pain. In cases of herpes zoster the same type of lesion is produced as a result of disturbance of the innervation of the affected part. The virus of herpes simplex is the causative agent not only of herpes on the lips or nostrils, but also of herpes genitalis and cornealis, herpetic (aphthous, Vincent's, or ulcerative) stomatitis, eczema herpeticum (a type of Kaposi's varicelliform eruption), and meningo-encephalitis. The last three conditions do not recur, but many individuals are subject throughout life to recurrent attacks of herpes around the lips and nose, of the genitalia, or of the cornea, and these develop in response to non-specific stimuli, such as sunburn, fever, or trauma and not through exposure to another source of herpes virus. In women, recurrence is often associated with the menstrual periods.

The vesicle fluid from herpes simplex lesions affecting the face, genitalia, or cornea may produce herpetic vesicles when inoculated into the skin or keratitis when applied to the conjunctiva of the rabbit, and it is therefore usually considered that all simple herpetic lesions are due to the same virus. There is, however, some doubt whether a virus can be demonstrated in all herpetic simplex lesions. According to Stoker, " there is no doubt that the virus is present during each of these recurrent attacks, because it can invariably be isolated in the early stages." It has been suggested (Burnet and Williams, 1939) that in recurrent cases herpetic infection occurs in childhood and persists throughout life. This is based on serological and skin tests, the sera of most adults containing antibodies against the virus. It is supposed that the virus remains within the epidermal cells, dividing with them, and normally causing no damage. A number of non-specific stimuli which lead to cell breakdown may release the virus particles.

Stalder and Zurukzoglu (1936) showed, however, that areas of facial skin subject to recurrent herpes no longer developed the disease if transplanted to another part of the body. Yet a recurrent attack usually occurs in roughly the same site. Because of this some favour the central nervous system, dorsal root ganglia, or cutaneous nerve endings as the permanent home of the virus. In this respect it will be recalled that the lesions of herpes zoster, which are due to infection with the herpetic zoster virus, are identical pathologically with those of herpes simplex, but the causative lesion for the skin change is found in the posterior nerve root ganglia (Lewis, 1927). It is thus by no means certain that the lesions of herpes simplex are always due to, or contain, a virus affecting the skin. It seems possible that this type of tissue reaction in the skin may result from various forms of irritation, of which the herpes simplex virus is one example ; that even in recurrent cases of herpes simplex local irritation plays a part in causing the recurrence, and that, as in cases of herpes zoster, disturbance of local nerve fibres may be a factor in causing this.

Whatever the explanation of recurrent herpes simplex, it seems that the appearance of the original lesion may predispose to malignant change in elderly subjects. Malignant change following herpes simplex may simply be an example of what may occur, especially in elderly subjects, at the site of any chronic irritation or inflammation, such as eczema or psoriasis, and not the specific result of virus infection. On the other hand, if all, and particularly recurrent, cases of herpes simplex are due to local infection with herpes simplex virus, and since the subjects may exhibit abnormal sensitivity to sunlight as do tar-workers and those subject to *x* rays or arsenical dermatitis and xeroderma pigmentosa, it may be that infection by the virus, which is widespread, is an important cause of malignant change. Since the buccal mucosa and the skin of the genitalia and other tissues may also be infected by herpes simplex there is a possibility that in some cases in these tissues, too, the infection may be related to the later appearance of malignancy.

Summary

Six cases of herpes simplex of the lips in old people followed by the development of squamous carcinoma six weeks to five years afterwards are described. The significance of the observation in relation to the virus theory of cancer causation is briefly considered.

The above observations were made while holding a Gordon Jacob Research Fellowship at the Royal Marsden Hospital. I should like to express my thanks to the Medical Committee of the hospital for permission to publish the brief case histories.

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MOTOR COMPLICATIONS OF HERPES ZOSTER

BY

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The occasional appearance of muscular weakness in association with herpes zoster has been recorded in numerous papers since Broadbent (1866) described a patient with extensive weakness of an arm preceded by a herpetic eruption. Head (1899) quotes as examples an eruption in the territory of the first dorsal root with severe hand weakness, ophthalmic herpes with oculomotor palsy, and facial palsy with an eruption in the second and third cervical area. Taylor (1896) drew attention to the occasional presence of weakness of the abdominal muscles with herpes of the trunk, and Ford (1944) has suggested that localized weakness of intercostal or abdominal muscles may be quite common, but may often pass unnoticed in the absence of disability. Other cases of lower motor neurone paralysis have been described by Joffroy (1882), Waller (1885), Buzzard (1902), and more recently by Cornil (1930), Barham-Carter and Dunlop (1941), Taterka and O'Sullivan (1943), Parkinson (1948), Scobey (1949), and McIntyre (1951).

