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A CLINICAL STUDY ON HERPES ZOSTER.

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FOREMOST in the rank of diseases affecting the skin, which may with measurable propriety be attributed to the influence of the nervous system, stands herpes, in its various forms and phases, and, central in the entire group, herpes zoster, zona, or shingles is recognized as intimately associated with direct lesions found *post-mortem* in the nerve elements related to the portions of skin affected. I will not do violence to the knowledge or experience of my readers by entering either into the ordinary clinical history of, or the microscopical conditions observed in this interesting disease, which are familiar to all, but will at once proceed with the history of a case of herpes zoster, which exhibits certain interesting and unusual features, and which has given rise to the thoughts herewith presented. I will reserve for another occasion a discussion of the varieties of herpes and their relations to each other.

I may premise that perhaps the most interesting feature, to many, in the case presented, is the history of the large glandular swelling in the neck on the same side as the herpes, and its rapid and complete disappearance under the internal use of arsenic. For the notes of this portion I am indebted to my friend, Dr. V. P. Gibney, under whose care the patient was at the time, and who kindly referred him to me on the appearance of the skin lesions.

John M., aged 73, on September 3, 1875, presented an extremely emaciated appearance, and exhibited an enormous tumour, located in the right cervical region anteriorly, extending from the angle of the jaw downwards, overlapping the clavicle; laterally it reached from the median line (at the pomum Adami) to within an inch or so of the acromion process. It was hard to the feel, the integumental covering was markedly discoloured, and the veins running through it large and tortuous.

The history was that it began almost imperceptibly, no cause being known, and was of comparatively recent origin; he was living in a damp basement, and the hygienic surroundings were lamentable. The case was sent to Dr. Frank Hamilton, who considered it a malignant growth, inclining strongly towards the diagnosis of "lympho-sarcoma." Removal was contra-indicated, he thought, by the age of the patient (over 70), his wretched cachexia, and the unfavourable habitation. It was agreed to make use of arsenic internally, and a change of residence was urged. He

received the liquor potassæ arsenitis, five drops thrice daily. On October 18th, six weeks and a half later, he was seen for the second time, and the change in his condition was so great that he was hardly recognized by Dr. Gibney. The tumour was at least three-quarters smaller, the general health good, and the old man seemed rejuvenated. He had taken the Fowler's solution regularly, and had recently succeeded in moving out of the basement to a floor above ground. The arsenic was ordered to be continued, and seven weeks later, December 8th, he again called and stated that the tumour had been gone for six weeks, and that he had discontinued the use of the arsenic since Nov. 1. It was then difficult to detect even a trace of the tumour. At this visit he called attention to the herpes zoster occupying the right arm, and was recommended to my care.

I find on my notes of the case that he appeared to be at that time rather uncommonly active and well preserved for one of his years, and that very careful examination failed to detect any tumour on its former site, but that there appeared to be a very slight thickening over the extent, perhaps, of two inches just about the centre of the space between the ear and the acromion process of the right side; this gave rather the feeling of a fatty deposit just beneath the skin, but not of any very great thickness.

The arm of that side (right) was the seat of a very abundant and rather peculiarly arranged eruption of herpes zoster. The chest, front and rear, was entirely free from eruption, there being not even any red or tender spots, sometimes the evidence of aborted eruptions—the surface of the thorax was healthy. The eruption began at the back of the shoulder, but quite low down, at least an inch and a half below the end of the humerus, and at about the same point, or a little lower down, on the anterior aspect of the arm. The groups here and elsewhere were pretty thickly set, and the inflammatory action was severe, as the vesicles here and also on the arm were large and flat, and many of them had run together, forming large, flat, bullous masses. The eruption wound around the arm, from behind forwards, in a band of about two inches in width, following closely the course of the cutaneous branch of the musculo-spiral nerve. Passing thus around from the back to the front of the arm, the lower portion of the upper arm, and the entire anterior and outer aspect of the forearm were covered with two or three bands of vesicles, irregularly traced and often touching, so that about one-third of the entire circumference of the limb was covered by the eruption.

Upon the hand the disease occupied also the radial aspect and extended down even to the tips of the thumb and forefinger; the pain in the thumb was so great as to keep the patient from sleeping. The eruption appeared to be in about the fourth or fifth day, and the clinical history corresponded to this. The patient was given phosphide of zinc with nux vomica, and did well; but the further history of the case does not concern us at present.

