procedure, which we may term "extracapsular" enucleation of the prostate, is the operation which Freyer has so prominently brought before our notice in the paper referred to, as well as in others subsequently published,¹ and in suitable cases is attended by very satisfactory results. The bladder having been opened from above the pubes, the mucous membrane and thinned-out sheath over the most prominent part of the swelling are divided with scalpel or scissors, or merely scratched through with the finger-nail. The enucleation is then effected entirely by the finger, which separates the sheath from the capsule above, externally, and below, as well as in front and behind, and by working close to the capsule the enucleation and removal of the gland is readily and quickly accomplished.

In cases of great hypertrophy the thinning of the sheath and capsule is so extreme that it is difficult to recognize these structures as such, and it is possible that under these circumstances the capsule becomes in places so stretched out and weakened that the lobulated glandular outgrowths actually burst through it. The gland may be enucleated *en masse*, but this necessitates tearing across, or removing with it, the prostatic portion of the urethra. This accident may be avoided by first dividing the tissue bridging over the urethra, the so-called "anterior commissure," and then working laterally round, and also below, the canal, which is pushed upwards and thus avoided. A safer method is to separate the lateral lobes from one another, and enucleate first one lobe and then the other, stripping them, as it were, from off the urethra which lies between them. If this is done, the urethra—in which a silver catheter should be retained to act as a guide—is less likely to be injured. If the surgeon stands on the left side of the patient and uses the right forefinger to enucleate the prostate, the presence of the left forefinger in the rectum will prove of great assistance, for by pressing the gland upwards it will steady it, and at the same time render it more accessible.

The haemorrhage, which may be free, is usually soon arrested by irrigating the bladder with hot lotion, and the subsequent treatment is identical with that after suprapubic cystotomy for bladder tumours or for other causes. A piece of large-sized drainage tube should be left in the suprapubic opening for a day or two, and until the wound closes, which usually takes place in from three to four weeks, the bladder should be washed out daily with some antiseptic lotion. As healing occurs the power of voluntary micturition gradually returns, the bladder regaining its expulsive power, even when this has been lost for a long period. The specimen, which I show you, is a good illustration of this method of treatment, the entire prostate being removed in its capsule in three portions, consisting of a large right lobe, a smaller left lobe, and a pedunculated third lobe, which was connected posteriorly with the right lobe. The patient, aged 59 years, who had suffered for eighteen months from retention of urine, requiring daily catheterism, made a good recovery from the operation, and completely regained the power of voluntary micturition in less than a month after its performance. Examination of the prostate after removal showed that the enlargement was due to the presence of numerous adenomatous growths embedded in the substance of each lobe.

Instead of removing the prostate in its capsule in the manner advised by Freyer we may enucleate separately the adenomatous growths embedded in its substance. In this method, which may be termed "intracapsular enucleation," the capsule is divided, as well as the mucous membrane and sheath, over the more prominent portion of each lobe. The finger is then passed through the opening in the capsule into the interior of each lobe, and the separate growths are easily detached from the surrounding gland tissue and enucleated one by one. This method, of course, does not so completely remove the obstruction as the "extracapsular enucleation," but it is probably attended by less haemorrhage, as the prostatic plexus of veins is very slightly interfered with. Moreover, there is less likelihood of injuring the prostatic urethra, as no doubt often happens in the more complete removal, and as yet our experience of the latter operation is not sufficient to say whether, if this complication occurs, troublesome contraction of the neck of the bladder may not possibly result in the future.

I adopted this procedure in the case of a gentleman, aged 61 years, in October, 1901, as he was not a good subject for any operation, and I thought it would be less severe than the method of complete enucleation which Freyer in his first paper, based on an experience of four cases, had published only a short time previously. A large number of adenomatous

growths, varying in size from a pea to a filbert, were shelled out of both lateral lobes, and after the suprapubic wound closed he regained and still possesses the power of voluntary micturition, which had been lost for a considerable period.

My subsequent experience, however, of the complete or extracapsular method of enucleation would lead me to adopt this procedure in future, though we must remember that it is not applicable to all cases of prostatic obstruction which call for surgical interference; and when we have the condition present to which I have referred, namely, a moderate fibro-myxomatous enlargement of the gland, it should not be attempted.

Under these circumstances, a partial prostatectomy will often give good results, and when this is not practicable, then cystotomy and bladder drainage will generally afford relief in the manner already described.

