OBSERVATIONS ON THE INCIDENCE AND SPREAD OF CANCER.

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INCIDENCE.

I HAVE collected 58 cases in which cancer began in the skin of the hand. All were squamous epitheliomata except one, a rodent ulcer on the back of the hand. In all cases except two the cancer began on the backs of the hands; the two exceptions were squamous epitheliomata, both of which began on the skin of the palms opposite the centre of the metacarpo-phalangeal articulations. Hence in 54 out of the 58 cases the disease began on the backs of the hands.

The points of incidence in these 54 cases are as follows: In 28 of them the disease began either exactly over or to one or the other side of the second metacarpal bone. In 16 of these 28 cases it began on the radial side of this bone (see Fig. 1). In 22 of the 54 cases the disease began about the middle of the shafts of the third and fourth metacarpal bones (see Fig. 2). In 4 out of the 54 cases the disease began on the ulna side of the fifth metacarpal bone near the wrist.

Out of the 58 cases 32 began on the right hand and 24 on the left. In 4 cases there were squamous epitheliomata of both hands (backs); in one of these patients there was in addition a rodent ulcer on the right temple. Data are not exact enough to be precise, but the majority of the cases are males.

Among these 58 cases the commonest point of incidence for cancer of the hand was on the skin covering the posterior surface of the second metacarpal bone and on its radial side. It is interesting to recall here that Dr. Henry Head¹ made himself the subject of the following experiment: Segments of his radial and two branches of his external cutaneous nerves were excised, and sensation was lost for tactile, pain and temperature impressions in the skin of the area which the nerves supplied. Eventually a trophic ulcer developed over a point on the radial side of the posterior surface of the second metacarpal bone; in fact, just upon the point which is the commonest site for the incidence of cancer on the hand. The question naturally arises, Can Dr. Head's experiment be brought into line with this site of origin in cancer of the hand? It demonstrated the point of most exposure to external irritation within the denervated area by the fact of a trophic ulcer forming upon it, and from this fact that the ulcer did not form until there had been a disturbance of the nerve supply to the part arises the problem as to whether cancer itself may be rendered possible only when there is a disturbance of nerve supply.

But it is not only in denervated areas that trophic lesions occur; Mr. James Sherren has kindly allowed me to quote the following facts from his book² entitled *Nerve Injuries and their Treatment*, which is still in the press. He says, in reference to cases in which the sensory nerves have been completely divided,

Blisters may originate spontaneously; they are often noticed on waking in the morning, and occur at a time when sensibility to prick is beginning to return to the affected portion of the limb.

And in the same book Mr. Sherren says, in reference to cases of incomplete division of a sensory nerve,

Blisters may make their appearance not only over the area of sensory loss, but also over the area in which there is hyperalgesia, but no loss of sensibility.

These important facts were not known to me, and I am very much obliged to Mr. Sherren for allowing me to use them.

The clinical connexion between external irritation and cancer is a factor too marked to be regarded only as a popular fallacy, and, while recognizing this fact, it is curious to observe that in the hand the back of it is the commonest position for cancer to begin, even when the fingers, front and back, are included. One would have imagined the knuckles and backs of the fingers would be as much exposed to external irritation as the other parts of the back of the hand. Why should it be that cancer most often starts along a line 2 in. broad drawn obliquely inwards and upwards across the back of the hand? Within that

line the nerves supplying the skin become cutaneous, and, as I have pointed out before, the incidence of cancer appears to me closely associated with those points at which nerves become cutaneous. In connexion with these points it is necessary to say, first, that the "maximum points" described by Dr. Head are points at which peripheral nerves become cutaneous; and secondly, that in two cases of cancer I found inflammatory changes in the posterior spinal root ganglion on whose cutaneous distribution each cancer began and that no inflammatory changes appeared within the ganglia into whose distributions the cancers spread. It must be realized that besides affecting the epithelium of the skin locally, external irritation also affects the posterior spinal root ganglion supplying that skin and its epithelium, so that really the changes in the skin which are observed when external irritation is applied to it may be partly, chiefly, or wholly due to impulses received or not received from the posterior spinal root ganglia. That this probably is so is supported by the fact that the skin on the backs of the hands of old people is thin, shiny, and wrinkled, and although its nerve supply is present it resembles in appearance the skin of a denervated area (Dr. Head and Mr. J. Sherren). I have also observed warts and superficial blackish-yellow pigmentary patches on the backs of hands in old people, the position of which coincides with the commonest points of incidence of cancer in this region.