A careful study of the distribution of this eruption as here recorded, in its relations to the distribution of the cutaneous nerves of the part, renders the conclusions inevitable that there must be some connection between the two. I am aware, of course, that the observation of a relation of the location and arrangement of the skin lesions of herpes zoster to nerve distribution is no new matter, but the observations in regard to this, if I mistake not, have hitherto been drawn largely, if not entirely, from the

distribution of the eruption on the chest, abdomen, and head, where the nerve tracts are more evident. In tracing it in this instance on the arm it is with the further view of seeking an etiological factor in the case before us, and of assisting thereby in a study of the etiology of the disease.

A comparison, then, of the distribution of the eruption with that of the cutaneous nerves, as given by Gray and Sappey, shows that the lesions were entirely confined to the regions innervated by the circumflex, musculo-spiral, musculo-cutaneous (or external cutaneous), median, and radial nerves. Thus the integument of the upper part of the arm, front and rear, up to within a short distance of the head of the humerus, is supplied by the circumflex, in its anterior and posterior branches, over which were groups of vesicles; a band of vesicles followed directly the course of the musculo-spiral nerve, twisting around from behind forwards; the mass of the eruption on the arm and forearm occupied the tract of the external cutaneous nerve along the anterior or radial aspect of the limb, even on to the thumb, which receives cutaneous filaments from this nerve; finally, the radial nerve sends branches to the skin of the back of the thumb and forefinger, and the median nerve to the inner surfaces of the same, all of which parts were also sprinkled with vesicles. These latter parts were the seat of the most pain, which was here very severe.

Tracing now these nerves to their origin, we find the musculo-spiral (from which the radial nerve is given off) and the circumflex nerves coming from the posterior cord of the brachial plexus, and the musculo-cutaneous (or external cutaneous), together with the median nerve, is formed from the outer cord (the median receiving also a branch from the inner cord). These two cords of the brachial plexus, the posterior and outer, are further found to be composed mainly of the fibres of the *upper of the two primary cords*, of the plexus (although the posterior cord receives also a branch from lower main cord); finally, this *upper* main cord is seen to be made up of the 5th, 6th, and 7th cervical nerves, the lower main cord being formed from the 8th cervical and 1st dorsal. Now there was no eruption upon the course of the nerves which are derived wholly from the *lower* main cord, the ulnar, and the internal cutaneous, and we trace, therefore, the eruption in this case to the *upper* of the two main primary cords of the brachial plexus, which we have found to be composed wholly of the 5th, 6th, and 7th cervical nerves (with a small fasciculus from the 4th cervical). Thus we are enabled to locate the nerve lesion somewhere about these large trunks or in the main cervical nerves, namely, the 5th, 6th, and 7th of the right side.

Turning now to the tumour which had occupied this patient's neck, on the same right side, we find that it extended from the angle of the jaw downward, overlapping the clavicle; laterally it reached from the median line to within one inch of the acromion process. It was hard to the feel, and seemed lobulated, the skin was tense over it. There can be little

oubt from the description and history of this tumour that it was connected in some way with the lymphatics; indeed, the opinion of Dr. Frank Hamilton was probably correct, that it was a lympho-sarcoma. I am the more strongly inclined to this opinion from the report of four similar cases by Tholen,[1] three of which, like this, were successfully treated by arsenic internally, in a manner previously employed by Billroth in two cases. Two of Tholen's cases resembled mine very closely; in the first one the tumour in the neck was so large as to interfere with the movements of the jaw. After six months' treatment with Fowler's solution, in from three to five drop doses, with occasional hypodermic injection of ten drops of the same into the tumour, it had entirely disappeared, and there was no return after two years. The second case was treated similarly, and in five months regained, nearly, its normal contour. In the third case a large bunch of glands in the supra-clavicular and axillary region yielded to arsenic at the end of two weeks, and subsequently disappeared entirely. Tholen states that benign lymphatic tumours in the neck treated in this way were not altered.

Now the deeper lymphatics are in very intimate relation with the deeper vessels and nerves, and those in the neck, which appeared to be most implicated are in very close proximity to the cervical nerves, especially the 5th, 6th, and 7th, which, as we have seen, are the ones supplying the parts to which the eruption of zoster was distributed; and the whole tumour, further, overlapped and pressed upon the upper part of the brachial plexus. I would, therefore, advance the opinion that pressure upon these, or alteration in some manner, or their irritation by the tumour, was the cause of the subsequent development of the zoster upon the arm.[2]

In studying the anatomical relations of the disease in this case, it first occurred to me quite strongly that the cause might be a disturbance of the sympathetic nerve, which sends communicating branches to the brachial plexus, as the middle and lower cervical ganglia of the sympathetic are situated just where pressure could be exerted by the tumour, but reflexion has made me exclude this element for reasons which will appear later, mainly, however, from the fact that the eruption of zoster has hitherto been conclusively proven to be in relation with the spinal nerves, and as they are also in a situation to be injured by the tumour in this case, they alone must be chargeable etiologically.