Evidence of direct involvement of the central nervous system was first observed by Brissaud (1896) and has since been described by Lhermitte and Nicolas (1924), Lhermitte and Vermes (1930), Worster-Drought and McMenemey (1933–4), and Whitty and Cooke (1949). Following the observations of Lhermitte and Nicolas of segmental changes in the spinal cord at the affected level, it has been suggested that the root entry zone of the cord is often if not always affected, and that many of the anomalous clinical findings in herpes zoster can best be explained by regarding the condition as a disease of the central nervous system in addition to the posterior root ganglion.

Denny-Brown, Adams, and Fitzgerald (1944) examined at necropsy the nervous system of a patient who had had the " Ramsey Hunt syndrome " and found no significant change in the geniculate ganglion. It has become well known since Ramsey Hunt's (1907) original description that wide discrepancies occur from patient to patient in the distribution of the eruption in relation to the facial palsy. Denny-Brown *et al.* postulated that herpes zoster may therefore be primarily a unilateral segmental polio-

myelitis in which the brunt of damage falls upon the dorsal part of the spinal cord, a view previously put forward by Wohlwill (1924) and since supported by most other writers.

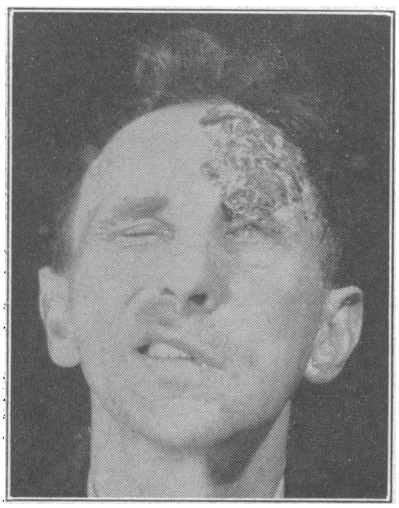
The cases described below show the considerable variation that occurs in the site and type of paralysis and the anatomical discrepancies between the cutaneous and nervous manifestations of the disease.

Herpes Involving Cranial Nerves

Case 1.—A man aged 60 began to have severe pain in the left side of the forehead on December 1, 1951. Two days later an extensive herpetic eruption appeared in the territory of the first and second divisions of the left trigeminal nerve. Twenty-four hours later he awoke to find the left eye closed, and was subsequently found to have a complete paralysis of the left third nerve. During the next three months he recovered from the ocular palsy with the exception of a mild degree of ptosis. The area of the skin supplied by the ophthalmic division of the left fifth nerve was anaesthetic and has remained so.

Case 2.—A woman aged 65 developed severe pain on the left side of the face on November 5, 1954, and a vesicular rash appeared in the territory of the second and third divisions of the left trigeminal nerve, on the left side of the tongue, and on the left side of the neck from C 2 to C 4. Two weeks later a complete left facial palsy appeared, with loss of sense of taste on the left side of the tongue. Recovery was complete in six months, without residual neuralgia.

Case 3.—In November, 1954, a man aged 62 developed a very severe left-sided ophthalmic herpes with corneal ulceration. Two weeks later a complete left facial palsy appeared and was associated with a generalized herpetic eruption on the trunk and limbs. Taste was lost on the affected side. (See Fig.) Complete motor recovery took place within two months.



Case 3. Photograph showing complete left facial palsy and extensive herpetic eruption.

Case 4.—A 70-year-old man experienced pain in the left mastoid region for 10 days. This was followed by a herpetic rash on the left pinna and by vesicles on the left faucial pillar. Almost simultaneously a complete left facial palsy appeared and was associated with a moderately severe left-sided nerve deafness. The latter remained permanently, but the facial palsy had recovered within three months.

Case 5.—A woman aged 81 developed a very extensive vesicular eruption extending from the left side of the vertex over the trigeminal area, the left side of the neck, and the left shoulder. A week later a complete left facial paralysis occurred with loss of taste. This was still present four months later, when she also had severe and diffuse neuralgic pain.