It is more difficult to collect cases of cancer of the fingers and the feet, and I have not yet enough of them to publish, but the regions of the big and little toes and the malleoli are apparently common points of incidence in the cancers of the feet. It is most difficult to secure records of any case of squamous epithelioma on the trunk. Mr. C. W. Rowntree has carefully examined the records of the Middlesex Hospital in the four years 1903-6; there were 935 cases of malignant tumours examined there during this time. Of these, 244 were cases of squamous epitheliomata, but not even one of them had its point of incidence on the trunk. I have seen only one case, that was one of a man who had two on his back, one over the back of the shoulder, and the other above the crest of the ilium. The two ulcers were removed, and the diagnosis confirmed by microscopic examination. Dr. Arthur Whitfield has a photograph of a case which was under his own care in which a female has the right axilla, side and front of the chest, covered with apparently discrete warts, some of which were removed for microscopical examination, and all of which were typical squamous epitheliomata.

I have collected 16 cases of squamous epithelioma which had developed on scars (no case of rodent ulcer on scar). The length of time which intervened between the injury which caused the scar and the appearance of cancer ranged between five and thirty years. There was no history of skin grafting. It does not seem essential that the scar should be large to become the seat of cancer, although in most of the cases the scar is very large. Nor is it essential that the wound should be healed, though in most cases complete healing had occurred. Curiously enough, the squamous epitheliomata of scars are limited at the edges of the scars, where the growth is apparently arrested. And lastly, the cancers seem to have begun well away from the margins of the scars which were the most extensive. I have not seen a case of cancer in a scar, therefore I cannot say that scars on which cancers develop exhibit abnormal states of nerve supply. But I have tested the tactile, pain, and temperature sensations of many scars, of many sizes and ages, and it is very striking how markedly abnormal most of them are.

THE SPREAD OF CANCER.

I wish to publish an area of occupation in cutaneous cancer. It can be seen in Figs. 3, 4, 5, 6, 7. By referring to Fig. 8 it will be seen that the anterior and inferior edges of these rodent ulcers correspond to the anterior and inferior limits of the skin supplied by the great auricular nerve, which is itself included in the supply of the second cervical posterior spinal root ganglion (see Figs. 9 and 10, and compare Fig. 7 with them). The anterior edge of the diseases in these figures also corresponds to the denervated area in Fig. 11. Mr. McAdam Eccles sent me a case of tertiary syphilis, in which the disease was extending symmetrically in the same areas.

I have a case of a cutaneous naevus which is occupying the region, and I have seen cases in which beards have become grey on the cheeks but not on the chins, and the

Fig. 7.—Dr. Sequeira's case of rodent ulcer; the disease began at the x behind the ear.

lines of demarcation between the two corresponded to the inferior margin of area of anaesthesia in Fig. 8.

Before leaving this subject, I want to draw fresh attention to the area occupied by the cancer in

Figs. 12, 13, 14, and 15. The corresponding area is mapped out in the herpes zoster in Fig. 16, and in the denervated area of the cheek in Fig. 18. Further, in Fig. 9 it will be seen that on the side of the head there is an area in which the distributions of the fifth cranial nerve and the second cervical spinal root ganglion overlap each other, and to a much smaller extent this area of overlap includes a portion of the parts supplied by the third cervical posterior spinal root ganglion. I want to draw attention to the differences of behaviour between the different cases of rodent ulcers which affect this region of overlap, and to show how they adopt mainly two distributions, either that of the fifth cranial nerve or area, or that belonging to the second cervical posterior spinal root ganglion,

Figs. 9 and 10.—Reproduced from Dr. Charles Sherrington's paper on Experiments in Examination of the Peripheral Distribution of the Nerves of the Posterior Spinal Roots of some Spinal Nerves. *Philosophical Transactions of the Royal Society of London, Series B, vol. 1898, pp. 45-186.*

example) in two different cases, yet in their subsequent growth they may cover one of two distinct and different areas of distribution. This fact seems to me to contra-

Fig. 16.—Dr. Henry Head's case of herpes zoster; the area affected corresponded to the cutaneous distribution of sensory fibres of the inframaxillary division of the 5th nerve. See *Brain*, autumn part, 1900.

indicate the assumption that these rodent ulcers are spreading in obedience to the mere anatomical arrangement of

uncontrolled lymphatic and blood-vascular systems, or any other mechanical or developmental arrangement; for, if such were the case, the distribution would be the same in all cases, and would not show these particular differences of distribution. There would not be the distinct anterior and inferior limitations which are seen in Figs. 3, 4, 5, 6, 7, where there is a distinct tendency to adhere to the second cervical area, even when traversing the fifth cranial nerve overlap. This fact suggests the argument that because a rodent ulcer which is spreading in the second cervical nerve area does not alter its course directly it reaches the fifth cranial nerve area;

that, therefore, there may be some factor of a nervous nature at work in the parts supplied by the second cervical posterior spinal root ganglion which is not present in the

Fig. 8.—Area of anaesthesia to touch, pain and temperature upon division of great auricular nerve. (The sensations of the pinna and external auditory meatus were not accurately tested.)

