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## PROGRESSIVE LETHAL GRANULOMATOUS ULCERATION OF THE NOSE\*

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DURING the last ten years several cases of a peculiar type of ulceration of the nose which correspond to no known pathological entity have come under our direct observation.

The ulceration was progressive and invariably ended fatally. Such cases left a painful impression which became mitigated by the passage of time, only to be intensified by the occurrence of another case.

I may, therefore, be pardoned for writing a paper composed of cases which at first sight appear to be rare and, because of their scarcity, demand more scientific than practical consideration. Similar cases met with at one time or another will probably be within the recollection of some.

The literature on this special form of ulceration is scanty, but an amazingly large field is opened up of similar ulcerative nasal conditions of known origin. It is beyond the scope of this paper to include ulceration due to malignant disease, syphilis, and tuberculosis, but other types of ulceration will be

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reviewed which have a close resemblance to the type of ulceration about to be described.

During investigation of this research, attention was drawn to a somewhat similar state of ulceration occurring in the pudenda. [Fig. 1.] The literature on this subject has been explored and may shed some light on the subject under discussion.

*Historical.*—The first case of progressive ulceration of the nose which ended fatally was recorded in the *Proceedings of the Laryngological Society of London*, 1896, by Peter McBride<sup>1</sup> under the title of “Case of Rapid Destruction of the Nose and Face”. Thereafter the literature on the subject is without addition until 1921, when Sir Robert Woods<sup>2</sup> published in the *British Medical Journal* the reports of two such cases under the name of “Malignant Granuloma of the Nose”. In 1925, under the same title, G. A. D. McArthur<sup>3</sup> reported another case in the *Journal of Laryngology and Otology* and, in 1929, L. Chatelier<sup>4</sup> added under the name of “Sarco-Lupus Pernio, Mutilant et Mortel” what we take to be a case which comes under the heading of our paper. [Fig. 2.] Finally, during 1931, George B. Wood<sup>5</sup> described a case of “Mutilating Granuloma of the Nose and Face with fatal ending” in the *Transactions of the American Laryngological Association*. [Figs. 3 and 4.] This is a summary of the literature proper which we have been able to collect.

To these, however, must be added three more cases which, though not characteristic of the ulceration with which we are dealing, are sufficiently similar to be included. They are: (a) “Esthiomenic Menstrual Ulcer of the Nose”, described by Macnaughton-Jones<sup>6</sup>; (b) “A Case of Undetermined Tropical Ulcer involving the Nose, Pharynx and Larynx with Histological Findings”, reported by John A. Fordyce<sup>7</sup>; and (c) “An obscure Case of Ulceration of the Nose in a Child, simulating an Epithelioma”, by David Nabarro.<sup>8</sup>

[*Note.*—Sir St Clair Thomson encountered two fatal cases—one a male, and the other a female. In both the ulceration started on the cutaneous aspect of the nose and steadily progressed until all the facial aspect of the nose and cheek were invaded.]

*Pathology.*—*Post mortem* examinations were made in five cases (Nos. I, III, V, IX and X), but in only two cases (Nos. III and V) was a description given of other organs apart from the

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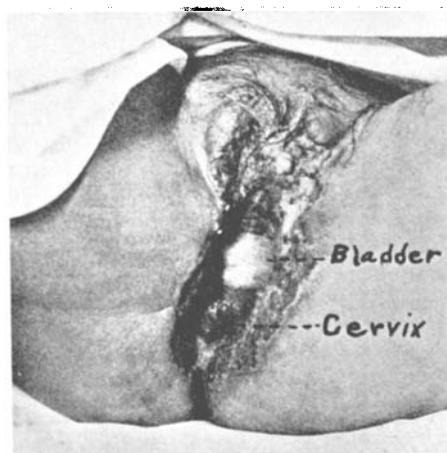


FIG. 1. After Rice <sup>14</sup>.

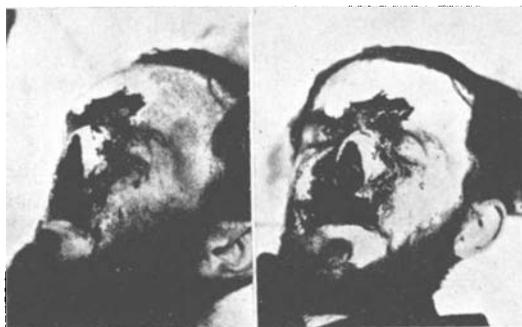


FIG. 2. After Chatelier <sup>4</sup>.

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FIG. 3. After Wood 5.

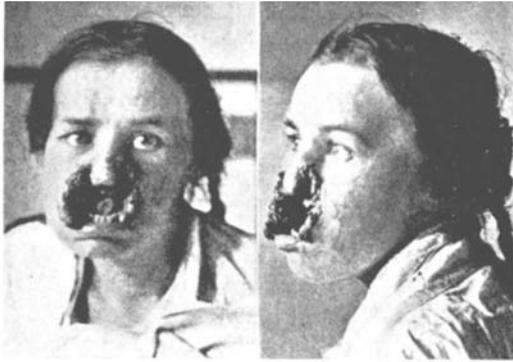


FIG. 4. After Wood 5.

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local condition. There was very little of note in the general examination. In Case III there was a general atrophy of the organs and in Case V, apart from dilatation of the heart and some enlargement of the liver, no pathological process was present.

Amyloidosis was not present. This change is generally found in cases of chronic suppuration of sufficiently long-standing, e.g. empyema with pocketing. In the cases under consideration the pus, when formed, escaped freely.

*Microscopic examination of diseased tissue removed at various times during life.* A fairly complete histological examination has been made from sections of diseased tissue taken from six of the cases (Nos. II, III, IV, V, VII and VIII). The general impression gained from a comparison of the material was that the affection was a chronic inflammatory process. Thus there was found proliferation of endothelial cells, lymphocytes and plasma cells, and the formation of granulation tissue, at first cellular, but later becoming fibrous. The inflammatory condition, it appears, starts in the subepithelial tissues. [Fig. 5.] In the material from the early cases there was principally a dense small round-celled infiltration with engorged vessels and scattered hæmorrhages. The epithelium which undergoes necrosis, being raised from its underlying tissue either by extravasation of blood [Fig. 6] or by œdema, gave the ulceration its typical picture.

As the disease progressed, fibrous tissue was laid down fairly loosely just below the surface and became more dense in its deeper parts. There was still among the fibrous tissue a small round-celled infiltration more marked when the fibrous tissue was less compact. The blood vessels in the early stages were proliferating and, in established conditions, showed enormous thickening of their walls and endarteritis with hyaline change. [Fig. 7.]

At the endosteal surface of the bone, absorption of its lamellae and Haversian systems was taking place. In sections from Case II new bone in its reticular form (see Stewart<sup>19</sup> on Histopathology of Mastoiditis) [Fig. 8] had taken place and it is interesting to note that the new bone was more resistant than the "old" bone which was being actively destroyed. [Fig. 9.] In some sections bone necrosis was present. The whole disease picture, therefore, was one of chronic inflammation.

The pathology of this disease is most obscure and an idea

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of this obscurity can be gained from the following opinions expressed as to its origin.

In McBride's case,<sup>1</sup> Robert Muir, then pathologist to the Royal Infirmary, Edinburgh, stated that the disease did not correspond to any type with which he was familiar. Syphilis, Yaws and Tuberculosis could definitely be excluded.

O'Sullivan, who examined Sir Robert Woods' specimens,<sup>2</sup> concluded that it seemed as if a wave of granulation tissue advanced irregularly into the healthy parts, breaking down behind as it advanced in front, so that there was never any great field of pathological growth present. The term "Malignant Granuloma" was suggested. The presumption was that granulation tissue, so far from being evidence of an attempt at healing, is itself primarily the cause of destruction. We understand what is meant by a cell taking on a malignant action. We cannot doubt that what happens to one kind of cell may happen to another and if we can have a malignant epithelioma why not a malignant granuloma?

In McArthur's case<sup>3</sup> microscopic examination was conducted by H. R. Dew, who concluded that "the growth was a peculiar one and did not appear to conform to any definite type of malignancy. The growth was not to be considered a sarcoma, but it did bear some resemblance to some of the very atypical spheroidal carcinomata seen in this region. It was believed to be of the same variety as that recently described by Sir Robert Woods under the heading of 'Malignant Granuloma'."

Chatelier, in describing his case,<sup>4</sup> said that lupus pernio itself is most certainly benign. Histologically the lesions were constituted by granulation tissue and he goes on to say that there exists a malignant form of lupus pernio which is mutilating and fatal. It is closely related to the sarcoids and, therefore, he thought he was justified in calling the disease "sarco-lupus pernio". Perhaps an explanatory note on Lupus Pernio may be given. In 1889 Besnier described a case in a male, *æt.* 34,<sup>1</sup> in whom a variety of lupus erythematosus was present on the face and then on the arms in the form of an erythematous pernio or local asphyxia, to which he gave the name Lupus Pernio or Lupus Asphyxia.

We now come to George B. Wood's case.<sup>5</sup> He received quite a number of opinions on his specimens. First we have that of Case, who reported that "the picture is neither

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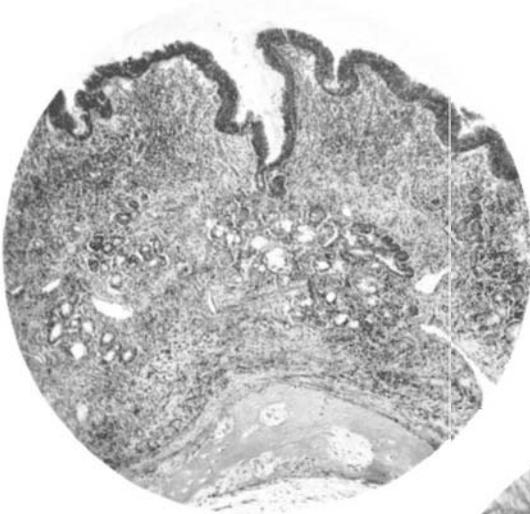


FIG. 5.

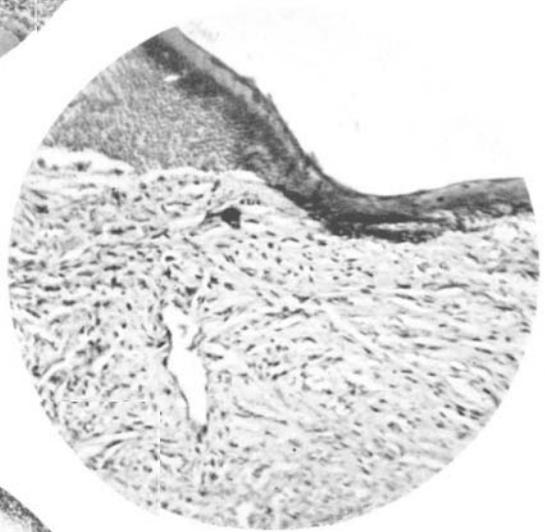


FIG. 6.



FIG. 7. [3]

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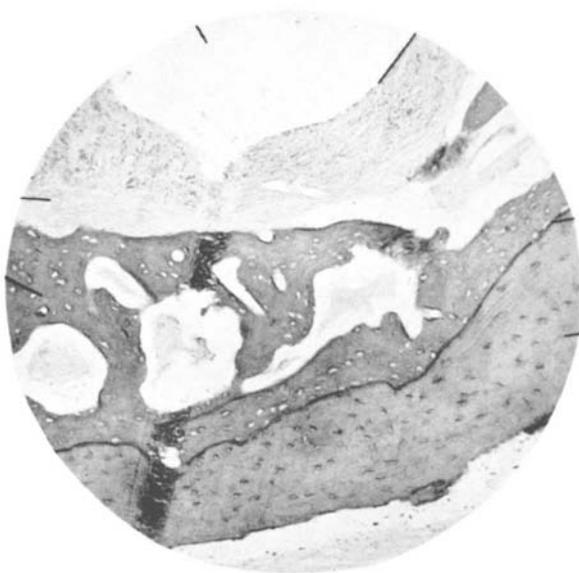


FIG. 9.

