Renal failure did not occur in Igersheimer's (1948) patient with lipodystrophy and hydronephrosis. Igersheimer maintained that lipodystrophy is due to a defect of the mesenchyme and described various mesenchymal abnormalities in his patient. He reviewed other published cases to support his view. The hydronephrosis in his patient was believed to be due to an aberrant renal artery. This was found at operation and cut. A subsequent intravenous pyelogram showed no change from the appearance before operation.

Igersheimer summarily dismisses the nervous, endocrine, and other causes suggested for lipodystrophia progressiva. The different hypotheses concerning aetiology have been fairly reviewed by Ellis (1951). There is much evidence to suggest that lipodystrophy may result from a lesion in the central nervous system (Warin and Ingram, 1950).

Besides that of associated mesenchymal defects or mere chance, there is another possible explanation for the occurrence together of uraemia and lipodystrophy. Lesions of two closely related areas of the brain, anterior to the hypothalamus, may be responsible for trophic changes and uraemia, both of these effects occurring if both areas are involved. Evidence that the cause of lipodystrophy may lie in a lesion related to the hypothalamus is found in the diencephalic syndrome (Russell, 1951), where profound wasting is a prominent feature. In Tizard's patient (1954) the profound wasting was a true lipodystrophy with disappearance of subcutaneous fat and no muscle-wasting. Dr. Russell, who saw this child, thought it likely that she had a diencephalic lesion. Evidence that trophic changes and uraemia can be due to lesions in closely related areas anterior to the hypothalamus is furnished by McLardy (1950). After prefrontal leucotomy, trophic changes with gross wasting and uraemia have often been described. These complications of the operation usually occur when the incisions go too far back (Freeman, 1953). McLardy has shown that prefrontal leucotomy can be followed by uraemia or trophic changes, depending upon which of two areas is damaged. Injury to posterior area 47 of the orbital cortex leads to uraemic death, and the severance of connexions between the caudate nucleus and Brodmann's (non-granular) cortical areas 8 and 6 is concerned with the trophic fatalities. The immediate cause of renal failure in McLardy's series of uraemic deaths is not known, but he mentions the work of Cort, who claimed to reproduce Trueta's renal shunt mechanism in cats by electrical stimulation of the cortex of area 13.

If renal failure in lipodystrophy is due to a lesion in the central nervous system, this could be caused by abnormal function of the autonomic innervation of the urinary tract, producing hydronephrosis, or of renal cortical arterioles, producing a Trueta shunt effect. Besides the evidence of the present case, hydronephrosis as a functional disorder of the urinary tract is common in man. The rare cortical necrosis of the kidney during pregnancy is the only disease which may be comparable to Trueta's shunt mechanism in the experimental animal.

Lesions affecting autonomic centres are responsible for diverse vegetative effects, including uraemia. The common idiopathic hydronephrosis with no organic obstruction may be due to disease of the central nervous system involving an autonomic centre regulating the function of the renal tract.

Summary

A case of lipodystrophia progressiva, temporary hydronephrosis, and recurrent uraemia is described.

The occurrence of renal disease with lipodystrophy is reviewed. The association of the two diseases may be fortuitous; the result of a mesenchymal defect; or the result of a lesion of adjacent centres in the central nervous system, responsible for the renal and trophic changes.

Evidence is submitted that a lesion anterior to the hypothalamus may be responsible for these changes.

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MALIGNANT GRANULOMA OF THE NOSE

BY

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The condition known as malignant granuloma of the nose is uncommon and almost invariably fatal. The chief purpose of this report is to present a unique result—a treated case which has remained healed for over five years. The secondary purpose is to present another case of a different and unusual type.

Only five cases of recovery appear in the literature, but closer examination of the case records and subsequent history reveals inconsistencies. Woods's case (1921) healed locally after interstitial irradiation, but the patient died within two years, of generalized sarcomatosis. The diagnosis of the original lesion must therefore be suspect. In the case of M'Arthur and Dew (1925) the local lesion healed after three doses of deep x rays, but the patient died four years after the last dose from what was called "miner's phthisis." No necropsy was permitted, and Stewart (1933) quotes a letter from M'Arthur in which the possibility of pulmonary sarcomatosis was envisaged. Schütz (1938) records eight cases, in one of which spontaneous resolution occurred, but the account is too brief to be entirely acceptable. Hoover (1941) describes an admittedly atypical case which apparently healed after excision of the granulomatous area followed by antisyphilitic treatment.