Case 6.—A man aged 45 developed chicken-pox on May 15, 1955. Three weeks later, when the last crust had almost disappeared, he developed a complete left facial palsy without impairment of sense of taste. Recovery was complete in three weeks.

Herpes with Flaccid Limb Paralysis

Case 7.—A woman aged 55 was first seen in August, 1954, three weeks after the onset of a severe herpetic eruption extending from the region of the right deltoid muscle, along the outer side of the arm to the radial side of the forearm. Simultaneous with the appearance of the rash, severe weakness of the hand and forearm was noticed. Examination showed complete paralysis of all the intrinsic muscles of the right hand, with severe weakness of the wrist and finger flexors. There was no weakness of the extensor muscles or of any muscles acting on the elbow or shoulder. Moderate recovery took place in about 18 months, leaving quite severe residual weakness and wasting of the interosseous muscles.

Case 8.—In September, 1951, a woman aged 57 had an extensive eruption in the distribution of C 7–8 and T 1 on the left side. At the same time the right trapezius, deltoid, pectoral, spinatus, and serratus muscles became completely paralysed. All the tendon reflexes in the right arm were abolished. There was complete cutaneous anaesthesia in the C 6–7 area. Recovery was complete in five months.

Case 9.—In July, 1951, a 76-year-old woman had a moderately severe herpetic rash in the left C 6 area, with moderate pain. This healed, with some scarring, in about six weeks. Two weeks later severe lancinating pain was experienced throughout the affected arm and was rapidly followed by complete paralysis of the whole arm. Examination showed a flicker of contraction in the triceps and extensor digitorum communis only; all other muscles acting on the left upper limb were paralysed; the tendon reflexes were absent; and there were severe impairment of cutaneous sensation corresponding to C 8–T 1 and loss of postural sensibility in the fingers. Recovery was very slow, but within nine months was complete in the shoulder muscles, biceps, and triceps. Weak grip returned in one year, but the hand remained very weak, with severe wasting of intrinsic muscles. Normal sensation returned within six months.

Case 10.—Two weeks after being exposed to chicken-pox a woman aged 23 developed a very severe and extensive herpetic eruption extending from C 2 to D 2 on the left side. Simultaneously she developed moderate weakness of the left deltoid, biceps, and triceps muscles. The biceps and triceps reflexes were lost. The next day a generalized herpetic eruption appeared and was associated with headache, fever, confusion, and slight nuchal rigidity. Recovery was uneventful and was complete within two months.

Case 11.—In October, 1954, a woman aged 60 developed severe pain in the right shoulder followed after four days by an eruption in the area C 2–6 on the right side. Ten days later complete paralysis of all muscles acting on the right shoulder and elbow developed, together with moderate weakness of the right hand. When examined four weeks from the onset there was minimal herpetic scarring over the neck and shoulder. Good grip was present, but she had severe wrist-drop and all other muscles in the right upper limb were paralysed. All the tendon reflexes in the arm were lost and there was dulling to perception of pin-prick over C 5–6. Recovery was progressive over 18 months, and after two years there was only minimal weakness in abduction of the shoulder.

Herpes with Involvement of Spinal Tracts

Case 12.—A married woman aged 38 noted the sudden onset in May, 1956, of pain in the right side of the chest associated with a weakness of the right lower limb. At that time a rash appeared in the painful area, at first petechial, later vesicular. About 24 hours later she complained of numbness of the left leg and left side of the abdomen. When examined three weeks from the onset there was evidence of a healing and quite slight herpetic rash corresponding to D 6–7 on the right side. She had a mild spastic

weakness of the right lower limb with an extensor plantar response, and impairment of superficial sensation on the left side below D 7. Three months later full motor recovery had taken place, but there was still some subjective alteration of sensation in the left lower limb.

Case 13.—A married woman aged 35 experienced the sudden onset of severe pain between her shoulders, radiating to the right breast. Twenty-four hours later a rash of moderate severity appeared in the distribution of D 5 on the right. During the following week she noticed an increasing weakness of the right leg, which subsequently started to improve. When examined two weeks from the onset a fairly extensive eruption, more marked posteriorly, was seen. The right abdominal reflexes were absent and there was a moderate spastic weakness of the right lower limb. Sensation was unaffected. Recovery was complete within two months.