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tuberculosis nor a neoplasm. However, there are cells whose appearance suggests tumour development which is not that of any particular type of tumour, but genetically I believe it should be placed amongst the sarcomas ”.

Ewing was of the opinion that the histological appearances most resembled syphilis, though lacking specific qualities. He further stated that “ unless we have an entirely new disease we are thrown back on syphilis or mycosis fungoides ”. He ends by saying that “ this I regret is the best I can do ”.

Frederick De F. Weidman was of opinion that it was not in a true sense a neoplasm. He did not think it was syphilis, tuberculosis or any disease he knew of, though it probably belonged to the so-called granulomas.

Cruickshank, of Aberdeen, examined material from Case IV. He stated there was no evidence of tuberculosis but a portion showed the structure of a cellular fibroma.

Another piece of tissue from this case was examined by F. E. Reynolds, who said that there was no definite evidence of neoplasm. It was not a carcinoma nor a sarcoma.

The late James W. Dawson reported on some tissue from Case II thus : “ Had I seen the specimen without any knowledge of the clinical history I would have looked upon it as Hodgkin’s lymphadenoma and have thought that it was becoming sarcomatous. One should consider the locally invasive and destructive properties of Hodgkin’s disease, which are features very prominent in this case, and I think this diagnosis applies more particularly to the slides.” My own view is that the appearance on examination is consistent with a chronic pyogenic infection.

In the similar maze of the rodent ulcers of the vulva, Rieck<sup>9</sup> seeks to prove a tuberculous origin.

To sum up, two investigators state that “ the tissue has no definite structure ”, one considers it “ Malignant Granuloma ”, one “ a so-called granuloma ”, one “ Sarco-Lupus Pernio ”, one that it “ resembles atypical spheroidal carcinoma ”, one that “ it is a manifestation of syphilis ”, one relegates it to the “ Sarcomata ”, one thought it was “ Hodgkin’s lymphadenoma becoming sarcomatous ” and, lastly, one that it was a “ Chronic Pyogenic Infection ”.

*Clinical Features.* Ten cases have been collected and are made up as follows : Edinburgh 5 cases, Sir Robert Woods 2 cases, McArthur 1 case, Chatelier 1 case, G. B. Wood 1 case.

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These comprise 9 males and 1 female. As regards ages, 2 cases occurred just under 30 years, 5 between 30-40 years, 1 between 40-50 years, and 2 cases between 60-70 years.

The symptoms may be divided into three stages.

First stage—prodromal. This period may exist for as long as four years. The patient is conscious of a stuffiness in the nose, usually accompanied by a watery or sero-sanguineous discharge. At this stage no active disease is present and a correction for deflection of the nasal septum or removal of enlarged conchae may be performed in order to provide more breathing space. When a submucous resection of the septum is performed, a perforation of the anterior part of the septum usually results on healing. During some years thereafter there may be little alleviation of symptoms.

Second stage—period of active disease. [Fig. 10.] The patient complains in practically every case of definite nasal obstruction accompanied by a foul smell and a purulent or sanguineo-purulent discharge. The disease tends to spread from the interior of the nose to the outside, so that the tip of the nose becomes swollen and indurated (3 cases). Involvement of the upper lip took place in two cases and, in addition, swelling of the adjoining cheek and lower eyelid occurred in three cases (in one a sinus in the cheek was present) and in three cases the swelling localised to the lower eyelid and tear sac was complicated by a sinus over the lachrymal sac. The swellings were, for the most part, painless. So much for the external appearances. The earliest indication of disease seen within the nose is usually a small brown ulcer on the inferior concha or the nasal septum. Later on, the affected side of the nose becomes filled up with odoriferous glutinous crusts which on removal reveal an ulcerating surface on the nasal septum and adjoining concha. Before long the cartilaginous portion of the septum becomes perforated and some minor hæmorrhages take place.

The disease is progressive and ulceration of the hard palate ensues, usually about its centre. Sequestra now come away—it may be a portion of the bony septum or perhaps the inferior concha. Abscess formation is present under the cheek and necessitates drainage, and the body of the maxilla must be denuded of its periosteum. There is fever with an irregular temperature and a very moderate leucocytosis or, as happened in one case, a leucopenia. (Highest white blood count was 14,800 and the lowest 2,200, with polymorphonuclears 70 per



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FIG. 10.

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FIG. II.



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cent and 45 per cent respectively.) The polymorphonuclear leucocytes retain their normal proportions. Agranulocytosis has never been present in any of the cases observed and septicæmia was absent, as indicated by the negative blood cultures. Hæmorrhages proved rather troublesome at this stage. The difficulty in packing a nose in which the floor is deficient and the septum has disappeared will be realised, and in at least two reported cases both external carotid arteries had to be ligated, one a short time after the other. Sequestra became frequent, those for example of the pterygoid process.

*The third or terminal phase.* [Fig. II.] The patient becomes exhausted on account of toxin absorption. The irregular temperature continues unabated. Only with difficulty can fluids be swallowed. Repeated hæmorrhages increase the exhaustion. But what of the local condition? The facial appearance is monstrous. Externally the eyelids are swollen and purulent discharge trickles from between the lids. Sloughing areas appear over the lachrymal sac or cheeks and the soft tissues about the external nose disappear, perhaps including the upper lip. This mutilating destruction was extreme in Chatelier's case and almost as great in McBride's. In these cases the hard and soft palates were completely destroyed and, through the mouth, the roof of the nose and nasopharynx were visible and the roof of the maxillary air sinus exposed by ulcerative destruction of the lateral wall of the nose. The alveolar processes were ulcerated and the teeth had either dropped out or were very loose. The posterior pharyngeal wall was covered with dirty grey necrotic material. The tongue remained unaffected. No sequestration of the basi-sphenoid occurred in any of the cases.

The course of the second and third stages generally lasted from one year to eighteen months and, on the whole, there were no complaints of pain.

*Result of Disease.*—In the Edinburgh group of cases death ensued despite all treatment. Taken collectively out of the ten cases, eight died from the direct effects of the disease, one died of sarcomatosis cutis seven months after the nasal condition had apparently been cured, and one lived for four years after cure of local condition and succumbed to "miners' phthisis", but no *post mortem* examination was obtained and McArthur, who reports the case, considered it possible that death was due to multiple sarcomata scattered throughout the lungs.

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*Differential Diagnosis.*—Ulceration of the nose instantly suggests firstly syphilis, secondly tuberculosis, and thirdly carcinoma. Even if the Wassermann reaction of the blood be negative, anti-syphilitic treatment is instituted and more or less vigorously carried out with not the slightest benefit. The diagnosis of syphilis should be not lightly undertaken and, in the absence of a positive Wassermann blood-reaction, anti-syphilitic treatment should not be adopted. Brown Kelly, who kindly discussed the nature of the disease with me, said that cases of this nature used to be considered in pre-Wassermann test days as “Malignant syphilis”. Each of the ten cases had been treated for venereal disease with no amelioration of their symptoms.

To eliminate the possibility of lupus, pieces of tissue are examined after biopsy and the discharge investigated by inoculation. Case IV was treated for tuberculosis for a considerable time and Chatelier evidently thought that this disease in his patient was a “malignant type” of lupus. The tissue examined previously rather excludes this diagnosis, but the destructive malign course of the disease makes it imperative to be quite sure that such a condition has not been missed. As an illustration, take Auxiliary Case I<sup>8</sup> “an obscure case of ulceration of the nose in a child simulating an epithelioma”. [Fig. 12.] The pathological investigation stated that “the material examined consisted of vascular granulation tissue. Throughout the section large collections of epithelial cells were present and keratinisation was well marked, with the formation of characteristic cell nests. Many of these cell nests were invaded and apparently destroyed by polymorphonuclear leucocytes and a small number of round cells. Between the masses of epithelial cells was a vascular and somewhat cellular connective tissue. A number of thin walled blood vessels were present, as well as extravasated blood. An occasional multinucleated or ‘giant’ cell was seen.” Nabarro goes on to say that “At first sight scrapings presented the characteristics of a squamous-celled carcinoma”. In view of the age of the patient and the result of treatment, doubt arose as to the correctness of the diagnosis. More opinions were given. Two of the consultants unhesitatingly said “epithelioma”, even in spite of the patient’s youth. Another thought it might be a proliferating papilloma, and yet another thought a granuloma with subsequent proliferation of the epithelium. Fischer said

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FIG. 12. After Nabarro <sup>8</sup>.



FIG. 13. After Carmody <sup>18</sup>.



FIG. 14. After Benjamins <sup>10</sup>.



FIG. 15. After Benjamins <sup>10</sup>.



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that the section reminded him of a case of verrucose tuberculosis of the skin.

The report on Case III shows that a snip taken from the ulcer of the hard palate was reported as showing a chronic inflammatory reaction, and a somewhat slowly growing carcinoma. Later sections, however, cast a doubt on this diagnosis.

After exclusion of these three diseases the next that demands attention is the mycosis group, i.e. actinomycosis, blastomycosis [Fig. 13], and sporotrichosis. [Fig. 13.] I do not propose to describe the nasal condition seen in those diseases, but I wish to draw attention to a blastomycytic<sup>18</sup> infection of the nose and of sporotrichosis. The fungus responsible for these diseases is easily seen in the pus films or on culture, e.g. sporotrichosis.

In practically every case of granulomatous ulceration, fungus was looked for and excluded, though blastomycosis was temporarily considered as a cause in Case III. (Physician's opinion.)

More difficulty in differential diagnosis is presented by tropical diseases which produce oropharyngeal or nasal ulceration. The individual in Case III had served during some time in the Army in Egypt. But after all, these diseases may be endemic in temperate climates and can occur in Europeans.

Auxiliary Case II should perhaps have been included in the cases proper. J. A. Fordyce,<sup>7</sup> who reported it, classifies it as only one of undetermined tropical ulcer because he had excluded other causes of ulceration and, therefore, thought it must be a tropical disease which would include these diseases, namely, leishmaniasis and rhino-pharyngitis mutilans (gangosa).

*Leishmaniasis.* The condition known as leishmaniasis has been divided into two forms, (a) cutaneous and (b) oro-naso-pharyngeal, the former being known as Oriental Sore and the latter as Espundia. It is caused by a parasite first demonstrated by Leishman and then independently by Donovan and designated "Leishman-Donovan bodies". It is chiefly found in subtropical countries and Europeans may be affected.

In espundia the victim, probably inoculated by an insect bite, develops at this site a small papule or papules which later ulcerate. This lesion is resistant to any local treatment but heals spontaneously within a few months. After a period of

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time varying from one to two years, the secondary state of esputia commences with manifestations in the nose. A small ulcerated area appears on the anterior part of the nasal septum accompanied by a mucopurulent blood-stained discharge having a peculiar odour. The ulceration spreads backwards as well as to the conchae; and the nasopharynx, pharynx, and tonsils, later become involved. The disease now appears on the facial surface of the nose and adjacent parts (upper lip, cheeks, etc.). [Figs. 15, 16.] The larynx, trachea and œsophagus may become involved by extension, but the tongue is not affected. The cartilage of the nasal septum may be completely destroyed, but the bones remain intact.

The disease reacts very favourably to tartar emetic, as discovered by Vianna in 1913, but if untreated death results from cachexia.

*Rhino-Pharyngitis Mutilans (Gangosa).*—We are indebted to C. E. Benjamins<sup>10</sup> for his masterly description of this disease. It was at one time thought that this affection was a particular form of yaws or of late syphilis.

The disease is found in sub-tropical countries and mostly affects the natives, though it has been found in Europeans.

Some investigators have isolated a "cryptococcus mutilans", others a yeast-like fungus of the nature of blastomycosis, while a "bacillus gangosa" has also been found. None of these, however, appear pathogenic for this disease.

The illness commences as a superficial ulcer which may be located on the posterior pharyngeal wall, palato-pharyngeal arch, or the free edge of the soft palate and is characterised by a dirty brown scab. Later the ulcer deepens and spreads forwards and upwards projecting into the choanae and destroying the bony and cartilaginous septum. The soft and hard palates ulcerate so that the nose, mouth and pharynx are converted into one large cavity. The tongue is never involved. In some cases ulceration attacks the outside of the nose and adjoining parts of the cheeks and the prognosis is then very grave. [Fig. 17.]