It can, of course, be objected that the eruption of zona did not occur

[1] Arch. für Klin. Chirurg. vol. xvii. Practitioner, Oct. 1875, p. 298.

[2] Lest it should occur to any that the herpes was *due to the arsenic* which this patient had been taking, as some writers have suggested, reporting cases where zona has appeared while using this drug, I would remind them of the far larger number of cases of shingles in patients who have never taken arsenic, and would say that my patient could hardly be considered to be under its influence, as he had taken none for full five weeks previous to the development of this eruption.

until the tumour had undergone absorption, and that, therefore, the latter could have had no effect in producing it. But it is quite possible that the active and rapid process of absorption of so large a tumour, for it had very largely disappeared after forty-five days' treatment, may have induced inflammatory changes in the parts which had formerly been compressed by it—the step between the absorptive process in a new growth and active inflammation is shorter than we are wont to realize.

Most of the observations heretofore published in regard to the etiology and pathological changes in zona have pointed to inflammation of the spinal nerves *near their origin*, and to inflammation of the *spinal ganglia*, and of the Casserian ganglion in cases of ophthalmic herpes, so that the ganglia have come to be looked upon as the *primary* seat of disease in this affection. But that this is but a single point from which to view the pathology of this interesting eruption is, I think, very evident upon study, to make which clear I will briefly allude to some facts to which I called attention, and some references which I quoted in an article some time since,[1] on "The relations of the nervous system to diseases of the skin."

Danielsen found the sixth left intercostal nerve, in thoracic shingles, swollen and reddened by a firm infiltration of the neurilemma, extending largely to the cutaneous branches of the nerve; the medullary portion was normal. Bärensprung found the intercostal nerves thickened and injected, and the same general condition has been noted by several other observers; and Haight gives a drawing of a microscopical section of a nerve in herpes zoster showing cell proliferation in and around the neurilemma, the nerves swollen, the medullary substance softened, and the axis cylinder eccentrically displaced. Charcot and Cotard found neuritis of the *cervical plexus* and corresponding ganglia of the posterior roots in a case of zona of the neck.

While, therefore, a number of post-mortem examinations of patients with ophthalmic herpes have demonstrated that the Casserian ganglion is in a state of inflammation, is of a grayish-red colour and succulent, and while in some reports concerning zoster in other regions the spinal ganglia are stated to have been inflamed, I would at the present time direct attention rather away from the ganglia to the nerves themselves, which many, if not all, the examinations have likewise shown to be the seat of inflammatory changes between the ganglia and the diseased skin; the anatomical proximity may, perhaps, in the case of ophthalmic herpes, account for the more frequent involvement of the Casserian ganglion. The weight of evidence seems to me to point to the cause of herpes zoster in a general neuritis

[1] Archives of Electrology and Neurology, Nov. 1874, and May, 1875. Where other references are not given the facts are quoted from this article and the references may be found in it.

rather than in a primary inflammation of the ganglia,[1] as the following facts show: 1. In cases such as that of Dr. Weir Mitchell's,[2] where severe brachial neuralgia is accompanied by herpetic eruptions, sections of the nerves which were performed for the neuralgia have shown them to have undergone certain definite changes; thus in the particular case referred to by Dr. Mitchell, "In very few of the rings of the secondary fasciculi could the axis cylinder be recognized, even with high powers, the individual nerve fibres being no longer clearly defined, but presenting a confused mass of concentric rings." 2. Cases are reported where other neural affections have accompanied, preceded, or followed herpes zoster in a manner which leaves little doubt that the eruption on the skin was closely connected with the other diseases. Thus, in two cases of shingles affecting the arm, Mr. Paget found the neuralgia to continue after the attack, and with it the fingers exhibited in a well-marked degree the features seen after an injury of the nerve, they became thin, tapering, smooth, hairless, glossy, pink, and blotched; in another case by the same gentleman necrosis and separation of a part of the jaw followed herpes of the right superior maxillary nerve. A number of instances are on record where paralysis has accompanied herpes zoster, affecting the muscles supplied by the nerves whose cutaneous branches innervated the affected skin. 3. Eruptions of herpes have been noted as following central nerve lesions, as after contusion of the vertebral column, in cancer of the vertebra, and in a case of pulmonary phthisis, with carious vertebra, where there was a collection of pus reaching into the sheaths of the spinal nerves; it has also been noted after fracture of the base of the cranium. Zoster has likewise been reported as occurring in connection with certain idiopathic diseases of the nerve centres, as chronic spinal meningitis, cerebro-spinal meningitis, locomotor ataxia, and apoplexy. 4th, and finally, zona has been frequently observed to follow very shortly after surgical operations, as M. Verneuil has particularly noted, and as has been well shown recently in a thesis by M. Picaud.[3]