Case 14.—A man aged 63 was first seen in March, 1950, with a history of a very severe attack of herpes affecting D 3–4 on the right side six weeks previously. Four weeks from the onset he complained of sudden pain on the inner border of the right arm, radiating to the fifth finger. This was followed rapidly by weakness of the right hand and of both lower limbs. Objectively there was severe weakness of the intrinsic muscles of the right hand, together with spastic weakness of the legs, more marked on the right side. Superficial sensation was impaired in the D 1 area on the right. Two weeks later definite wasting was present in the affected hand. Two months later the lower limbs were normal, there was still a minor degree of wasting and weakness in the right hand, and sensation was normal.

Discussion

During the period 1950–6 I have seen, in addition to the cases described above, nine other instances of facial palsy associated with herpetic eruption on the pinna, face, or palate, and in the same period 76 patients with "Bell's palsy" have been examined. It is perhaps justifiable to speculate whether some of the latter may have been instances of herpes sine herpete. Aitken and Brain (1933) carried out complement-fixation tests for herpes and obtained positive results in 9 out of 9 instances of the Ramsey Hunt syndrome and in 4 out of 22 instances of Bell's palsy. It would therefore seem at least possible that a small proportion of the cases of Bell's palsy may be due to herpes zoster, and in this connexion the occasional occurrence of very severe pain in the mastoid and upper cervical region prior to the paralysis may be a significant pointer.

Clinical Findings in Seven Cases of Neuralgic Amyotrophy

Case	Age and Sex	Pain Site	Duration of Pain Before Weakness	Weakness	Reflexes	Sensory Loss	Recovery
A	53 F	Severe, left C 5–6	7 days	C 5–7 (severe)	Absent left arm	None	Almost complete in 6 months
B	39 F	Severe, left C 5–7	4 ,,	Deltoid, biceps, triceps (moderate)	Biceps, triceps, (absent)	C 7	Complete in 4 months
C	57 M	Severe, right shoulder and D 1	5 ,,	D 1 muscles	Normal	D 1	Complete in 3 months
D	33 M	Severe, left shoulder and upper arm	10 ,,	Serratus magnus. Extensors of wrist and fingers	,,	C 7	None in 2 years
E	46 M	Moderate, right shoulder and arm	2 ,,	D 1 muscles (slight)	,,	D 1	Complete in 3 months
F	65 M	Severe, left side of neck, left shoulder and arm	Hours	C 5–6 muscles	Biceps absent	C 5–6	Almost complete in 9 months
G	45 M	Moderately severe, interscapular and left arm	2 days	C 5–D 1 (slight)	Normal	D 1	Complete in 3 months

On the same basis it is of interest to compare the clinical manifestations of paralytic zoster in the limbs with the findings in neuralgic amyotrophy (Turner and Parsonage, 1948). The clinical findings in seven patients suffering from this condition are set out in the Table. It will be seen that in each instance the pattern of the history and findings follows very closely that of herpetic paralysis in the upper limbs, differing clinically only in the absence of the rash. It would seem likely that neuralgic amyotrophy may, in some cases at least, bear a similar relationship to herpes as facial palsy. In general, it may be said that motor weakness or paralysis is a not uncommon accompaniment of herpes zoster and that the prognosis is as a rule quite good, with complete or almost complete return of muscle function.

The anatomical relationships of the eruption and the paralysis are by no means constant, and frequently do not coincide—a feature which supports very strongly the contention that herpes is essentially a disease of the spinal cord or brain stem and not a radicular disorder as was originally supposed. Case 6 is unusual in that facial palsy appeared to be related to chicken-pox.

Summary

Fourteen cases are described in which the patients suffered paralysis as a result of herpes zoster infection.

The distribution of the paralysis varies greatly but corresponds approximately to the distribution of the rash.

It is now generally accepted that herpes is essentially an affection of the central nervous system rather than of the dorsal root ganglia, thus making the not infrequent appearance of motor symptoms more logical.

It is suggested that a certain number of patients with "Bell's palsy" may, in fact, be suffering from the Ramsey Hunt syndrome, and the points of similarity between zoster paralysis in the upper limbs and the clinical condition described as neuralgic amyotrophy are such that there may be grounds for considering the two conditions as aetiologically similar.

The prognosis in zoster paralysis is on the whole good, but the incidence of recovery of facial paralysis due to this cause is not so satisfactory as in true Bell's palsy. Recovery of paralysed limbs is usually nearly complete.

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