The diagnosis is made by exclusion. Up to the present no therapeutic agent has proved of benefit.

Apart from these, a case has been reported of "Trophic Post-Encephalitic Ulcer Formation of the Outer Nose and Cheek" by Schlittler.<sup>11</sup> Briefly "such changes are connected with central localised phenomena in the mid-brain with changes

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FIG. 16. After Benjamins <sup>10</sup>.



FIG. 17. After Benjamins <sup>10</sup>.



FIG. 18. After Schlittler <sup>11</sup>.



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in the region of the ganglion cell group which lie in the convolutions of the third ventricle and possess vegetative and trophic functions." The affection occurred in a male aet. 20, the subject of encephalitis lethargica. Following a superficial scratch of the nose a rapidly increasing ulceration appeared on the right ala nasi. Application of ointment caused improvement but the ulcer never completely healed. On examination the whole right ala nasi was found to be destroyed by a crater-like granulating, slightly hæmorrhagic ulcer, the wall-like edges of which were slightly thickened and covered with thin sanguineous crusts, while the parts of the mucous membrane of the interior of the nose directly bordering the ulcer display only increased redness, a white discoloration being present on the septum in consequence of epithelial metaplasia. The ulcer-granulations were soft but there was no fœtor. From the lower edges of the large ulcer a second superficial ulcer stretched from the right upper lip towards the right angle of the mouth without much infiltration of the deeper soft parts. The ulcerated area was very irritable. The ulcer increased in spite of anti-syphilitic treatment and violent inflammatory manifestations appeared around the soft parts of the nose and cheek. [Fig. 18.] The point of the nose was not infiltrated. During six months there was no material improvement, but a year later the ulcer healed spontaneously. Death occurred from pneumonia in the following month.

*Agranulocytosis* bears more than a resemblance to progressive lethal granulomatous ulceration of the nose, face and pharynx. The ulceration in agranulocytosis tends to occur in the immediate neighbourhood of possible sepsis, for example in the perinæum, or in the pharynx or nose, and when that ulceration occurs there is little reaction because the granulocytes of the blood are inhibited in their formation and, after a period of three days, more or less completely disappear from the blood stream on account of their natural destruction.

In progressive granulomatous ulceration, on the other hand, one of the most striking factors is the lack of resistance on the part of the patient. But there is no agranulocytosis present in the blood, the granulocytes, either in leucocytosis or leucopenia, remaining in their normal proportions. Therefore, the lack of resistance can be attributed in agranulocytosis to the absence of the granulocytes but no cause is apparent for the absence of resistance in progressive lethal granulomatous ulceration.

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### Ulceration occurring in Female Pudenda

A somewhat similar ulceration to that which we are discussing occurs in the pudenda and here investigators are faced with the same problem as to its cause. All ulcers of that locality used to be grouped under the term *Esthiomène*, which implies a rapid destruction, and Eugene Deschamps<sup>12</sup> made an attempt in 1885 to classify these various types of ulcer. The term *Esthiomène*, however, has been used by some authors to designate the condition of *lupus exedens*.

True *esthiomènic* ulceration of the pudenda attacks only the soft tissues and does not involve the bone, thus differing from the condition in the nose. The bony septum, hard palate, pterygoid lamina, etc., depend for their blood supply solely on the overlying periosteum—they are extremely thin and when subperiosteal affection denudes them of their coverings they come away as sequestra.

*Rodent Ulcer of Vulva—Esthiomène.*—Rieck<sup>9</sup> has written a very interesting paper on this subject. He maintains that all ulcers described as *Esthiomène* have a uniform cause. The local appearances show a slow ulceration with spreading margins. The ulceration progresses beyond the more highly differentiated tissues such as the urethra and intestine and, above all, there is the great tendency to the formation of fistulae.

He rules out syphilis, gonorrhœa, *ulcus molle* and carcinoma and, apart from these and tropical diseases, only non-specific causes remain. Koch states that these ulcers are due to a local disturbance of nutrition such as the destruction or extirpation of the inguinal lymph nodes. Rieck refutes this theory on the grounds that the epidermis would be the first to suffer from this central disturbance and that the rodent ulcer presents an extreme disease of the subcutaneous connective tissues; also apart from the face there is scarcely another region of the body so well supplied by vessels as the sexual region. Local uncleanliness is also ruled out as a cause.

Rieck further states that these ulcers have all the characteristics of primary tuberculosis such as chronicity, hypertrophic proliferation, sinus formation, little cicatricial formation and destruction of specialised tissue, e.g. the urethra, despite the fact that no tubercle bacilli or any other ætiological factor was found. He looks for a slight swelling and redness in an otherwise healthy region near the ulcer, in which a fine sinus

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has just formed, and he extirpates this tissue, which is then cut in serial sections, in which tuberculosis may then be demonstrated. He emphasises the great difficulty in demonstrating the bacillus in tissue and the need for repeated examinations. In one of his cases tubercle bacilli were demonstrated only once. In another case of vulvar rodent ulcer, tubercle bacilli were not demonstrated though there was associated uro-genital tuberculosis.

The failure to find tubercle bacilli (histological research, inoculations, etc.) does not preclude tuberculosis. At times tuberculosis need be present only to quite a small degree.

In this connection Macnaughton Jones<sup>6</sup> published a case of Esthiomènic Menstrual Ulcer of the Nose.

*Esthiomènic Menstrual Ulcer of the Nose.*—In November, 1895, an adult female developed a small ulcer on the right side of the columna nasi. The ulcer was flat and covered with a thin brown scab and slightly raised. A red blush extended over a small area around it. At the menstrual period the ulcer became more active. The nose was affected for seven months, but in the inter-menstrual periods the inflammation subsided. Increasing severity of the ulceration suggested a tuberculous origin. Treatment had no effect.

In January, 1896, the disease was progressing and half of the ala nasi had become involved. The ulcer was scraped and acid applied, but the wash-leather character of the slough, its extreme tenacity and incorporation with subjacent tissue, made any attempt at scraping impossible and it had to be shaved off with a knife before applying alembroth wool as a dressing. This was repeated twice during January and was followed by considerable improvement. Just before menstruation in February there was a recurrence of all the old activity—rapid spreading of inflammation and increase in size of the black slough. At times the agony was extreme. The whole margin of the nose, including the columella and the skin as far as the mucous membrane of the lip, became involved. Dermatologists were consulted and considered it to be of a cancrroid nature akin to cancrum oris. The blush then extended to the skin of the left nostril and was associated with a sickening and most unpleasant odour. The entire slough was cut away and nitric acid applied and this was followed by improvement, but there still remained a tendency to the formation of crusts.

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By August the ulceration had healed and though in October a recurrence took place on the right nostril at the site of the original sore, Salactol proved to have a beneficial effect and the ulcer healed with very little mutilation and very little contraction.

*Granuloma Venereum or Granuloma Inguinale.*—This disease, which is described as being confined to the tropics, has occurred in the temperate zone of the United States of America in an endemic form. It is seldom seen before puberty and rarely after the forty-fifth year (Randal, Small and Belk<sup>13</sup>). It usually begins on the outer genitals as a small nodule which breaks down and refuses to heal. The ulceration spreads rapidly and has little tendency to penetrate deeply.

The diagnosis is dependent on the isolation from the bacterial examination of the local smear of "Donovan bodies".

Local applications and excision have no effect. Radio-therapy has proved of benefit but has to be continued for a year to eighteen months and 50 per cent of the cases so treated recur (Randal, etc.). Best<sup>15</sup> records a case which showed no response to radio-therapy or radium, but was cured by antimony. The condition clears up rapidly on the intravenous administration of tartar emetic, the dose of which can be increased up to 0.1 gm. without bad effects.

A case of this disease occurring in the nose has been published by Bonne and Verhagen.<sup>16</sup> An ulcer appeared at the junction of the nasal orifice and the upper lip and spread gradually into the nose and mouth, involving also the mucous membrane of the cheeks and lower lip. Later on, swelling of the face gave the patient a monstrous appearance. Donovan bodies were isolated from scrapings and the condition cleared up with the administration of antimony. Randal, Small and Belk<sup>13</sup> conclude their monograph by stating that any pudendal sore resistant to ordinary antiseptics, unimproved by arsenical therapy, of long duration and, especially when devoid of pain, should be searched for the specific organisms of granuloma inguinale and given the advantage of treatment with antimony. Is it worth while applying that principle to the nose?

*Bacteriology.*—An interesting paper somewhat related to the disease under discussion has been published by F. Hector Scotson<sup>17</sup> on "Progressive Post-Operative Gangrene of the Skin". In his summary he states that "a type of wound infection is described which leads to progressive gangrenous

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ulceration of the skin. The affected skin is first red, then finally gangrenous, and the area is intensely painful and tender. The organism most commonly found is a streptococcus but in at least three of the above cases there has been found in addition a staphylococcus, lending support to the theory of Brewer and Meleny that the ætiology of this condition may be a symbiosis of these organisms."

Detailed bacteriological examination is noted in seven of the ten cases under review. In six of these cases streptococci were reported as having been isolated from among many organisms and in the above cases they have been associated with staphylococci. In the seventh case only were staphylococci isolated.

Can this be correlated with the ulceration which is the subject of this paper? Rigorous search was carried out to locate tubercle bacilli. Direct films of the secretion, together with cultures and inoculation of guinea pigs were always negative. The Wassermann test was taken a few times in every case and no spirochætes were ever demonstrated.

*Treatment.*—In reviewing the various forms of treatment carried out, especial interest is attached to those cases which recovered.

*Local Treatment* consisted in keeping the parts clean, combating the tendency to crust formation, and evacuating any accumulations of pus. Calomel ointment, peroxide of hydrogen douches, tincture of iodine douches, mercurochrome and cauterisation, constituted the local applications.

*General Treatment.*—Each individual was given anti-syphilitic treatment without benefit. It is interesting to note that in Case V injections of tartar emetic caused no mitigation of the disease. "Cuprum" and "205" Bayer, as well as sodium iodide, were administered intravenously. Surgical diathermy was tried but proved unsuccessful.

It was found that in comparatively early cases in which there was a skin involvement, surface radio-therapy gave good results, but if this treatment were carried out later when the disease was strongly established, good effects did not follow. Deep radio-therapy, on the other hand, was successful in Case VIII, which indeed seems to be so far the only case thus treated.

Radium therapy, on the other hand, was employed in two cases. In Case VII it was followed by apparent recovery—certainly the local condition cleared up, but this satisfactory

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result is somewhat neutralised by Case II, in which after the first application of radium the symptoms abated, only to return with increasing severity notwithstanding a second and third application.

The information detailed above would indicate that anti-syphilitic treatment is of no practical use. Surgical diathermy is also useless. Radium was responsible for improvement of the local condition in one, but aggravated the local symptoms in another case. Deep radio-therapy was employed only in one case with successful results, but too few cases have been so treated to make any trustworthy evaluation possible.

### Synopsis

1. A disease is described to which we cannot give a definite name and whose cause is very obscure. In our opinion the most descriptive term is "Progressive lethal granulomatous ulceration of the nose".

2. Ten cases of this disease are reviewed.

3. The disease is practically confined to the male sex, the ratio being 9 males to 1 female.

4. Eight of the ten cases occurred between the ages of 28 and 42 years.

5. The pathological basis is unknown. From the clinical and microscopic appearances, the writer concludes that the disease is not one of tumour but essentially a pyogenic one, a chronic inflammatory process. Malignant Granuloma is an unjustifiable designation. The writer finds no connection between this disease and Hodgkin's lymphogranuloma. The disease is not one of formation but of destruction, while the presence of granulation tissue may approve the term "progressive granulomatous ulceration".

6. The clinical picture is one of progressive destruction of the nose, face and pharynx. The disease is characterised by a mild leucocytosis (14,800), or a leucopenia (2,200), with the white blood cells in their normal proportions. There is prolonged and hectic fever and frequent and severe hæmorrhages.