Though doubts were expressed by several surgeons as to the possibility of complete removal of the prostate—mainly on anatomical grounds—in the course of a somewhat prolonged correspondence on this subject, which appeared in the *BRITISH MEDICAL JOURNAL*² shortly after the publication of Freyer's early cases, it is my opinion that when the pathological changes to which I have alluded have taken place in the prostate, giving rise to the adenomatous form of hypertrophy, then its total enucleation is quite feasible.

This conclusion is based upon my own experience of the operation, and also upon an examination of many of Freyer's specimens, which were exhibited at the recent meeting of the British Medical Association held at Manchester.

I believe, therefore, that suprapubic prostatectomy on the lines laid down by Freyer is not only possible in properly-selected cases, but that it is an operation which will soon establish for itself a recognized place in surgery.

REFERENCES.

¹ *BRITISH MEDICAL JOURNAL*, November 8th, 1902, p. 1495. ² *Clin. Soc. Trans.*, 1888, vol. xxi, p. 52. ³ *BRITISH MEDICAL JOURNAL*, October 19th, 1889, p. 863. ⁴ *Ibid.*, July 20th, 1901. ⁵ *Ibid.*, February 1st, 1902, p. 249; November 8th, p. 1492. ⁶ *Ibid.*, July 27th to September 14th, 1901.

NOTE UPON A POSSIBLE RELATIONSHIP BETWEEN CARCINOMA AND NERVE OR TROPHIC AREAS.*

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In this communication I wish to point out certain features in the pathology of cancer when it is viewed stripped of the masking effects produced by the presence of secondary deposits.

The features to which I allude are mainly two: First, that there is a proportion of cases which show a marked relationship between the spread of the primary focus and the distribution of nerves and trophic areas. Arising out of this observation is the practical issue that the extent of these areas should be taken into consideration in marking out incisions when removal of cancer is contemplated. I do not wish to detract from the importance we now attach to the lymphatic pathways of distribution; I only desire to add another factor.

My second point is that there is reason for thinking that the incidence of cancer within a nerve area is not a fortuitous circumstance, but that it may be due to the direct or indirect nervous influence over that area.

I will take these two points separately, and will attempt to demonstrate my meaning by showing cases of rodent ulcer, Hutchinson's crateriform ulcer and squamous epithelioma, as they affect the head and face. Before doing so I will remind you of the close central connexion which exists between the fifth cranial, the glosso-pharyngeal, and pneumogastric nerves.

The mode of distribution in the cases remind one of the distribution of herpes, morphea, moles, naevi, and of certain infective processes.

The particular nerves are sensory, but I am not prepared to say whether the following phenomena are due to the influence of peripheral nerves or whether they are due to a central

* Read before the Pathological Society of London. It may be mentioned that the illustrations published with this paper are only a few of the total number shown by the author at the meeting.

nervous influence exhibiting itself in its peripheral nerve areas. (Dr. Head advised me to be particularly careful to lay stress upon this point.)

In the absence of precise knowledge concerning trophic influences a definite statement cannot be made. But during the consideration of my paper I must press you to bear in mind the possibility of conditions indicating "central" nervous influence. In any case I cannot believe that areas occupied by disease in the following cases are merely due to the promiscuous presence of lymphatic and blood vessels. Their share in the effect appears to me to be one presided over by a nervous influence, nor can the areas of occupation be entirely due to a relationship to developmental fissures and other anatomical conditions. One nerve area after the other is mapped out in too marked a manner to be overlooked, and this, too, in spite of the following factors which act against limitation, namely:

(a) Diminution of a normal skin area occurs when it lacks the support of the parts lost by ulceration, and its elasticity is rendered free to exert uncontrolled power of contraction. Unsupported skin flaps always atrophy.

(b) Imperfect operative procedures and infection will enlarge the area, and scar tissue modifies the direction of growth in cancer.

(c) Nerve areas overlap each other, and there are many variations to the usual manner of peripheral nerve distribution.

Rodent Ulcer.

I will show rodent ulcer first because it is the commonest form of cancer in which secondary deposits in lymphatic glands are rare. In the grossest and most extensive lesions of the head and face which I have seen the whole of the areas supplied by the two fifth cranial nerves have been destroyed.

Fig. 1.—Mr. G. D. Thane's diagram of the distribution of the areas of the head and face supplied by the fifth cranial and the cervical spinal nerves. Taken from Dr. Head's article in *Brain*, vol. xvii, page 468, "On the Disturbances of Sensation and the Pain of Visceral Disease."

