied by any eruption in the areas of fifth cranial nerve distribution.

Optic neuritis is a rare complication. Bowman, Paton, and others have seen cases in which marked secondary optic atrophy was visible in the affected eye after an attack of ophthalmic zoster.

Sequelae.—It has been stated above that keratitis, iridocyclitis, etc., may follow at some considerable time after an attack. Residual opacities of the cornea, phthisis bulbi, and secondary glaucoma have also been discussed. Other sequelae to be mentioned are:

1. Impaired corneal sensation.
2. Scleritis.
3. Patches of atrophy in the iris.

The reason why corneal sensation is recovered in some cases but not in others, is made intelligible by the pathological researches of Head and Campbell, who found that the inflammatory damage sustained by the Gasserian ganglion varied greatly among different patients. In a severe case many of the nerve-cells are completely destroyed from the first, or afterwards become strangled in a mass of organising scar-tissue. A mild attack, however, does not preclude complete recovery of the infected cells. Impaired corneal sensation is in most cases evident for many months after the attack. There are many examples recorded in which sensation had not fully recovered several years later.

Scleritis appears in the form of one or more nodules about two months after the rash has disappeared. Most of the reported instances have occurred in association with iridocyclitis. The nodules are painful and irritable. They usually remain active for several months, and when they fade away their site is marked by a permanent slate-coloured scar.

Patches of atrophy in the iris are an exceedingly characteristic sequel. They are, as we should expect, commoner and more extensive in eyes which have had iridocyclitis, but are often to be found in uncomplicated cases. These patches present the customary atrophic features of thinning and discolouration of the iris stroma.

In addition to these ocular sequelae, an attack of herpes zoster ophthalmicus may be the forerunner of most unpleasant after-pains referred to the skin areas which were attacked by the rash.
These pains may persist for years, and are associated with abolition or impairment of sensibility in the affected skin. Hutchinson believed that older people are particularly subject to this troublesome sequel. One elderly patient of Forget suffered so grievously in this manner that he was incited to suicide.

**Association with Chicken-pox.**—During the last few years attention has frequently been directed to the close connection which exists between herpes zoster and chicken-pox. In hospitals and other institutions the presence of a case of herpes zoster has often been held responsible for an otherwise inexplicable outbreak of the other disease. This association has been so commonly remarked that it can hardly be attributed to a series of coincidences. Moreover, there have been cases reported in which a typical chicken-pox rash and an attack of herpes zoster have assailed the same patient within a few hours. The prevailing opinion is that both conditions are due to infection by closely-related ultra-microscopic viruses. That the viruses are not identical is shown by the failure of an attack of chicken-pox to confer immunity from herpes zoster. Mayou had two cases in which influenza heralded a herpetic eruption, but, in view of the wide prevalence of influenza in this country, it would be necessary to collate an enormous number of similar instances before any affinity could be proved between the two maladies.

**Symptomatic herpes.**—Symptomatic herpes zoster ophthalmicus may be the result of cerebral tumour, tabes, or syphilitic basal meningitis. It may also be caused by drugs, among which arsenic is apparently the most noxious to the Gasserian ganglion. Hutchinson reported a case of herpes frontalis in a middle-aged woman who had been using Fowler’s solution (liquor arsenicalis) as a remedy for psoriasis. Bruere found some form of neuropathic keratitis in a syphilitic patient who had undergone salvarsan injections. A man under the care of Hegner sustained sloughing of the cornea after two injections of neo-salvarsan for syphilis. Pearce published interesting notes of a child, aged seven, who developed ophthalmic zoster after a course of Fowler’s solution employed in the treatment of chorea. The most likely interpretation seemed to be that the child was afflicted with symptomatic herpes zoster due to arsenical poisoning of the Gasserian ganglion. In the same ward, however, another child developed chicken-pox three days later. This second child had remained in the ward for the preceding thirty days, during which time there had been no other visitation of chicken-pox or herpes zoster, apart from that of the above-mentioned first child; who may therefore be regarded as a probable case of epidemic herpes zoster, not imputable to the ingestion of arsenic.
Pathology.—More than seventy years ago von Baerensprung expressed the opinion that herpes zoster should be ascribed to lesions of the nervous system. He found support for this opinion in a post-mortem examination which he was soon afterwards enabled to make on a suitable case. Weidner in 1870 found pathological changes in the cells and connective tissue of the Gasserian ganglion during the autopsy performed on a man who had suffered from herpes zoster ophthalmicus five years previously. In the following year Wyss noted softening and congestion of the ganglion; haemorrhages chiefly affecting the cells governing the first division of the nerve; and histological changes in the nerve branches from the ophthalmic division, as contrasted with offshoots of the second and third divisions investigated as controls. The work of Head and Campbell was still more conclusive, consisting, as it did, of exhaustive observations at all stages in a series of cases. They found ganglionic haemorrhages in recent cases, sclerosis in old cases, and destruction of nerve-cells in proportion to the severity of the infection. On sifting the clinical records of more than four hundred cases they could discover only four examples of a patient being attacked twice.