7. The duration of the illness is from one to two years.

8. The most marked feature of this disease is the complete absence of resistance of the patient to the infection.

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9. The disease must be differentiated from ulceration occurring in the nose due to the following diseases: syphilis, tuberculosis, malignancy, agranulocytosis, mycosis and myiasis group, yaws or frambœsia, leprosy, rhinoscleroma, leishmaniasis, rhino-pharyngitis mutilans (gangosa) and trophic post-encephalitic ulceration.

10. In six out of the seven cases, when bacteriological findings were given, the presence of a streptococcus in combination with a staphylococcus was reported.

11. As regards treatment, local applications proved unavailing. Radium treatment was employed in two cases with indefinite results; but deep radio-therapy promised more success and deserves further trial.

12. *Results.*—Eight patients died from the direct effects of the disease, namely, sapræmic cachexia and repeated hæmorrhage. One survived for four months after local cure before succumbing to generalised sarcomatosis cutis, and one died from atypical “miners’ phthisis” four years after recovery from the local affection.

In conclusion I have great pleasure in expressing my thanks to the following for permission to include their cases in the present paper:—

Case I. Peter McBride.

Case II. M. J. Gibson (Dundee).

Case III. J. S. Fraser.

Case IV. J. M. Johnston (Tor-na-Dee) and A. Logan Turner.

Case V. J. S. Fraser and Prof. D. P. D. Wilkie.

Cases VI and VII. Sir Robert Woods (Dublin).

Case VIII. G. A. D. McArthur (Sydney, Australia).

Case IX. L. Chatelier (Paris).

Case X. George B. Wood (U.S.A.).

D. Middleton Greig, Conservator of the Museum of the Royal College of Surgeons, Edinburgh, has taken an immense amount of trouble both in his suggestions and in his revision of this paper. The translations of the literature were again ably carried out by Miss Mary Ritchie.

Finally, this piece of work has been greatly facilitated by the enthusiasm of J. S. Fraser and his unfailing devotion in the cause of research.

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## ILLUSTRATIONS

The undernoted illustrations have been taken from the following articles :—

- Fig. 1. F. W. Rice, Ref. 14.
- Fig. 2. L. Chatelier, Ref. 4.
- Figs. 3 and 4. George B. Wood, Ref. 5.
- Fig. 7. Microscopic section from G. A. D. McArthur.
- Fig. 12. David Nabarro, Ref. 8.
- Fig. 13. T. E. Carmody, Ref. 18.
- Figs. 14, 15, 16 and 17. C. E. Benjamins, Ref. 10.
- Fig. 18. E. Schlittler, Ref. 11.

## CASE I.

A.P., aged 28, male.

*December*, 1895, scratched his nose on the inside of the left ala with his finger. This became irritable and sore : in a week the skin began to be œdematous.

*January*, 1896.—Much the same only the left side of the nose and corresponding cheek were swollen and painful. An ulcer was seen on the inner side of the left ala covered with a dirty white slough. Examination of ulcer for tuberculosis was negative. Antispecific treatment employed.

*March*.—Erysipelatous-looking swelling of the left ala, cheek and lower eyelid, a pustule beginning to form on the exterior of the left ala—bare bone in the middle concha region with crusting. Pustule soon changed into a fistula and destruction of surrounding parts followed. Guinea pig inoculated with negative results. Caustics extensively employed coupled with antispecific treatment but with no effect. Progress of case characterised by great rises of temperature (of a septicæmic type) associated with marked œdema of the face and eyelids. Several hæmorrhages occurred from the ulcerated area, and one necessitated plugging. Cultivations showed numerous cocci and bacilli. The destructive ulceration continued and the patient died on *December 18th*. No glandular enlargement.

*Post mortem*.—Destruction of the face was very extensive, the bone being exposed from malar to malar ( $3\frac{1}{2}$  inches), whilst the whole external nose and most of the upper lip were destroyed.

## CASE II.

J.E.W., male, aged 36.

13.6.24.—Patient gave a history of trouble in the nose for the last two years. A feeling of stuffiness was first experienced, neither pain nor discharge being present. *On examination* the septum

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was deviated to the left and a small brownish ulcer was present on the left inferior concha. Septum resected and teeth removed. Wassermann reaction negative even after provocative dose.

30.7.24.—Examination showed the left side of the nose to be red and swollen and the ulcer had now reached the margins of the ala nasi and the upper lip on the left side. The septum showed a large perforation and the nose was blocked by yellowish-green foul smelling discharge and crusts. The right side of the nose was affected to a certain extent. There was nothing abnormal in the fossae or pharynx and posterior rhinoscopy revealed nothing abnormal. The left drumhead was bulging and showed a small posterior perforation. The report on the tissue removed at the first operation stated that there was a simple inflammatory condition but no evidence of malignancy. Patient seen by a skin specialist as the condition was now affecting the skin. The latter reported that he thought this case was syphilitic. Report on tissue removed at second operation stated that a chronic inflammatory condition was present. Anti-syphilitic treatment suggested. The X-ray photographs showed no apparent disease of the sinuses.

20.8.24.—Patient reported. Œdema and swelling present over the left side of the face. No pain and no temperature. The skin surface over the left alar cartilage was raised and looked like a case of erysipelas. The pores of the skin were distended with the yellowish secretion. On palpation the tumour was firm and there was no tenderness. Again the left side of the nose was filled with foul smelling crusts. The left middle concha was healthy. Nothing abnormal was seen on transillumination. Patient treated on the ordinary lines of ozæna and asked to report again.

15.9.24.—Nose a little cleaner. The ulceration on the left side has now involved the vestibule and there was a yellowish crust all round the ala nasi. Piece of tissue removed and material from it injected into a guinea pig. The results were entirely negative. Bacteriologist's report on piece of granular tissue showed that microscopic examination indicated the presence of a large number of micro-organisms including staphylococci, streptococci and pneumococci. These have been verified on culture. A gram negative bacillus apparently of the proteus group was also found. No tubercle bacilli were seen.

Wassermann reaction again taken and found negative. Acute mastoid infection has developed and a simple mastoid operation performed. Patient has made good progress as regards the mastoid condition. There is an ulcer over the left alar cartilage. On examining the inside of the nose it was discovered that the left ramus of the maxilla was bare and that there was a collection of pus under the soft tissues of the cheek extending up to the left infra-orbital margin. The whole of the tissues of the eyelid and left side of

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cheek showed swelling and œdema but no tenderness. Anti-syphilitic treatment was given. As time advanced there was more of the maxilla laid bare.

25.9.24.—As anti-syphilitic treatment was having no effect patient was again seen by another specialist who suggested malignant granuloma. Piece was removed for inspection.

30.9.24.—Patient has been getting progressively worse. A small ulcer was present on the hard palate.

11.10.24.—Radium applied, four platinum needles on a flat surface applicator being used. The result has been very good, although there has been an increase in swelling of the tissues and the discharge has become more profuse.

23.10.24.—Patient has made progressive improvement. 30 mg. of radium applied. The resulting reaction was mild and patient made good progress.

13.11.24.—Another 30 mg. of radium was applied for four and a half hours. Radium treatment continued.

The second and third applications of radium did more harm than good.

13.12.24.—The report stated that only a small piece of soft portion of tissue could be obtained, the remainder was bone and was being decalcified. Present section showed the presence of necrotic and inflammatory cells with no specific cell reaction. Report on hard tissue: The bone has been decalcified and showed a considerable degree of rarefaction of the bone trabeculae with the presence of a delicate fibrous tissue in the enlarged intertrabecular spaces and foci of cells of a chronic inflammatory type suggestive of a granulomatous condition. There was no evidence of tubercle or of syphilis.

In *February*, 1925, X-ray treatment was tried but nothing would stop the progress of the disease.

In *March*, 1925, the hard palate was perforated and he had such a free hæmorrhage from the nose that the external carotid artery was tied.

On 21.4.25 the patient died.

### CASE III.

Case O.L., male, aged 31, dental surgeon, came for consultation on 8.4.25.

He complained of nasal obstruction on the right side of three months' duration and a thick discharge which had been lasting for a week.

On examination a good deal of œdema and swelling below the right lower eyelid was noticed. A sinus was present about half an inch below the medial canthus of the right eye over the tear sac area.

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Anterior Rhinoscopy.—There was a marked deviation of the nasal septum to the right side narrowing this side very considerably and this, in addition to a swelling of the outer wall, practically completely blocked this side of the nose. This made it impossible to see into the upper regions of the nose. The left side of the nose was clear.

A great deal of post-nasal discharge was present.

Posterior Rhinoscopy could not be made.

Transillumination.—In spite of the swelling below the right eye the right maxillary sinus illuminated well. Both frontal sinuses illuminated.

Wassermann Reaction.—Negative. (The patient had had treatment for syphilis which did nothing to alleviate the condition. This diagnosis had ultimately to be abandoned. The local condition, even in the later stages, looked remarkably like a broken down gumma. Except for this there was nothing else that pointed to a syphilitic infection. During the war he was on active service in the East and was stationed in Egypt for a long while.)

He was referred to the Eye Department.

8.4.25.—He gave the history that he had an acute abscess over the inner corner of the eye last January which burst towards the end of the month. A discharge at intervals had been troubling him since then. It was found that a sinus from the lachrymal sac was discharging.

28.4.25.—A very large tear sac was excised.

4.5.25.—The wound was still open in the centre and oozing. He was sent back to the Ear and Throat Department.

6.5.25.—A swab from the nose was examined for bacteria. A growth of pneumococci, streptococci, staphylococci and diphtheroid bacilli was obtained.

11.5.25.—Area over the wound was still very œdematous and inflamed. Pus was exuded from the duct on pressure.

15.5.25.—An X-ray photograph showed an obscured right maxillary air sinus. A proof puncture of the right maxillary sinus was performed and a clot of mucus was obtained.

27.5.25.—The nose was much clearer and cleaner. The discharge from the tear sac wound had greatly diminished. A slight inflammatory element was still present and the œdema still marked.

10.6.25.—There was a little stream of pus coming down from high up and far forward in the right side of the nose. During the examination the right inferior concha was touched and it came away completely as a sequestrum.

26.6.25.—A snip was taken from an ulcer which appeared in the centre of the hard palate. A report by the pathologist was that it showed a chronic inflammatory reaction and a somewhat slowly

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growing epithelioma. The patient was told to douche his nose regularly as prescribed and to keep it clean. He was told to have his nose seen to again if there was no relief.

14.8.25.—The patient was sent to the Infirmary late in the evening with a note that he had been bleeding profusely from the nose and that it could not be stopped by anterior plugging. On admission he was very agitated and suffering from profuse hæmorrhage.

When a post-nasal plug was introduced the posterior edge of the nasal septum was felt to crumble, as also was the posterior edge of the hard palate. The bleeding could not be controlled in this way and it was found necessary to ligate the external carotid. This was done at 1 a.m. and soon effectively controlled the hæmorrhage.

27.8.25.—A foul smelling breath was noticed. Pus was noticed far back on the hard palate and it appeared as though a sequestrum was going to come away. He did not complain of pain.

4.9.25.—A well marked perforation of the hard palate was now present and a very foul greyish discharge, scanty in amount, was coming through the perforation. He complained of a sore throat and the uvula was somewhat œdematous.

5.9.25.—A snip from the edge of the perforation in the hard palate was taken and examined. The report was that there was no indication of a carcinomatous growth. There was a large amount of inflammatory reaction. There was no evidence of specific infection.

In view of the fact that no apparent causative organism had been found and the obviously granulomatous appearance of the lesion, a course of mercury salicylate was started.

8.9.25.—Swabs from the nose and the palate were examined and the findings in both instances were the same. No streptothrices were seen on direct film and anærobic culture. The organisms were chiefly streptococci and staphylococci.

21.9.25.—Temperature remained high. More discharge was coming from the nose. Another blood culture was made. The results again proved negative.

1.10.25.—The mercury salicylate treatment showed no visible effect and a course of sulpharsenol administered intramuscularly was commenced.

9.10.25.—The posterior pharyngeal wall had a sloughy appearance, greyish in colour, more so on the left than on the right side. The hard palate on the left side was greyish and sloughy. On the right side the perforation was extending into the alveolar margin. Comparatively little actual discharge of pus was taking place.

19.10.25.—The sulpharsenol up to now had not given any visible satisfactory result.