In these cases there seems to be an absence of spread to those areas supplied by the cervical spinal nerves, and this limitation to the fifth is more permanent on the head than

Fig. 2.—Mr. Malcolm Morris's case. The disease began near the right orbit. (Rodent ulcer.)

on the face (see Figs. 2 and 3.) The fifth nerve of one side can

Fig. 3.—Dr. Sequeira's case. The disease began on the side of the head above the attachment of the ear to the side of the head. The state of things since this photograph was taken eight months ago is that extension has occurred upwards and forwards, but not backwards. It is interesting to observe the ulcerated part of the pinna corresponds almost exactly with the peripheral distribution of the auriculo-temporal nerve. (Rodent ulcer.)

be sharply marked off from the advancing disease of the opposite fifth (see Figs. 4, 5, 8, and 11), and the nerve areas of

Fig. 4.—Mr. Watson Cheyne's case. The rounded swelling at the upper limit of the ulcer is the oedematous upper eyelid. (Rodent ulcer.)

one fifth can be sharply demarcated from the disease of contiguous nerve areas of the same fifth (see Figs. 2, 3, 5, 8 and 12).

Where the disease begins at the meeting place of two or more peripheral nerve areas they tend to be mapped out before the disease spreads to others (see Fig. 5). Should such areas be situated on one side at the middle line (Fig. 5) the corresponding and contiguous areas of the opposite side are frequently attacked and will then produce a bilateral lesion which appears central (See Fig. 6). This is an area mapped out in other diseases such as syphilis (see Fig. 7). In Fig. 8 the infraorbital nerve area is seen ulcerated and should this lesion become bilateral it will map out an area seen in Fig. 9. This is an area mapped out in other diseases, such as glanders (see Fig. 10).

In studying the sites of origin which correspond to a single nerve area one sees that the disease often begins at the point where the particular nerve becomes cutaneous. That point in relation to the infratrochlear nerve is probably the most frequent site of incidence in rodent ulcer. A mole is frequently observed about this region, but if one can believe patients' histories a rodent will begin here when no mole previously existed.

Fig. 13 shows rodent ulcer occurring in the cervical spinal nerve area and its progress of ulceration is spreading away from the areas of the fifth nerve. I have already pointed out

Fig. 5.—Dr. Sequeira's case, in which the disease began on the side of the nose behind the ala, where the nasal nerve area joins that of the infraorbital nerve. The disease was spreading downwards towards the lip, and represents a type of distribution. (Rodent ulcer.)

Fig. 6.—Dr. Sequeira's case. The disease began on the right side of the nose. (Rodent ulcer.)

Fig. 7.—Mr. Watson Cheyne's case. Congenital syphilis marking out same area as the rodent ulcer in Fig. 6.

Fig. 8.—A case from Mr. Hutchinson's collection at the Polyclinic.

Fig. 10.—A plaster cast of glands affecting the same area as the rodent ulcer in Fig. 9. From the Museum of St. Mary's Hospital.

Fig. 11.—Dr. Whitfield's case, showing the area of first division of the fifth nerve on the right side in course of destruction. (Rodent ulcer.)

that the areas on the face supplied by the nerves of cervical spinal region are more liable to invasion than the areas on the head that are supplied from the same sources, and although the disappearance of the skin on the face may be more apparent than real there can be no doubt that the cervical nerve areas in the region do in some marked cases eventually succumb.

Squamous Epithelioma and the Crateriform Ulcer.

Hutchinson's crateriform ulcer, which may or may not be a squamous epithelioma, very frequently arises on the points at which nerves become cutaneous. The same may be said of typical squamous epithelioma.

Fig. 14 shows the naso-labial area as mapped out in herpes; and, in a patient who refused operation, I have seen the same area in the course of destruction by a cancer which began on the lower lip.

Fig. 15 shows an example of the same state of things arising from a cancer which began on the lower lip. It appears that it may be regarded as the eventual area of occupation when the cancer begins in either the lower lip and at or near the angle of the mouth. I have seen a cancer of the lower lip which began on and spread superficially along the whole mucous membrane of the lower lip. I have also seen two cases of so-called recurrent cancer of the lower lip beginning to map out this area in a more or less complete manner. It is a compound nerve area, [the infraorbital, buccal, and mental nerves being involved.

Fig. 9.—A case from the collection of the Cancer Hospital, London. (Rodent ulcer.)

I may here say that herpes occurred in this region in a case of pneumonia which died the Gasserian ganglion being the seat of a haemorrhage, supplying evidence of a central nerve connexion to this area. The recognition of this area as being the eventual site of occupation for the growth appears to me an indication for modifying the V-shaped incision now considered sufficient for removing cancer of this region. To

devise preliminary incisions for the removal of cancer according to the delimitation of similar areas elsewhere appears to me of first importance.