I do not intend to question the fact that herpes zoster has to do with the sensitive nerves, whose fibres are ultimately gathered together and form the posterior roots of the spinal nerves, upon which are developed the ganglia, but only to indicate the improbability of a *primary* inflammation of the ganglion as a cause of zoster, unless, indeed, as before suggested, the ganglion becomes inflamed secondary to a neuritis (and this

[1] It will be observed that I use the term "*primary* inflammation of the ganglia," for I could not deny the post-mortem evidence that the ganglia are involved, but I believe it to be *secondary* to the neuritis, as lymphatic ganglia are inflamed in lymphangitis, although I know the simile does not hold good in every respect.

[2] Amer. Journ. Med. Sci., July, 1874, p. 26, and April, 1876, p. 321.

[3] Des Eruptions Cutanées Consécutives aux Lesions Traumatiques. A. Picaud, Paris, 1875.

neuritis may be from the effect of cold on the terminal filaments). The impression may be, then, supposed to travel backward towards the spinal column, becoming transformed in the spinal ganglion to a trophic nerve action, which latter is transmitted centrifugally along the same nerve bundle, and produces the inflammatory disturbance in the cells of the part to which it is distributed; the difference between the normal nutrition of the part and the abnormal excitation of disease exhibits itself in the disturbed or irritated and inflamed condition of the ganglion. The subject of the influence of the nerves on normal and abnormal nutrition, or trophic nerve force, is one of very great interest and of great obscurity, and is yet far from solution. I am not aware of this explanation, which has occurred to me from the present study, having been demonstrated to be untenable, and if it has been proposed by others I have not been able to find reference to it; it finds support in Kölliker's[1] description of certain nerve fibres which take their origin in the spinal ganglia and proceed centrifugally with the sensitive nerves, and go to make up the complete mixed spinal nerves.

A further confirmation of neuritis as a cause of zona is found in a remarkably peculiar case of this disease reported lately by Kaposi.[2] In this case the eruption affected the right arm of a woman, aged 42 years, and there had been four recurrences of the same (that is, five attacks in all) within a space of eighteen months (I see that he has still more recently recorded a sixth attack in the same patient). There were many unusual features in the case in regard to the seat, form, and development of the vesicles, etc., which I need not dwell on, but mention the case to make this single quotation: "In this case the brachial plexus in the right supra-clavicular fossa (the affected side) was swollen to the touch and painful to pressure, the pain extending along the inner surface of the upper arm to near the region of the elbow." The frequent returns of the eruption were probably due to a continued inflammation of the bundles of the brachial plexus, the cause of which we are of course as ignorant of as we are of the exciting cause of idiopathic inflammation or disease of any one organ or part of the body.

If, now, my line of thought and illustration have been clear, I trust that I have assisted in bringing forward prominently certain facts in regard to the etiology of herpes zoster but little considered hitherto, which, together with our knowledge respecting this disease, may be thus briefly recapitulated:—

I. Whatever may be the cause of the nerve irritation, herpes zoster is always of nerve origin, that is, it is an inflammatory lesion of the skin wherein the local cell action, resulting in the production of vesicles, is but

[1] Handbuch der Geweblehre des Menschen. Leipzig, 1867. 5th Aufl. p. 316.

[2] Wien Med. Wochensch. Vierteljahresschrift f. Derm. u. Syph. 1874, p. 411, and 1875, p. 521.

a result of nerve influence, a perverted cell action caused by perverted innervation.[1]

II. From the almost constant changes found in the ganglia developed on the posterior or sensitive roots of the spinal nerves of the affected regions, we must infer that the trophic changes observed in the skin have to do with the sensitive nerves, which marks a certain advance in the study of the physiological relations of the trophic nerves or nerves of nutrition.

III. We are not to conclude, however, that zoster is the result of inflammation of the sensitive ganglia alone, for the entire nerve on the distal side of the ganglion has been always found to be inflamed, and abundant proof exists of eruptions of zoster due to various nerve lesions, peripheral and central, injuries and disease of the transmitting nerves and of the cord and encephalon.

IV. In certain cases the origin may be shown to be idiopathic inflammation of conducting nerves (as in Kaposi's case quoted), or they may be affected by pressure or other alteration caused by the presence of a tumour (as in the case given here), or the disease may be the result of surgical or other injury.