The application of X-ray locally was given once weekly. (Initial dosage 1/3 pastille.)

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26.10.25.—The local condition had remained more or less stationary since the X-ray therapy had been commenced.

4.11.25.—Scrapings from various parts of the ulcerating areas were taken and swabs from the *spreading* margins. (Particular care was taken that the swabs were from the spreading margins.)

There was an improvement of the nasal condition on the right side.

The bacteriological findings from the above swabs revealed yeast-like bodies in addition to organisms previously found.

Another Wassermann reaction proved negative.

Intensive sodium iodide treatment by mouth was then given and tinct. iod. nit. was applied locally.

9.11.25.—He had a slight hæmorrhage in the morning which was soon stopped by a peroxide gargle.

13.11.25.—The ulcerating margin in the hard palate was clearing up favourably. The bone included in the ulcerating area had become denuded and a fair sized sequestrum was noticed. The posterior wall of the oropharynx was also showing signs of clearing up, though patches of sloughy material were still present. The right side of the posterior wall showed areas in which pus was oozing from crevices (*sinuses from underlying bone*). The patient felt fairly comfortable.

16.11.25.—The margins of the palatal ulcer were almost clean. The pharyngeal wall still showed some thick greyish purulent discharge. There was a persistent purulent discharge, moderate in amount, from a sinus in the right side of the oropharynx.

Although on the whole the local condition was much cleaner and better than it was before the intensive iodide treatment, there was not much difference now between the present condition and that after the first week of treatment.

Blood count W.B.C. 11,800.

A film showed the presence of *immature white cells*.

18.11.25.—He had a slight hæmorrhage in the morning which was controlled by a strong peroxide gargle. Practically all the raw surfaces were oozing. Later in the day he dislodged some of the blood clot that had formed and had a very sharp hæmorrhage. The patient became extremely agitated.

It was decided to ligate the left external carotid artery in case of a hæmorrhage occurring, similar to the one when the right artery had to be ligated. Further bleeding was soon arrested.

23.11.25.—The healing process locally was very slow if existent, especially that of the oropharynx.

Posterior Rhinoscopy.—The hard palate was just a thin shelf of bone. Pus was coming from several points in the roof of the nasopharynx. The hard palate was still fairly firm. The medial pterygoid lamina on the right side had become bare.

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29.11.25.—His temperature was swinging very badly but he said he felt quite well and appeared quite bright.

Locally it seemed as if the healing process was progressing. The hard palate was still quite firm as also was the pterygoid process.

10.12.25.—No apparent change was seen in the local condition for the last twelve days. There were very persistent discharging foci, especially in the nasopharynx on the posterior wall. Drops of pus were coming from sinuses extending, apparently, into the sphenoid. The hard palate and pterygoid process on the right side had become movable. Iodide by mouth was stopped as this method of administration did not show the same effect as it had in the beginning.

12.12.25.—Locally there was more pus on the pharyngeal wall than previously. Pulling on the pterygoid process caused extensive bone movement.

Intravenous injection of sodium iodide was commenced and was administered every second day in doses of 100 c.cm. of a 10 per cent solution.

14.12.25.—The hard palate, which was denuded of soft tissues, was removed. This removal extended to within a short distance of the incisor teeth. The upper surfaces of the horizontal processes of the palatine bones and the palatine plates of the maxillae were covered with thick greyish pus. The pus seemed to be held together by a network of fine strands like those of a cobweb. The pterygoid process was quite loose but the patient could not endure further manipulations. One also feared the removal of this process as it seemed likely that a large piece of bone might come away and so expose the dura mater.

A view of the nasopharynx and the roof of the nose showed an extensive greyish sloughy-looking surface covered with somewhat scanty thick pus.

17.12.25.—The local condition had become decidedly worse. His breath was extremely fœtid. A prominent swelling was noticed over the medial end of the lower right eyelid. The conjunctival sac contained a small amount of yellowish grey fluid pus unlike the pus seen elsewhere. The temperature was swinging above 101°.

Blood count W.B.C. 12,000.

Differential count: Large numbers of miniature white cells were seen.

26.12.25.—What remained of the left side of the hard palate had become extensively involved and was covered with foul-smelling greyish sloughs. The surfaces in the right pterygo-palatine area were covered with similar greyish sloughs and a amount of pus was to be noticed. The alveolus on the right side

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posteriorly was extensively involved and the teeth were quite loose.

Posterior Rhinoscopy.—The appearance of the nasopharynx and the roof of the nose was the same as that seen elsewhere. The bony septum had almost completely disappeared.

27.12.25.—A small amount of blood was lost from a capillary hæmorrhage.

The right pterygoid medial lamina came away as a sequestrum. Blood clot was removed later and in doing this a large amount of sloughing tissue was removed from the posterior pharyngeal wall and the roof of the nasopharynx, including a small sequestrum which from its shape was apparently the remains of the vomer.

30.12.25.—He had been in a semi-comatose state for the last few days and in a very weak condition. There were no signs of meningitis.

Patient died on 1.1.26.

### *Post mortem.*

*General Appearances.*—The body was that of a very emaciated adult male.

*Body Cavities.*—On opening the body cavities almost complete disappearance of subcutaneous and other body fat was seen.

*Nasal Cavities and Nasopharynx.*—On looking at the nasal and nasopharyngeal cavities from below, the roof of the nose and nasopharynx could be seen, owing to almost complete destruction of the hard and soft palates, with exception of the extreme anterior portion of hard palate and nasal septum. The roof of the right maxillary sinus and a portion of the roof of the left antrum could be seen; the latter cavity contained pus.

On the right side, the inferior and middle concha and lateral nasal wall had disappeared.

On the left side, there were the remains of the left middle concha.

In the mesial plane the upper part of the nasal septum remained, along with ethmoidal cells laterally. These areas were bathed in pus.

The vault of the nasopharynx was exposed to view and was covered by dirty, necrotic tissue.

The ulcerated, necrotic area was very extensive and included the nasal structures enumerated above. In addition it involved the lateral and posterior walls of the nasopharynx and pharynx, reaching as low as the level of the aryepiglottic folds on each side.

The alveolar margins were intact, but the upper molars on the right side were loose.

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*Cranium and Contents.*—There was some excess of clear cerebrospinal fluid. Otherwise the skull, meninges and brain showed no pathological changes.

The base of the brain was normal.

*Other Organs.*—All the organs showed general atrophy, but otherwise there were no pathological changes to be seen by the naked eye.

The blood culture yielded no growth.

The agglutination test against yeast was difficult to carry out as there was difficulty in preparing a perfectly homogeneous emulsion of the organism.

There was, however, definite agglutination at 1/10 and 1/20 dilution of the patient's serum, doubtful agglutination at 1/40.

### CASE IV.

G.H., male, aged 39.

*October, 1927*, admitted to a Sanatorium for treatment, when the following history was obtained from him. Fourteen years ago he had a motor bicycle accident, when the right jaw was injured. Three years ago he had an aching pain behind the upper jaw for which some teeth were extracted without, however, any relief. Two years ago the left maxillary air sinus discharged spontaneously into his nose, when a small operation was performed on it. One year ago he had some pain in his left maxillary air sinus and it was found, on examination, that the maxillary air sinus appeared to be healthy and had free drainage. He then had all the upper and lower teeth removed, with no subsequent alleviation of his pain.

Six months ago he suffered from an ischio-rectal abscess which was operated upon successfully. The left maxillary air sinus then flared up twelve days after the ischio-rectal abscess had been operated upon and pus burst through the facial maxillary wall of the air sinus. An operation was performed on the air sinus and a tuberculous infection was then suspected. Four months ago a piece of dead bone was removed from the left upper jaw and a sinus appeared in the roof of the mouth. Six weeks ago the patient had a severe hæmorrhage from the left maxillary air sinus which necessitated operative treatment. He was then admitted to the Sanatorium as a case of suspected tuberculosis. On examination, there was a large opening in the roof of the mouth about three-quarters of an inch in diameter into the left air sinus which also involved the whole of the left upper jaw region. Granulations and pus were present in the air sinus.

Blood count showed R.B.C. 4,350,000. H.B. 65%.

W.B.C. 14,800; Differential count:

Polymorphonuclears 70%. Small lymphocytes 24. Large lymphocytes 5. Eosinophils 1%.

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Blood sedimentation seventeen minutes—accelerated.

Wassermann reaction negative.

Patient complained of severe neuralgic pain in the head. Confined to bed and has run a septic type of temperature. Has been treated with ultra-violet light daily with no beneficial effects.

21.11.27.—Piece of tissue excised for examination. Reported on by Professor Cruickshank, Aberdeen, who stated that there was considerable infiltration with lymphocytes but no evidence of tuberculosis.

A second piece of tissue showed the structure of a cellular fibroma.

14.11.27.—Patient has been sleeping badly and losing weight. Has been kept in bed and temperature is still raised.

As regards the local condition, there seems to be a burrowing into the bone on the posterior wall of the cavity with foul discharge. Pain is considerable and is located chiefly in the trigeminal area.

3.12.27.—Left maxillary air sinus cavity scraped out and swabbed with pure alcohol with a view to destroying the nerve-endings. Almost the whole of the malar bone seemed to be necrosed, also the soft tissues of the left upper jaw.

X-ray therapy advised.

January, 1928.—Hard palate has necrosed and pain very much worse. The free edge of the palate has been irregular in outline due to active ulceration. Pus also present from pterygoid fossa.

15.1.28.—Hæmorrhage occurred.

23.1.28.—Swelling of face greatly increased and fluctuation present. Pus obtained on puncture and free opening made into soft tissues through mouth. Discharged from Sanatorium as non-tubercular.

Bacteriologist's report.—Swabs from palate and diseased areas were consistently negative for T.B. Pus from cheek showed numerous organisms, chiefly Gram positive cocci in short chains and Gram negative bacilli. A few Gram negative diplococci of catarrhalis type also present.

For the above notes I am indebted to Dr. J. M. Johnston, Physician Superintendent, Tor-na-Dee Sanatorium.

16.2.28.—Case under the charge of Dr. A. Logan Turner.

Another piece of tissue removed for microscopic examination. No definite structure of any neoplasm could be found but ulceration with tissue infection and a soft or cellular-like fibrous structure was seen. It was not a carcinoma or a sarcoma.

On examination there was a spreading destruction of the soft palate and left maxilla, including all the bony walls of the left antrum also extensive ulceration of the left cheek.

Treatment with surgical diathermy given, which made not the

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slightest difference to the progress of the disease. X-ray therapy was equally useless.

The patient finally died from pneumonia on 18.10.28, the period of active disease being just under two years.

### CASE V.

C.T., male, aged 36.

In *July*, 1930, patient first noticed a painless swelling on the right side of his nose. He consulted his doctor in *September*, by which time there was a foul smelling, whitish yellow discharge from the nose. Patient was sent to Dr. J. S. Fraser and admitted to the Ear, Nose and Throat Department. A specimen of tissue was taken but microscopic examination revealed no tubercle bacilli. Operation was considered but, as he was running a temperature of  $104.5^{\circ}$  it was postponed. Dr. Logan Turner was consulted and found that patient was fit, except for the temperature. Urine, sputum and blood were tested and found negative.

By this time the swelling had increased in size and the nasal discharge became more profuse, the right nasal passage being completely obstructed. Patient was examined by Dr. Cranston Low and erysipelas was ruled out and injections were suggested. Two injections were therefore given into the arm. In *October* the patient had X-ray treatment. As a result of this his temperature came down to normal and the swelling in the nose was rapidly going down. He was allowed up and, after further examination by Dr. J. S. Fraser, was allowed to go home.

Three weeks later the patient had further X-ray treatment as an out-patient. He returned a month later but X-ray treatment was not repeated as the swelling had nearly gone and the nose had cleared. He reported again to Dr. Cranston Low in *November* and was pronounced fit and no further treatment was advised.