Fig. 12.—Mr. Watson Cheyne's case. The disease has begun in the area of the nasal division of the fifth and has not involved the infraorbital nerve supply to the ala nasi. (Rodent ulcer.)

In the tongue is seen remarkable limitation occurring at the middle line when cancer begins on the side of that organ (Fig. 16). The epithelium at the tip of the tongue on the side of the disease often remains free, and the overlapping of nerves at this point is of course considerable. I can see no mechanical or vascular reasons for the disease being arrested even temporarily in the epithelium of the middle line.

Fig. 13.—Dr. Sequeira's case. The rodent ulcer is occupying the cervical spinal nerve area.

Fig. 14.—From Dr. Head's articles in *Brain*, vol. xvii, p. 384, showing the nasolabial region occupied by an eruption of herpes.

I would like to point out that an epithelial surface disappears during the cancer process in two ways. One in which the normal surface can be seen actually breaking down into cancer, and the other is atrophy of the epithelium due to the

increasing pressure of the subjacent growth. Where disease begins at the mid-line of the tongue then both areas are simultaneously involved. (See Fig. 17.) Here no arrest of growth is visible at the middle line. One would have thought it would have shown if vascular arrangements or developmental clefts account wholly for limitation.

Fig. 15.—Approximately the same area as 14, occupied by squamous epithelioma which began in the lower lip. From the Royal College of Surgeons Museum.

My second main point is that there is some reason for inferring that carcinoma may originate in a nerve area as a result of the nervous influence over that area.

Fig. 16.—Mr. Watson Cheyne's case. A squamous epithelioma of left side of tongue, the epithelioma at the tip of the left side is still free. The disease began on the left side of the tongue.

The usual occurrence of a single rodent ulcer, 64 out of 66 cases (Bowlby), or a squamous epithelioma on the area supplied by the fifth nerve may not with justification convey any connexion between the two facts. But that connexion is made stronger, I think, when it is associated with cases in which the fifth areas either singly or combined are the seats of multiple discrete rodent ulcers. To make myself clear I will enumerate a few cases.

- Case I.—A rodent on right ala nasi and one on left temple.
- Case II.—Two rodents on right fifth area and one on left.
- Case III.—Two rodents on left fifth area and one on right.
- Case IV.—A squamous epithelioma on fifth of one side and a rodent on the fifth of the opposite side.
- Case V.—Nine rodents over the areas of the two fifth nerves. (Mr. Bruce Clarke's case.)
- Case VI.—Two rodent ulcers on fifth area of left side.
- Case VII.—Five rodents on fifth area of right side. (Mr. Malcolm Morris's case.)
- Case VIII.—A rodent ulcer on left upper lip and on front of tip of left ear.

It will be seen that rodent ulcers may be multiple on the two areas of the fifth nerves at the same time; and that they may be multiple on the area of one fifth nerve; and no lesion elsewhere. Mr. McAdam Eccles had a case of two rodents on one fifth, and many others on the body and legs.

[I have omitted any reference to multiple epithelioma on the areas of the fifth, because the question of secondary deposits may be a factor in their appearance.]

I can quite appreciate the criticism that, singly or otherwise, infective processes can be shown occupying the same regions; but the incidence of cancer may not be due to the mere influence of infection as claimed by several observers.

Cancer, belonging essentially to the period of bodily degeneration, is a point which seems to me of some importance in considering the following facts. Lugaro has proved that peripheral irritation causes central changes of degeneration in the posterior root ganglia of the spinal nerves. In these the ganglia cells are seen swollen and rounded. The Nissl bodies break up; the nucleus is eccentric, and often quite at the periphery. Apart from senile degeneration there is, then, the fact that peripheral irritation can induce visible changes in the ganglion controlling the irritated area. At the same time I fully realize the importance of recognizing that central nerve impulses may

be abnormal, although nothing abnormal can be seen in the central nerve ganglia.

Before I knew of Lugaro's experiments I examined the posterior ganglion of the fifth dorsal spinal nerve of the right side, which I took away from a woman for the relief of agonizing pain in an inoperable cancer in the right breast, and Dr. Purves Stewart, who kindly stained the ganglion for me, found the same changes as described by Lugaro occurring in some of the ganglion cells.

I do not wish to infer that a degeneration of the ganglion preceded the carcinoma in this case, because I know not if this really occurred.

At the same time I cannot help alluding to the clinical fact that irritation is a great precursor of cancer, and added to this it causes degeneration in the particular ganglia whose peripheral ramifications are irritated.

Carcinoma often appears in tissues which are associated with disorders of growth such as moles, and these moles are themselves associated with definite nerve areas and the incidence of cancer. (See Fig. 18.)