Fig. 14.—Dr. Crombie's (North Berwick) case of rodent ulcer.

Figs. 18 and 19.—Represent Dr. Harvey Cushing's case of the distribution of herpes zoster on both sides of the face and neck. The right Gasserian ganglion had been previously removed by him and the oblique lines in Fig. 18 represent the area of anaesthesia.

see Figs. 3, 4, 5, 6, 7 for the former case, and Figs. 12, 13, 14, 15 for the latter. Therefore, although two rodent ulcers may begin on the same spot (in front of ear, for

fifth cranial nerve system. Further, it must be realized that the spread of cancer begins directly upon the first division and proliferation of the parent cell or cells of cancer, and hence if a nerve influence on the growth becomes clinically evident at a nerve limit, then

Fig. 3.—Dr. Harrison's (of Bristol) case of rodent ulcer. The disease began in front of the ear.

Fig. 4.—Mr. Madden's (Cairo) case of rodent ulcer.

Fig. 1.—Squamous epithelioma on back of hand. (Guy's Hospital Museum.)

Fig. 15.—Rodent ulcer.

Fig. 2.—Squamous epithelioma on back of hand.

Fig. 5.—McMaddin's (Cairo) case of squamous epithelioma.

Fig. 6.—Rodent ulcer. Mr. J. R. Lunn's case.

Fig. 11.—A case of Dr. Harvey Cushing's (Baltimore), which shows the segmental area of tactile anaesthesia after removal of second and third posterior spinal root ganglia.

Fig. 12.—Rodent ulcer. (Cancer Hospital Museum.)

Fig. 13.—Rodent ulcer.

Fig. 17.—Dr. Sequeira's case of rodent ulcer.

it may also be exhibiting the same influence on the first division of the parent cell or cells of cancer. On the other hand, it may be said that the nervous influence (supposing it exists) which controls the spread of rodent ulcers may be called into operation only when cancer has started, and has by its presence affected such reflex nerve impulses as those of vaso-constriction or vaso-dilatation, for example. But, if such were the case, one would not expect to see the marked tendency to adhere to one of the areas where two or three overlap, and the rodent ulcer would not elect to spread in one of them in preference to another, and consequently both would be equally affected, and no definite nerve distribution would be visible.

I have another curious rodent ulcer distribution kindly sent to me by Dr. Sequeira. (See Fig. 17.) The disease began in the centre of the cheek. This might be said to be a pure spread in the lymphatic vessels of the part, but it may also be said, first, to be too transverse in direction for that to be the correct explanation; and, secondly, that its area of occupation may be one of a nerve distribution, because practically the same region is occupied by herpes zoster in Dr. Harvey Cushing's case, Fig. 19.

The case of Dr. Harvey Cushing depicted in Figs. 18 and 19 suggests that if the right Gasserian ganglion had been intact the distribution of herpes zoster on both sides would have been symmetrical. It is highly probable that the existence of a peripheral nerve is essential for the occurrence of herpes zoster as a conductor of irritant impulses from the ganglion, yet this is the only case I know which can be said to demonstrate this point. And suppose the spread of cancer be influenced by ganglionic disturbances they must be conveyed or not conveyed by peripheral nerves, and when a peripheral nerve is exposed and irritated by cancer and septic conditions, its power of conducting afferent and efferent impulses must be profoundly changed and the normal spread of cancer modified in consequence. In fact I have already shown grounds for believing that the growth of rodent ulcers are arrested, or at any rate do not spread so rapidly in denervated areas as elsewhere except when irritated by antiseptics, etc.² I have also pointed out inflammatory changes in posterior spinal root ganglion on whose cutaneous distribution cancer began and that I could not observe the same changes in the posterior spinal root ganglia into whose cutaneous distribution the cancer had spread.³ Whether the changes which existed in the ganglion were primary or secondary to the appearance of the growth I will not now discuss, but it is as difficult to imagine how their presence can fail to influence the state of cancer as it is to comprehend how the influence acts or what it precisely is. In the present state of our knowledge one can only speculate upon the possibility of its being an active or irritative influence rather than one of a passive or an inhibiting nature.

REFERENCES.