During the first week of *December* the patient's eye began to water. He bathed it with boracic lotion which improved the condition for two days. A fortnight later the side of his nose and the medial canthus of the eye became swollen and painful. The pain was so severe that on *December 30th* he went to bed. Two days later, as there was no improvement, he returned to the Ear, Nose and Throat Department. He was referred to the Eye Department as it was thought that the lachrymal sac was involved. Hot fomentations were recommended and the following day the swelling on the side of the nose burst just below the medial canthus of the eye and greenish matter was exuded. He returned to the Eye Department and was told to report when the inflammation had subsided, after which the lachrymal sac was to be removed. Patient was seen by Dr. Traquair, who did not consider that the tear sac was the cause

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of the trouble. He was then transferred to the wards of Professor D. P. Wilkie to whom we are indebted for the following notes :—

Patient is a moderate smoker and drinker. At work he is exposed to weather and inhales petrol fumes.

Previous history—nothing of note.

Family history—nothing of note.

On examination patient looks healthy and well nourished. Colour good.

*Face.*—There is a swelling on the right side of the face involving the side of the nose, the medial canthus of the right eye, the lower eyelid and extending down to the cheek and right ala of the nose. It is red, brawny, shiny and feels hot to the touch. About 1 cm. below and medial to the medial canthus of the eye, there is a small hole from which a clear, syrupy fluid escapes. There is also a pustule about the size of a threepenny bit in the groove between the ala and cheek. There is pain in the swelling and a dull ache is felt on pressure over the cheek. There is also some tenderness in the lower jaw. The swelling has a brawny, hard portion in the region of the cheek but no definite outline can be made out. Below the eye the swelling is softer. Fluctuation can be detected.

The right nostril is completely blocked by bulging mucous membrane and between the contiguous surfaces of the mucous membrane a yellowish green matter exudes.

*Teeth.*—Artificial.

*Tongue.*—Clean.

*Abdomen.*—Quite normal.

*Cardiovascular System.*—Pulse—regular in time and force. Heart—not enlarged, sounds pure.

*Respiratory System.*—Normal vesicular breathing.

*Blood Examination.*

|        |    |    |    |    |           |
|--------|----|----|----|----|-----------|
| R.B.C. | .. | .. | .. | .. | 4,210,000 |
| W.B.C. | .. | .. | .. | .. | 4,600     |
| H.B.   | .. | .. | .. | .. | 82%       |

*Differential Count.*

|                   |    |    |    |    |       |
|-------------------|----|----|----|----|-------|
| Polymorphs        | .. | .. | .. | .. | 45·7% |
| Large lymphocytes | .. | .. | .. | .. | 18%   |
| Small lymphocytes | .. | .. | .. | .. | 32%   |
| Large hyalines    | .. | .. | .. | .. | 4%    |

5.2.31.—X-ray of the nasal sinuses showed obscurity of the right maxillary antrum and right ethmoidal cells.

6.2.31.—Operation. Professor Wilkie. Gas and oxygen anæsthesia. Small incision over centre of swelling in the right cheek. Sinus forceps introduced but no pus evacuated. A culture of the blood-stained fluid was taken, also a culture of the foul smelling discharge from the nose.

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|                 |    |    |    |    |                  |
|-----------------|----|----|----|----|------------------|
| 8.2.31.—W.B.C.  | .. | .. | .. | .. | 3,000            |
| 11.2.31.—W.B.C. | .. | .. | .. | .. | 5,000            |
|                 |    |    |    |    | (before nuclein) |
| H.B.            | .. | .. | .. | .. | 52%              |

Report on exudate from swelling of cheek showed red blood cells, some pus cells and some epithelial cells: Diphtheroids and staphylococcus albus were present, along with a very minute streptococcus; the latter could not be obtained on culture. Some filaments were present but no true streptothrix was found in films or obtained on culture.

### 25.2.31.—*Differential Count.*

|                   |    |    |    |    |       |
|-------------------|----|----|----|----|-------|
| Polymorphs        | .. | .. | .. | .. | 53·7% |
| Small Lymphocytes | .. | .. | .. | .. | 33·5% |
| Large Lymphocytes | .. | .. | .. | .. | 8%    |
| Myelocytes        | .. | .. | .. | .. | 5%    |

### 2.3.31.—*Blood Count.*

|                  |    |    |    |    |                     |
|------------------|----|----|----|----|---------------------|
| R.B.C.           | .. | .. | .. | .. | 4,800,000           |
| W.B.C.           | .. | .. | .. | .. | 6,500               |
| H.B.             | .. | .. | .. | .. | 70%                 |
| C.I.             | .. | .. | .. | .. | 0·73                |
| Bleeding time    | .. | .. | .. | .. | 4 minutes           |
| Coagulation time | .. | .. | .. | .. | 6½ minutes          |
|                  |    |    |    |    | (Control 7 minutes) |
| Platelets        | .. | .. | .. | .. | 210,000             |
| Reticulocytes    | .. | .. | .. | .. | None seen           |

### *Fragility.*

|                    |    |    |    |    |        |
|--------------------|----|----|----|----|--------|
| Partial hæmolysis  | .. | .. | .. | .. | =0·4%  |
| Complete hæmolysis | .. | .. | .. | .. | =0·35% |

### *Differential Count.*

|                        |    |    |    |    |     |
|------------------------|----|----|----|----|-----|
| Polymorphs             | .. | .. | .. | .. | 46% |
| Small Lymphocytes      | .. | .. | .. | .. | 28% |
| Large Lymphocytes      | .. | .. | .. | .. | 11% |
| Transitionals          | .. | .. | .. | .. | 12% |
| Eosinophils            | .. | .. | .. | .. | 3%  |
| Degenerate polymorphs. |    |    |    |    |     |
| No abnormal reds.      |    |    |    |    |     |

*Progress.*—Patient has been given six intravenous injections of 5% nucleic acid given every other day, starting on 9.2.31. After each of these he had a very marked reaction—a rigor would come on within twenty minutes to half an hour after the injection, the temperature rose on each occasion to between 105° and 106·2°, pulse between 130 and 142.

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The white blood count on the first occasion before nucleic acid was 5,600, after 7,650.

|                                       |        |
|---------------------------------------|--------|
| On the second occasion before nucleic | 5,000. |
| after „                               | 8,200. |
| On the third occasion before „        | 4,200. |
| after „                               | 8,400. |
| On the fourth occasion before „       | 3,600. |
| Taken whilst the rigor was present    | 6,200. |
| and afterwards                        | 5,800. |
| On the last occasion it started at    | 5,200. |
| after                                 | 7,000. |

21.2.31.—Patient was given .45 gr. neokharsivan intravenously. He had a slight reaction after this. The following day the temperature rose to 103.2°. There was some local reaction.

There has been no improvement in the patient's condition. There was a steady but gradual increase in the size of the sloughing area at the side of the nose. The associated reaction and swelling of the face varies from day to day, on some days the eye is completely closed and on others it is not. The discharge is always foul smelling.

3.3.31 and 4.3.31.—5 gr. tartar emetic.

5.3.31.—.45 gr. neokharsivan followed by very little general reaction and no perceptible local reaction.

The ulcer appears to be gradually but slowly increasing in size; the edges are well defined and the bone is covered by a greenish yellow slough which is foul smelling. The surrounding œdema varies from day to day. Still no swelling of lymph nodes in the neck.

11.3.31.—Patient given local X-ray treatment followed by local erythematous reaction.

12.3.31.—W.B.C. .. .. . 4,200

Wassermann reaction negative.

17.3.31.—W.B.C. .. .. . 3,000

22.3.31.—Started on radiostolium.

25.3.31.—Second application of X-ray treatment. Started on liver extract 1 dr. b.i.d. Given 1 c.cm. of cuprum intramuscularly.

The ulcer on the side of the nose appears to be increasing in size. There is a small point higher up on the side of the nose where the skin has broken down and a discharge is seen coming from this point.

Patient is still running a temperature varying from 99°-102°.

8.4.31.—*Blood Count.*

|                |           |
|----------------|-----------|
| R.B.C. .. .. . | 4,020,000 |
| W.B.C. .. .. . | 4,200     |

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14.4.31.—*X-ray Examination.* No bone lesions demonstrated—but there is always a difficulty in demonstrating lesions of face bones. Marked density of right maxillary air sinus.

15.4.31.—*Blood Count.*

|        |    |    |    |    |           |
|--------|----|----|----|----|-----------|
| R.B.C. | .. | .. | .. | .. | 3,800,000 |
| W.B.C. | .. | .. | .. | .. | 4,000     |

*Differential Count.*

|                    |    |    |    |    |           |
|--------------------|----|----|----|----|-----------|
| Polymorphs         | .. | .. | .. | .. | 65%       |
| Small lymphocytes  | .. | .. | .. | .. | 26%       |
| Large lymphocytes  | .. | .. | .. | .. | 8%        |
| Transitional cells | .. | .. | .. | .. | 1%        |
| 24.4.31.—W.B.C.    | .. | .. | .. | .. | 3,200     |
| 25.4.31.—W.B.C.    | .. | .. | .. | .. | 2,200     |
| 12.5.31.—R.B.C.    | .. | .. | .. | .. | 3,870,000 |
| W.B.C.             | .. | .. | .. | .. | 4,000     |

14.5.31.—*Differential Count.*

|                     |    |    |    |    |     |
|---------------------|----|----|----|----|-----|
| Polymorphs          | .. | .. | .. | .. | 75% |
| Large lymphocytes   | .. | .. | .. | .. | 7%  |
| Small lymphocytes   | .. | .. | .. | .. | 15% |
| Mononuclear         | .. | .. | .. | .. | 2%  |
| Transitional        | .. | .. | .. | .. | 1%  |
| 15.5.31.—Polymorphs | .. | .. | .. | .. | 73% |
| Large lymphocytes   | .. | .. | .. | .. | 6%  |
| Small lymphocytes   | .. | .. | .. | .. | 17% |
| Mononuclear         | .. | .. | .. | .. | 1   |
| Transitional        | .. | .. | .. | .. | 1   |

*Treatment and Progress.*

9.2.31.—Given nuclein 5 c.cm. intravenously.

11.2.31.—Temperature down to 98°. Nuclein 5 c.cm. intravenously.

13.2.31.—Nuclein 5 c.cm. intravenously. Temperature rising. No improvement in condition of face.

15.2.31.—Nuclein 5 c.cm. intravenously.

17th and 19th.—Nuclein 5 c.cm. intravenously.

26.2.31.—Temperature settled.

2.3.31.—0.5 gm. tartar emetic intravenously.

3.3.31.—Repeated.

4.3.31.—Blood pressure 58/38.

5.3.31.—0.45 gr. neokharsivan.

11.3.31.—X-ray treatment.

24.3.31.—Condition spreading, right eye and upper lip involved. Liver extract dr. 1 b.i.d. X-ray treatment. Cuprum 1 c.cm. intramuscularly.

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- 27.3.31.—Cuprum 2 c.cm. intramuscularly.  
29.3.31.        "    3 c.cm.        "  
3.4.31.        "       "        "  
5.4.31.        "       "        "        Temperature rising.  
8.4.31.        "       "        "  
9.4.31.        "       "        "  
13.4.31.       "       "        "        Swelling spread over to  
  the left. Cheek and  
  upper lip involved.
- 17.4.31.       "       "        "  
21.4.31.—Sterile milk 5 c.cm. intramuscularly.  
25.4.31.—Bayer " 205 " 10,000 units intravenously.  
28.4.31.—X-ray treatment. Bayer " 205 " intravenously.  
Whole face involved. Both eyes closed. Developed a visible  
tremor. Getting weaker. Mind beginning to wander.  
1.5.31.—Bayer " 205 " intravenously.  
9.5.31.        "       "        "        Condition much worse.  
16.5.31.       "       "        "  
17.5.31.—Temperature down. Patient very weak.  
18.5.31.—Death.
- 10.3.31.—Report on blood in broth and Trypsin broth showed  
that a growth of a gram positive bacillus has been obtained from  
both cultures. It ferments no sugars, is apparently non-spore  
bearing, is aerobic. The probability is that it is a contamination,  
as it does not seem to conform to any known pathogenic type likely  
to cause a blood infection.
- 16.3.31.—Flocculation test of serum for syphilis (Sachs Georgi  
reaction)—negative.  
Arginase reaction of serum (frequently positive in malignant  
disease)—negative.  
Blood culture 12.3.31—negative.
- Bacteriological examination of secretion from right nostril and  
from surface of ulcer in right cheek :—Microscopical examination  
and aerobic and anaerobic culture showed many cocci and bacilli of  
probably saprophytic importance but no pathogenic species was  
recognised. No acid-fast organisms found.
- 15.4.31.—From a small sinus which recently opened below the  
inner canthus of the right eye, microscopical preparations and  
cultures have been made on two occasions, with the following  
results :—  
Hæmolytic streptococci in large numbers.  
Staphylococci.  
Diphtheroid bacilli.  
No evidence of streptothrix actinomyces has been found.
- 11.5.31.—Blood culture in Trypsin broth and in ordinary broth.  
Trypsin broth : A growth of staphylococcus albus only, was

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obtained. Ordinary broth: A good growth of Pfeiffer's Bacillus has been obtained together with some diphtheroids.