Illustrative Cases.—The following cases furnish examples of the more important ocular complications:

Case I, a woman, aged 51 years, was confined to bed for two months at the beginning of 1931 with an attack of left herpes zoster ophthalmicus in which the rash involved the forehead, lower lid, and side of the nose. Severe kerato-irido-cyclitis arose as a complication. Eighteen months later the cornea displayed numerous large, superficial new vessels, and a great deal of dense opacity affecting all the layers. The pupil was completely immobile as a result of extensive posterior synechiae. Tension was raised, and the eye was quite blind. One interesting feature in this case was the existence of several slate-coloured scleral scars, two of which had occasioned so much thinning of the sclera as to produce localised staphylomata, resembling small, dark-blue berries.

Case II, a woman, aged 47 years, who came up to hospital complaining of pain in the right eye for the last two days. Her attack of herpes zoster had begun nearly a fortnight previously, so that the rash, which had alighted on the forehead and side of the nose, was in process of settling down. On examination the epithelium of the right cornea was uniformly bedewed; there was faint, generalised haze of the substantia propria; and numerous keratic precipitates were seen on the posterior surface. The pupil was small and inactive. The iris showed loss of pattern, lack of lustre, and vascular engorgement. Several coagulated flakes were adhering to the anterior lens capsule. The pupil responded well
to the repeated instillation of atropine, there being only one un-
resolved posterior synechia at the end of two hours. When she 
attended again a week later, having in the meantime used atropine 
drops thrice daily, that last synechia had broken free, and the 
iridocyclitis was progressing favourably. Since her previous visit 
she had developed a right sixth cranial nerve palsy; but, the right 
eye having been covered, no diplopia had been appreciated. This 
palsy cleared away in rather less than a month. The outcome of 
the iridocyclitis was also favourable, corrected vision of 6/9 
being recovered by the right eye at the end of the attack.

Case III, a man, aged 63 years, came to the hospital suffering 
from left herpes zoster ophthalmicus. For the past eight days he 
had felt sharp neuralgic pains, and the characteristic rash appeared 
three days ago. Herpetic sores, associated with redness and 
swelling of the skin, occupied the forehead and part of the lower 
lid margin. Sensation to light touch was lacking on the eyelids. 
The corneal epithelium was oedematous, as expressed by the 
presence of many minute vesicles of inconstant size. A few cracks 
and striae were noticed in the deeper layers of the substantia 
propria. Visible particles were circulating in the anterior chamber. 
The patient was put to bed. During the next few days the rash 
developed further, spots appearing at the margin of the upper lid, 
and down the left side of the nose; but he escaped serious eye 
trouble. The keratitis was mild, so that when he was seen a few 
weeks after his discharge from hospital, there were merely a few 
small, irregular opacities situated in various layers of the substantia 
propria.

Case IV was one of symptomatic zoster. A girl, aged 17 years, 
undergoing treatment in hospital for juvenile tabes, developed 
the typical rash over the inner half of her right upper orbital 
margin, accompanied by acute muco-purulent conjunctivitis. At 
this stage the cornea was perfectly clear. On the following day 
three small, distinct blebs, visible to the naked eye, and resembling 
those that appear in cases of herpes febrilis, were found on the 
cornea. The ulcers resulting from the rupture of these vesicles 
healed quickly. During the next three days the characteristic 
picture of zoster keratitis was produced; all layers of the corneal 
substance showing general haziness interspersed with zones of 
denser opacity, and vision being reduced to finger-counting. After 
a weeks treatment with atropine the cornea cleared enough to 
allow keratic precipitates to be seen on its posterior surface. 
Corrected vision improved to 6/18 within a month of the onset. 
The only residual signs in the cornea were a few scattered, irregular 
areas of opacity, affecting chiefly the middle layers of the sub-
stantia propria; also some shrunken precipitates. There was no 
vascularisation of the cornea.
The chief point of interest in this case, as it seems to me in retrospect, was the appearance of blebs on the surface of the cornea before typical zoster keratitis arose. It has been already mentioned that epithelial bedewing is a common, and possibly a constant feature in the cornea of patients suffering from epidemic herpes zoster ophthalmicus, quite apart from the consideration whether or not keratitis is going to complicate the picture; but I have never seen actual blebs visible to the naked eye in an epidemic case. I do not know whether blebs are a common finding in symptomatic cases, like that of the girl described above, but their occurrence may perhaps be regarded as forming a stage in the transition between herpes zoster and herpes febrilis, between which diseases border-line cases sometimes occur, not conforming to the usual classification.

I wish to express my gratitude to the Moorfields surgeons for allowing me access to their clinical material. Especially I wish to thank my teachers, Sir John Parsons, and Mr. C. B. Goulden, for their instruction and guidance.

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