V. The origin, therefore, of herpes zoster is a direct nerve irritation and inflammation, and in ordinary, apparently idiopathic cases, the explanation of this is to be sought for in the same causes as give rise to neuralgias in general, some of which are traceable, many are not. The gouty habit, inducing neuralgia, can likewise give occasion to herpes; the direct exposure to cold of the terminal branches of a nerve, as in the head and neck or elsewhere, can cause painful excitation of the nerve itself, or neuralgia, and is equally a cause of zoster; malaria can originate neuralgia, and may not therefore some of the cases of zona be due to a malarial influence?—certainly the prompt action of citrate of iron and quinia in some cases might point to a malarial element.

VI. In considering, then, the true nature of herpes zoster we are rather led away from the skin lesion to the antecedent neuritis, whose manifestations are neuralgia, more or less marked, and disturbances of sensation in the area of nerve distribution, represented by hyperalgesia, hyperæsthesia, and anæsthesia, while at the same time other results of nerve disturbance may occur, as paralysis of muscles, trophic alterations in the tissues, and

[1] I do not deny the influence also of capillary congestion, but as normal nutrition is rather the result of a proper appropriating of the needed nourishment and a giving up of unneeded and effete elements by the cells of a part, so under abnormal innervation the amount of fluid called for by the cells contiguous to the bloodvessels is larger than is needed, and forms the vesicles; by a lowered vitality endosmosis of the cells of the skin is in excess, as is seen outside of the body in dead animal tissues. Vaso-motor action, being also a trophic affair, is undoubtedly likewise disturbed.

even necrosis and separation of bone. In other words, the eruption of zoster is an epi-phenomenon to a primary neuritis and neuralgia.

VII. The clinical history and therapeutics of herpes zoster are in themselves almost convincing proofs of the neurotic nature of the disease. In most cases, especially in younger patients, the treatment is purely expectative, while in severe cases and in elderly persons the neuralgia is the principal element requiring attention, and this is remedied by measures directed to the nervous system. In the majority of instances the nerve irritation or inflammation subsides spontaneously, the whole train of morbid phenomena occupying about the same length of time taken by other self-limited inflammations, as pneumonia and erysipelas, while under certain circumstances the *sequelæ* require attention, as in other diseases. The local destruction of tissue is sometimes a troublesome feature in the way of ulceration or necrosis of the skin, or the neuralgia persists to a distressing degree even under the most intelligent treatment.

VIII. Three therapeutic agents seem to have marked control over herpes zoster, whose cutaneous manifestations as well as painful element they appear to arrest. First, phosphorus, which, used in the form of phosphide of zinc, one-third of a grain with one-third of a grain of extract of nux vomica, every three hours, will pretty certainly *abort* the disease if given early as recommended by Dr. Ashburton Thompson.[1] I should presume that the tincture of phosphorus, or what is known as Thompson's solution of phosphorus, as now used so successfully for neuralgias,[2] would have the same effect. I have not tried them in this disease, but have used the phosphide repeatedly and with most excellent results. Second, electricity: the galvanic current passed directly through the affected nerves, their trunks and peripheral distributions, will have the effect of causing the eruption either to abort, if used early, or will make the newly formed vesicles dry up much sooner than otherwise, and will pretty certainly check the pain. Third, quinia with iron will, I think, if pushed early in the disease, shorten the duration much and relieve many unpleasant symptoms.

Whether ergot, which has been of great service in neuralgia in the hands of some, would check this congestive neurosis I cannot say, but should hope much from it. The hypodermic injection of morphia, as we know, relieves the neuralgia, and if used early and repeatedly, might abort the disease by checking the nerve-irritation, especially if conjoined with atropia. Painting the surface with collodion or colloid coating containing morphia would serve the same purpose—some assert that it is a very valuable measure. Ordinarily the only local treatment required is protection of the inflamed surface, and this is best accomplished by powdering

[1] Glasgow Med. Journ., Oct. 1874, p. 460. Braithwaite, July, 1875, p. 169.

[2] Transactions of the Amer. Neurolog. Assoc., vol. i. p. 224. New York, 1875.

it with starch and keeping a single thickness of muslin firmly applied, and left on till the vesicles are dried.

In conclusion, I would, as a suggestive thought in regard to the subject of the nerve relations of the disease in question, and perhaps of other affections, mention a remark of Handfield Jones, when writing on herpes zoster:[1] "One can hardly avoid surmising," says he, "that in many cases of pleurisy with effusion the pathological action is quite the same as in pleurodynia with cutaneous vesicular eruption, only that the pleural vasomotor nerves are paralyzed, and not those of the integument."

[1] Journal of Cutaneous Medicine. London, 1868, vol. ii. p. 132.