6.2.31.—Report on (1) swab from nostril, (2) swab from lachrymal sac. Direct films showed staphylococci. Cultures made from both swabs (1 and 2). Good growth of staphylococcus on each.

19.5.31.—Report on heart-blood culture—*post mortem*. A mixed growth of a non-hæmolytic streptococcus and a group 4 pneumococcus was obtained.

### *Post Mortem.*

*General Appearances.*—The body was that of a fairly well nourished male without developmental anomaly. *Post mortem* rigidity was marked and lividity was present on the back.

*Face.*—The right side of the face was greatly swollen. The right eye was closed, but purulent fluid was escaping from between the lids. There was no redness of the skin, and the swelling was chiefly due to œdema.

The right nostril opened into a greatly-widened nasal cavity and from this, also, pus was escaping.

A Fergusson incision was made to expose the maxilla and lower margin of the orbit.

The anterior surface of the maxilla and floor of the orbit were removed and the antrum displayed. The antrum was much larger than usual and was filled by a yellow, gelatinous, purulent substance. The mucous wall of the antrum appeared to be absent and the cavity was lined by thin bone with a granular surface. This granular appearance was also present on the bone forming the floor of the orbit and also on the nasal aspect of the maxilla.

The soft tissues of the face were uniformly œdematous.

There was no inflammation in the tissues of the neck.

*Serous Sacs.*—Peritoneal Cavity—contained no free fluid and its walls were healthy.

*Pleural Sacs.*—no free fluid and no adhesions present.

*Pericardial Sac.*—contained perhaps 2 oz. of clear yellow fluid.

*Circulatory System.*—Heart—was enlarged. The right atrium and ventricle were dilated and the tricuspid valve admitted four fingers easily.

The chambers of the left side of the heart were also dilated and the mitral valve admitted three fingers easily.

The heart muscle was fairly firm and of quite a good colour.

The aortic valve was competent and the cusps of all four valves were healthy.

*Respiratory System.*—Larynx—the mucous membrane was healthy, but in its posterior part the cricoid cartilage was completely necrosed and replaced by a minute abscess cavity the size of a pea and containing greenish necrotic material and pus.

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Trachea—bore a congested mucous membrane in its lower part and contained a good deal of mucoid secretion.

Lungs—both were uniformly congested and highly œdematous.

*Alimentary System.*—Œsophagus—was healthy apart from *post mortem* erosion.

Stomach—was contracted. It contained a small quantity of clear yellow fluid, and its walls were healthy.

Duodenum and Intestines—were healthy.

Liver—was enlarged. Its surface was smooth and regular. The cut surface was pale and soft.

Spleen—was perhaps slightly enlarged. The cut surface was dark purple in colour but of firm consistency.

Pancreas—was healthy.

*Genito-Urinary System.*—Kidneys—neither kidney was enlarged. The capsule on each side stripped easily to leave a smooth surface and, on section, the usual appearance of cortex and medulla was maintained.

Ureters and Bladder—were healthy.

*Bone Marrow.*—The bone marrow was gelatinous and its colour did not differ from the normal.

### CASE VI.

Male, aged 68, reported in *February*, 1914.

On examination the bridge of the nose was seen to be sunken just below the nasal bones. Region of right lachrymal sac was swollen and there was a fistula below the inner canthus. Both sides of the nose were filled with foetid crusts; cartilaginous septum gone; walls of nose in a condition of ulceration. Wassermann reaction negative. Specimen of blood taken and found to be normal. Salvarsan administered intravenously. Mercury and potassium iodide prescribed, but all without the slightest obvious effect on the disease. Interior of nose cauterised. In every examination granulation tissue was the dominant feature, but in one place at least it developed into something very like a sarcoma. Iodine injected subcutaneously for some time but without effect. Several tests of the blood gave a negative Wassermann reaction. Patient admitted to hospital for some weeks, during which time the temperature remained normal. Two months later the left lachrymal sac was swollen as the right originally was, but the fistula on the right side had healed. Patient attended hospital intermittently during 1915. Early in 1916 the disease, which had hitherto been marked by the absence of obvious tumour, began to infiltrate the soft palate and back of the nose. In *June* a necrotic area developed on the right side of the soft palate and at the end of *July* it perforated the palate. X-ray therapy given. This treatment was carried out

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at the end of *July* and during *August*. No improvement resulted. On *September 17th* the soft palate was infiltrated in its whole extent. The perforation had increased in size, the increase being towards the middle line. The edges of this perforation were very definite and sharp. The floor of the ulcer was covered with a greyish slough. *November, 1916*, ulceration had progressed. Patient put on large doses of potassium iodide three times a day. Patient's condition became steadily worse—septum and turbinated bones were completely destroyed, but the tissues of the face were never attacked.

Patient died at home in *October, 1918*, four and a half years after the onset of the disease.

### CASE VII.

Male, aged 67. First seen in *February, 1920*, when he complained of discomfort in his nose.

On examination, both sides of the nose were filled with glutinous crusts; the septal cartilage was almost completely destroyed; the ulceration appeared to be spreading along the floor of the left side of the nose. No sinking in of the nose below the bridge. Wassermann test negative. Piece of ulcerated tissue removed for microscopic examination which showed a very cellular granulation tissue invading the nasal cartilage with many polymorphs in the tissue. The vessel walls were not thickened. Mercury and potassium iodide were prescribed and a dose of novarsenobillon administered. A week after this injection a necrotic area appeared on the roof of the mouth on the left side of the hard palate. Through the floor of the slough, necrosed bone could be felt by the probe. Wassermann reaction again negative. The condition of patient grew steadily worse. The necrosis spread to the neighbouring parts of the maxilla, burrowing under the tissues of the cheek. Severe pain set in on the left side of the face in *June*. The nasal process and a large adjacent portion of the left maxilla was isolated and necrotic. The tissues of the face were attacked above the fold of the nostril and necrosed, leaving a large perforation with tender granular edges between the nose and the cheek through which dead bone could be seen and felt over a large area. Treatment consisted of cauterisation of the ulcerated surfaces by mechanical cauteries but with no avail. Treatment with radium began in *June*. In about two weeks it was evident that great improvement had resulted—the posterior part of the palatal perforation had epithelialised. Another dose of radium was given on *July 17th* and in ten days' time the change was startling—the swelling had subsided, the tenderness was very much reduced and the pain had ceased to such an extent that the patient could sleep without drugs. In *October* the front of the left maxilla, which had become quite loose, was easily removed through the

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palatal perforation. In the latter half of 1920 the patient put on weight. In *April*, 1922, a swelling appeared in the inner wall of the left nose, near the body of the sphenoid. This was certainly a recurrence but disappeared in ten days after an exposure of radium.

On *November 22nd*, 1922, patient was admitted to hospital with a nodular purpurul swelling on each shin. Piece removed for examination appeared to be a small round celled sarcoma to which the name "sarcomatosis cutis" was given. It was treated with radium, without apparent success. A similar swelling appeared on each thigh and, later, on the anterior abdominal wall. He died on *December 22nd*, 1922.

*Post mortem* examination showed secondary deposits of small round celled sarcoma in the liver, lungs and both testicles. There was no recurrence in the nose.

### CASE VIII.

Male, aged 42.

Four years ago submucous resection of the nasal septum was performed. A small perforation was noticed in the anterior region of the septum following operation. Patient experienced relief for a time but then began to blow crusts from his nose and the obstruction returned.

Examined in *April*, 1922, when it was seen that in the anterior region of the septum there was a large perforation which was bordered by a broad fungating mass of tissue which greatly obstructed the airway. In parts the mass was covered by glutinous crusts which had a foetid odour. The mass was removed and examined microscopically. Wassermann reaction was negative.

*August*, 1922.—An apparent recurrence of the growth was noticed in the upper anterior and upper posterior regions of the perforation. This gradually subsided after the application of radium emanations.

*November*, 1922.—A perforation appeared in the centre of the hard palate which slowly increased in size. Radium was applied to the perforation but had no apparent effect. Another blood test was negative. Patient put on potassium iodide. Culture from the tissue in the palatal perforation yielded a growth of staphylococcus aureus. Several doses of ordinary X-rays produced no improvement.

*February*, 1923.—Perforation appeared in the soft palate. Anti-syphilitic treatment was pushed. In spite of this treatment ulceration spread rapidly, so that a month later the uvula had sloughed away and the whole of the palato-pharyngeal arch was in a condition of ulceration. The anterior end of the right inferior turbinate was ulcerated. There was swelling and tenderness of the face over the right maxilla. Patient complained of pain at night

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which prevented sleep. A third blood test was performed, but was found negative. Deep X-ray therapy was given with marked improvement. However, later on, a bare area of bone was discovered on the alveolus of the right maxilla and it was evident that the whole of this bone was necrotic. Patient complained of pain round the right eye and the lid became puffy. He also complained of double vision. Second dose of deep X-ray therapy was given and this was followed by relief of pain and he gradually recovered from the diplopia.

*September, 1923.*—Third dose of deep X-ray therapy given. The necrotic maxilla gradually came away spontaneously in sequestra of various sizes. A year has elapsed since the last dose and there has been no recurrence.

Dr. McArthur kindly wrote to me about the subsequent course of this patient and also sent me a microscopical section of the tissue which he had removed. Patient died in 1927 from erysipelas and broncho-pneumonia. For about two years before his death he had attended the Out-Patient Department of the Melbourne Hospital for “miners’ phthisis”. I do not know if tubercle bacilli were ever found in his sputum. He also remarked that if the nasal condition had been tuberculous why did it respond in such a remarkable way to deep X-ray therapy. He added that in this case it might have been possible for multiple sarcomata scattered throughout the lungs to give a clinical picture of fibroid phthisis and in this case no autopsy had been permitted.

### CASE IX.

Male, aged 29, seen in 1923 for a nasal catarrh persisting for two years, with mucopurulent secretion, adherent crusts and nasal hæmorrhages. During the four months the disease had settled with a progressive thickening on the root of the nose. There is also a swelling at the extremity of the nose making it almost double in size.

Local State: Swelling of nose. Considerable enlargement of root which fills up space between the eyes. This region appears to be invaded by an infiltration which spreads already to the eyelids and spreads on each side towards the internal angle of the eyes. Infiltration red and glistening, extending to lower part of nose, which is doubled in size, and on to the narine which appears to be tumefied. From left nostril infiltration descends to upper lip. Skin over root of nose adherent to bone. Examination of narine orifices shows a congested and infiltrated mucous membrane. Intense alveolar inflammation in the mouth. Papular-pustular rash appeared on forehead, lips, ears and thorax.

Condition progresses. Below the left narine, ulceration develops. Mastication difficult—upper jaw teeth commencing to drop out.

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Wassermann reaction always negative. Cartilaginous septum perforated then slowly destroyed. Mucopurulent secretion with formation of crusts and slight hæmorrhages. Respiration only possible through mouth. Hard palate is ulcerating away. Fever irregular. Pustulo-papular eruption spreading over body—superficial sarcoid. No glands. No enlargement of spleen. Naso-maxillary lesion spreading rapidly. Upper lip wholly infiltrated—central portion necrosing. Only a rag of mucous membrane and skin join the labial extremities. Central ulceration—fœtid odour—covered over with black crusts is continuous with nasal lesions. Septum entirely destroyed—left nares disappeared, right nares largely encroached upon and in the bottom of this ulceration one sees the bone proper denuded of nose and osseous septum. Floor of nares necrosed. Nose and mouth form one single cavity. The peripheral involvement has progressed in all directions between the eyelids and on to the forehead. Same eruption on body—sarcoid. Ulceration destroys left nares and the right nares completely. Upper lip has disappeared. Died *February*, 1929. Negative blood cultures. Inoculation of vaccines negative.