¹ Head and Sherren, Injury to Peripheral Nerves in Man, *Brain*, cx, p. 252. ² BRITISH MEDICAL JOURNAL, December 12th, 1903. ³ *Ibid.*, July 20th, 1907.

A FORM OF ORAL FILTER TO BE WORN DURING OPERATIONS BY ALL PERSONS INSIDE THE OPERATING ROOM.

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OWING to Mikulicz of Breslau and Dr. Mendes de Leon, considerable attention has been drawn of late to the question of the surgeon's breath as a source of wound infection.

The fear of infection is not from micro-organisms given forth in the ordinary act of expiration, but in the act of talking.

It has been shown by numerous observers that micro-organisms are not given off in the breath in ordinary quiet expiration; in fact, the expired air is sterile.

The buccal secretions of healthy people contain micro-organisms, and an enumeration is given of the organisms found.

Examinations of healthy buccal saliva prove that the following organisms are commonly present: *Streptococcus brevis* (Lingelsheim), *Streptococcus medius*, *Streptococcus*

conglomeratus, *Streptococcus longus*. All the above cocci were found by Gordon to be present to the extent of from 10 to 100 million per c.cm. of saliva. Staphylococci in less numbers, 1 to 10 million per c.cm. No staphylococcus of the aureus variety was found. Bacilli were conspicuous by their absence. In addition to the above normally-found micro-organisms, every medical man is well aware of the accidental pathogenic cocci and bacilli that are to be found in the throats of apparently healthy individuals, such as the pneumococcus, bacillus of diphtheria, *Micrococcus tetragenus* (Koch and Gaffky). In the way of literature on the micro-organisms in the mouth there are: *The Mycology of the Mouth*, Goadby, London, 1903; *Die Mikroorganismen der Mundhöhle*, Miller, second edition, Leipzig, 1892; *Microbes de la Bouche*, David, Paris, 1890.

In ordinary speaking, loud talking, orating, singing, shouting, sneezing, coughing, etc., organisms are projected from the mouths of healthy and unhealthy people in saliva droplets to various distances and in various directions. Flugge, and also others of his school, made extensive experiments in proof of the above. Papers by Flugge, Laschtschenko, Beninde, Heyman, and Koeniger are to be found in *Zeitschrift für Hygiene*, Bande 30, 34, 38. Modelled on the above experiments, we have those of more recent date by Dr. Gordon. Details of the technique are given at great length in Appendix B, No. 2. Sections 1 to 7 of the Thirty-second Annual Report of the Local Government Board, 1902-3, also an interesting paper by Dr. Rupert Collins, An Experimental Inquiry into the Infection of Operative Wounds from the Skin, the Breath, and the Air. This paper will be found in the BRITISH MEDICAL JOURNAL, July 15th, 1905, p. 121. Gordon found that salivary micro-organisms were capable of being projected in the salivary droplets to a distance of 40 ft. in front and 12 ft. behind the speaker. In all his experiments control tests were most rigorously carried out.

The organisms such as are projected in the salivary droplets of healthy individuals are capable of pyogenesis on a suitable soil. In the medical officer's report, Local Government Board, 1903-4, Dr. Gordon, in the "Differentiation of Streptococci," finds that two of his streptococci isolated from patients suffering from ulcerative endocarditis gave reactions identical with the two found to occur with the greatest frequency in normal saliva. The virulent streptococcus which occurred with greatest frequency in septic processes was fourth in order of frequency amongst salivary streptococci.

If there be truth in the foregoing statements, I would submit that it is in the best interests of the patient who is undergoing operation that those in the operating room should wear some form of mask or mouth filter.

The form of filter is a simple one, consisting of a square of butter muslin measuring 3 ft. 1 in. along each border. This square is folded up like an ordinary handkerchief and is sterilized with the dressings. After the surgeon, his assistants, and others in the operating room have sterilized their hands and put on their operating coats they will apply the muslin filter in this manner. Unfold the muslin from its handkerchief form until one fold remains, that is, the muslin is simply

Fig. 1.

folded once, its area being halved. Grasp the folded edge with both hands and fling the muslin over the head bring the centre of the folded edge down to the centre of the forehead just above the eye-brows, pass the folded edges behind both the ears exposing the free ends down over the shoulders on to the front of the chest. (See Fig. 1.) Now strip (on both sides) the anterior free edge from the posterior free edge up to the level of the lobe of the ear. (This stripping is shown in Fig. 1 on the left shoulder, whilst the fold on the right has not yet been touched.) Now bring the posterior free edge across the face at the level of the bridge of the nose. (See Fig. 2.) Likewise the remaining posterior free edge across the nose tucking the end in, about midway between the outer canthus of the eye and the external auditory canal. Now pull up