Dr. Whitfield has pointed out to me that Foldau has shown that nerve fibres can be traced into these moles.

I wish it to be understood that I do not claim to have enunciated a new theory of cancer, but to have shown that there is reason to justify us in taking into consideration the possibility that the genesis and spread of cancer, even when considered apart, may be connected directly or indirectly with the nerve influences which preside over the areas affected. In conclusion, I thank Dr. Sequeira for the unreserved manner in which he placed his large clinic and wide experience at my disposal. My thanks are also due to Dr. Scott, from whose thesis upon rodent ulcer I gleaned a few cases. Major Pinch kindly gave me permission in Mr. Hutchinson's absence to copy many of Mr. Hutchinson's pictures in the Polyclinic. Dr. Andrews and Dr. Broadbent allowed me to reproduce some specimens from the respective museums over which they preside.

Fig. 17.—A tongue from the museum of St. Bartholomew's Hospital. The squamous epithelioma began in a wart which was situated in the centre of the tongue and occurred at a point on which the end of a clay pipe habitually impinged.

Fig. 18.—Dr. Sequeira's case, showing the distribution of moles and on the left side of the man's face was a squamous epithelioma.

ON THE ETIOLOGY OF SLEEPING SICKNESS.*

BY

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THE bacteriological researches which we have prosecuted in investigating the etiology of sleeping sickness were principally on the organic tissues and liquids, for being guided by the knowledge of former pathological observations, and by the result obtained in the first necropsies made by us, we were aware that the principal lesions of this African disease were anatomically those of a meningo-encephalo-myelitis.

In our first report of June 9th, 1901, regarding the 6 cases observed in Principe, we said that the preliminary and restricted investigations up to that time accomplished seemed to "guide us in the sense of the infectious nature of the sleeping sickness."

Two months later, on August 10th, in Loanda, we first discovered the existence of a diplo-streptococcus in the cerebro-spinal fluid *intra vitam* (6 results positive in 9 cases) and in the subarachnoid exudate (in 13 necropsies), and we described the principal characters of the germ in an incomplete and summary way. These results were published in September, 1901.¹

In Lisbon on August 7th, 1902, we finally brought forward the results of our researches in a public conference, illustrating our communication by projections and by the demonstration of pathological specimens, cultures, and microscopical preparations which were collected from a great number of examinations, both of the cerebro-spinal fluid obtained by lumbar puncture *intra vitam*, of the exudate in the ventricles obtained at the necropsy, of the blood, ganglia, and spleen, and demonstrating also in numerous microscopical sections, especially of the nervous tissues, the existence of the micro-organism both inside and outside the vessels.

We were particular in pointing out, in order to avoid error, that the micro-organism in question ought to be included in the streptococcus group, and we proposed therefore to call it the hypnococcus.²

We wrote as follows: "The general description of the principal characteristics of the hypnococcus being given, let us see if it is possible to determine its place in bacteriological classification."

In our first report we were rather disposed to consider it as a type transitional between the streptococcus and Fraenkel's diplococcus. We can, however, now affirm that it is easy to distinguish it from the latter.

It will be sufficient to say that it grows on gelatine and in other media at a temperature below 24° C. in order to clearly separate it from Fraenkel's diplococcus.

But in order to go further, we followed the method proposed by His to establish the differential diagnosis between the pneumococcus and the bacteria of the streptococcus group. To water and ox's serum in equal portions, conveniently alkalized and sterilized, we added 1 per cent. of inuline. This sugar is fermented by the pneumococcus, giving a change in reaction from alkaline to acid, and producing the coagulation of the medium. Our diplococcus grew well in this fluid, the reaction was not modified, nor did the fluid coagulate even after a month's stay in the incubating oven.

We read recently in the *BRITISH MEDICAL JOURNAL*, March 14th, a preliminary report of the bacteriologist Castellani, a member of the English Commission sent to Uganda to study the sleeping sickness, in which he states that he had found, as we had already done, a streptococcus both in the cerebro-spinal fluid of living patients and *post mortem*, which he considers is different from ours.

This idea may probably be due to the fact that Dr. Castellani only knew of our first reports, which were erroneously translated before they came out in the *Journal of Tropical Medicine* in May and June, 1902, from which the description of our bacterium might reasonably give rise to some doubts in regard to its bacteriological classification.³ However, after this work we described it more precisely, and considered it as belonging to the large streptococcus group (August, 7th, 1902). It is necessary to say that though some divergences exist between what we said in our first report

* This note belongs to the first part of the chapter, *Recherches Factiologiques*, of our report now in the press.