### CASE X.

*September*, 1929.—Female, age 32. Complained of swelling and soreness at tip of nose with difficulty in breathing.

Present illness started in *March*, 1929, the patient developed severe watery nasal discharge. Condition persisted. Wassermann negative. In latter part of *August* given anti-syphilitic treatment.

*August*, 1929.—On examination perforation of septum, extensive crusting and very marked swelling in the floor of the nose, more marked on the right side, were seen. Wassermann negative. Anti-specific treatment no effect.

*September 26th*.—The nose was swollen, especially around the tip, and was reddened and infiltrated. Infiltration did not show the hardness of scleroma. Odour similar to that of advanced case of atrophic rhinitis. Anterior portions of both nostrils filled with a necrotic mass which involved the lower portion of the cartilage of the septum and the floor of the nose. On removing this material with forceps a bleeding granulating surface was exposed, through which rather extensive areas of exposed bone in the floor of the nose could easily be probed. The picture was typical of a breaking-down gumma of the septum and surrounding area. There was some tenderness around the upper incisor teeth, but no marked pathological condition of the mouth could be noted. There was a very slight enlargement of the cervical lymph nodes.

In spite of the negative history, negative Wassermann, and negative therapeutic results, a provisional diagnosis of tertiary syphilis of the nose was made.

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She was seen in consultation by Dr. Sigmund S. Greenbaum, who agreed with this opinion, and she was placed on active antiluetic treatment, consisting of 0.45 gm. of neoarsphenamine intravenously every five days with 1 gm. bismuth intramuscularly.

The subsequent course of the case was one of gradual progression in spite of all types of treatment.

During the early part of her stay at the hospital she ran a normal temperature and normal pulse-rate. After the disease had become more extensive, her temperature, at times, showed some evidence of general sepsis, never rising, however, above 102°F.

For the first few weeks there was possibly a slight improvement in the local condition, certainly lessening of pain. This, however, was very transitory. The infiltration gradually spread laterally and downwards, involving the alae of the nose and upper lip. At one time distinct nodular swellings could be seen in the skin of the right nasal vestibule. As the infiltration advanced, the ulcerative or destructive area kept pace with it so that the interior of the nose, the septum, the alae and nostrils were more and more excavated and larger areas of denuded bone were exposed.

Because of the extreme tenderness she was given a general anaesthetic three times for purposes of examination, treatment and for obtaining material for biopsies. In the anterior part of the nasal fossae there were always some areas resembling a neoplasm which cut with the resistance of rather firm fibrous tissue.

Pain was a fairly prominent symptom and the use of narcotics became more and more necessary as the condition grew worse. The extreme tenderness of the nose and surrounding areas was very noticeable.

Careful physical examination made at various times failed to reveal any other evidence of disease. A Roentgen-ray of her chest was negative, and there did not at any time seem to be any involvement of the accessory sinuses of the nose.

On *October 13th*, 1929, a spinal puncture was done. Pressure was 15 mm. Hg. The fluid was clear and negative for Wassermann test. The pressure increased on coughing. The cell count was 4 cells per c.mm. Globulin was not increased. Colloidal gold was 0,000,111,000.

Laboratory findings were practically all negative as far as the diagnosis was concerned. Both secretion and tissues were examined for actinomycosis, but no ray fungus was found. There were no Bacillus mallei and the complement-fixation test for glanders was also negative. Rhinoscleroma was ruled out both by a biopsy and the absence of bacillus of rhinoscleroma. Cultures taken at various times showed numerous pyogenic organisms of various types, such as hæmolytic streptococci, non-hæmolytic streptococci, staphylococcus albus, diphtheroids, some Gram-positive cocci and Bacillus

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subtilis. No streptothrix or sporothrix were ever found. Although for three or four days, at one time, acid-fast bacilli were found in fairly large numbers in the secretions, they were never found in the tissues, and the biopsy failed to show any histology which would make a diagnosis of tuberculosis justifiable. For a few days after the acid-fast bacilli were found, the possibility of leprosy was considered, but this was finally absolutely ruled out.

Several guinea-pigs were inoculated, but all with negative results as far as tuberculosis was concerned. Several of them died from septicæmia.

Her leucocyte count varied from 14,000 to 6,000, with from 72 to 80 per cent polymorphonuclears. Her red cells varied from 3,470,000 to 3,800,000. Urine examination while at the hospital was always negative.

At the time of her leaving the Graduate Hospital the condition had so spread as to involve the cheeks on both sides with dilatation of the nostrils so that it was possible to view anteriorly the nasal cavities without speculum and perforation between mouth and nasal cavities behind the upper lip seemed imminent. She left the Graduate Hospital on *December 31st, 1929*, and was admitted to the Hazleton Hospital on the same day, where she stayed until the time of her death, *September 4th, 1930*.

As a local treatment her nose was douched bi-daily with a 1 to 3,000 potassium manganate solution and the eroded area covered with calomel ointment. Later on 25 per cent chaulmoogra oil was used, and this seemed to give more local relief than anything. A weak solution of iodine was also used as a douche. The interior of the nose was from time to time painted with mercurochrome. Sodium perborate was also tried for a while.

However, nothing that we did for her had any lasting effect, the destructive process kept slowly advancing, sometimes with more pain and sometimes with less.

During her stay at the Hazleton Hospital the destruction of her face gradually increased in extent, as can be seen by the illustrations, until at the time of her death practically all the structures between her eyes and lower jaw had become involved. Her death was due to general exhaustion. Unfortunately no *post mortem* was done, but a piece of the soft tissue surrounding the ulcerative area was removed and sent for examination (with a description of her appearance at the time of her death) to Dr. R. A. Gaughan, Superintendent Surgeon of the Hazleton State Hospital. Dr. Gaughan's letter was as follows :

“ The entire upper jaw was affected. The lower jaw was normal, excepting slight necrosis of the inner surface of the lower lip. The lower teeth and tongue appeared normal.

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“ The affected area extended from the corners of the mouth outward into the soft tissues of the cheeks to a point opposite the first molar teeth on each side of the face, then upward to the lower border of the orbital cavity. Both sides of the face seemed to be equally involved. The soft tissues of the nose were gone, leaving the posterior portion of the nasal bones and the nasal septum intact. The anterior portion of the nasal bones and the septum were eroded and the remaining portions were blackened and moth-eaten in appearance. The upper teeth were out. The superior maxillae were both exposed and had the same blackened appearance, as if the moths had eaten it. The horizontal plates of the palatine bones were eroded and destroyed, leaving the nasal and the orbital cavity as one.

“ The edges of the lesion along the cheeks were covered with blackened crusts, appearing like dried, clotted blood and crumbling when touched. The tissues immediately adjacent were hardened, and indurated with rolled, heaped-up edges.

“ There was no discharge of any kind, but there was a distinct very foul odour.

“ As near as 3 cm. from the edges the skin appeared normal, excepting extreme pallor. The eyes were not involved, except that the conjunctivae were reddened and oedematous. The upper lids were swollen until the eyes were almost closed. Sight was not affected until the last few days of life.”

### AUXILIARY CASE I.

Female, aged 11 years, admitted *April 21st*, 1913. In *September*, 1912, a small pimple appeared on the nose. This gradually became larger and the surrounding skin was discoloured. Ulceration occurred later and the lesion gradually spread. On admission the tip of the nose and a considerable area of the alae on either side of it was the site of an ulcer, the base of which was covered with vascular granulations bathed in purulent discharge. No outlying areas of ulceration and no “ apple-jelly ” nodules. The disease did not appear to have eroded the nasal cartilages to any extent and there was no evidence of extension to inner aspect of nostrils. No glandular enlargement.

*April 23rd*, ulcer scraped and cauterised.

*May 6th*, X-ray treatment. Continued for several weeks. Local condition showed no improvement. Ulceration seemed to be spreading. General condition remained good. Sections cut of scrapings looked like an epithelioma and this opinion was confirmed by one of our foremost morbid histologists. The extract of *alnus glutinosa* (the common alder) was used. Dosage—first day, half a minim plus ac. t.i.d., p.c. Second day, one minim t.i.d. Third day,

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eight minims t.i.d. Dose rapidly increased to half a drachm t.i.d. Within a fortnight of starting, the ulcer was entirely healed. Area was covered with epithelium and the nose has remained perfectly well ever since.

### AUXILIARY CASE II.

Case under observation for eight months. Interesting because of unusual clinical picture. Diagnosis of syphilitic ulcer made. Active anti-luetic medication employed without influencing process. Failure of treatment strengthened opinion that ulceration was due to tuberculosis. Repeated examinations failed to demonstrate T.B. Then thought process might be tropical ulceration contracted while the patient was in Panama.

J.B., aged 44, native of Panama, admitted City Hospital 1904. Complained of nasal obstruction and ulceration causing continual mucopurulent discharge, bleeding, pain and nasal obstruction. Began six years ago in Panama, his symptoms being annoying and offensive mucopurulent discharge from nose and gradually increasing difficulty in breathing. Polypus removed but only seemed to aggravate condition. A year later small ulcers appeared about the nasal orifices. On examination, nose very broad and ulcerated at external meatus; tip sunken. From *September 28th to October 19th*, temperature varied from  $98.2^{\circ}$  to  $101.2^{\circ}$ . Discharged on latter date but returned *November 7th*. On that day had severe rigor which lasted twenty minutes and temperature rose to  $103.8^{\circ}$ . Discharged again and returned *March 22nd* when he had another rigor. Most striking feature of foregoing history was involvement of mucous membranes and underlying tissues of nose, pharynx and larynx by a chronic ulcerative process.

Nose—great ulceration around edges of nostrils, involving part of upper lip. Septum gone and anterior nares one necrotic sloughing mass.

Larynx and pharynx—ulcerated areas.

Plate 1 shows only the later extension of the disease to the anterior nares, upper lip, right nasal duct and lachrymal sac.

Unfortunately the man was discharged so that ultimate result of disease could not be determined.

Histology—tissue examined—no fungi found. Section from diseased edge one half of surface ulcerated, the other showed a proliferated epidermis. The former covered with blood and fibrin but underneath dense cellular infiltration extending to muscle tissue of lip. Cells consist largely of small lymphocytes. Only few polynuclear leucocytes present. Epithelioid cells and hyperplastic fibroblasts. Giant cells irregularly distributed.

Summary—lesion a granuloma whose nature could not be determined by methods employed. It could be differentiated from

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blastomycosis, actinomycosis, rhinoscleroma and leprosy by the absence of their specific micro-organisms. From mycosis fungoides by character of infiltrate and absence of fragmentation. Histological picture might readily be mistaken for T.B. as the giant cells were numerous with nuclei arranged peripherally. The epidermic hyperplasia was such as is met with in hypertrophic lupus. It is seen also in blastomycotic dermatitis. Existence of T.B. conclusively disproved. Affection distinct from yaws. Syphilis excluded.

Fungous or protozoan forms not demonstrated in any sections examined.

Der Verfasser hat in dieser Arbeit zehn Fälle dieser ausserordentlich seltenen Erkrankung gesammelt. Die Ursache ist noch unbekannt, ebenso das pathologisch-anatomische Substrat. Die wesentlichen Merkmale sind die progressive Zerstörung von Nase, Gesicht und Rachen und die gänzlich fehlende Widerstandskraft des Kranken gegenüber dieser Infektion. Es geht aus der Zusammenstellung hervor, dass der Ausgang fast stets ein unglücklicher ist, obwohl die Dauer des Leidens ein bis zwei Jahre betragen kann.

L'auteur décrit dans cet exposé dix cas de cette maladie qui est extrêmement rare et dont la cause est obscure et l'origine pathologique inconnue. Les signes les plus marquants sont la destruction progressive du nez, de la face et du pharynx et le fait que le malade n'oppose aucune résistance à cette infection. On verra que l'issue en est presque toujours fatale quoique la maladie peut durer d'un à deux ans.