An exhaustive survey of the literature by Williams (1949) failed to reveal any cases of survival other than those cited above. His discussion of the pathology is most instructive, particularly in assessing a link with periarteritis nodosa and with certain types of hypersensitivity reactions. Following upon this paper, Williams and Hochfilzer (1950), Moore *et al.* (1951), and Woodburn and Harris (1951) have had some success with cortisone and A.C.T.H., but the follow-up period recorded is too short for appraisal.

Finally, Sneddon and Colquhoun (1952) claim a cure with chlortetracycline ("aureomycin") and chloramphenicol, but the patient died a year or so later, and, furthermore, the precise nature of the lesion was never identified by biopsy. They considered the lesion to be staphylococcal in origin, but no other case has been recorded in which the local lesion healed with antibiotics (Breckenridge *et al.*, 1954).

Case 1

A married woman aged 28 was first seen at the Royal National Throat, Nose, and Ear Hospital on June 24, 1947, complaining of right-sided nasal obstruction, an intermittent swelling in the right nasal cavity, a purulent nasal discharge, and considerable crusting with fetor. Some of the symptoms had been present for over two years. There was a large septal perforation, crusts in both nasal cavities, mucopus in the nasopharynx, and a nodular swelling of the right side of the palate. A radiographic opacity of the right antrum was present and antral lavage revealed pus and crusts. The W.R. was negative. On a tentative diagnosis of atrophic rhinitis, she was advised to use an alkaline nasal douche and a nasal paint of glycerin and glucose, night and morning, and this kept her relatively comfortable. As this diagnosis was not convincing, she was kept under close observation, attending frequently at short intervals, until on October 7 a large piece of necrotic bone, thought to be a sequestrum of the septum, was removed from the left side of the nose.

A few weeks later she was admitted to a hospital nearer her home because of acute maxillary sinusitis. This occurred

FIG. 1.—Case 1. Showing the external extent of the ulcer with necrotic bone in the margins.

FIG. 2.—Case 1. Showing the nodular enlargement of the palate.

FIG. 3.—Case 1. Showing the pleomorphic cellular reaction and the absence of focal necrosis and of necrotizing angitis. ($\times 230$.)

three times during the next fifteen months, necessitating her readmission on each occasion. These attacks were treated with penicillin and antral lavage, and in September, 1948, by a Caldwell-Luc operation on the right side. After this operation the right side of the nose and the tissues underlying it literally melted away, and an ulcer appeared which rapidly spread upwards almost to the margin of the right orbit. At this stage I saw her again, quite fortuitously, in my out-patient clinic at another hospital, where she was referred by her doctor. It was now evident that this ulcer was the external opening of a large fistula into the right nasal cavity, right ethmoidal region, and right antrum, and that its margins consisted of necrotic bone and of granulation tissue (Fig. 1). The mucosa on the buccal surface of the palate was thickened and nodular, although still intact (Fig. 2), but on palpation it was found that the bone of the hard palate had been almost completely destroyed. A diagnosis of malignant granuloma now sprang to mind, and, so far as confirmation is possible, this diagnosis was confirmed by biopsies from the edge of the ulcer and from the swelling on the palate.

Dr. I. Friedmann's report is as follows: "The histological appearances (Fig. 3) of this case are characteristic of malignant granuloma of the nose in so far as they consist of a chronic fibrous non-specific inflammatory granulation tissue infiltrated by pleomorphic inflammatory cells, including plasmacytes and lymphocytes. There are no giant cells present and there is no evidence of focal necrosis, frequently seen in similar cases. A small artery found in the biopsy specimen shows no evidence of necrotizing angitis. This histological picture virtually excludes all known forms of specific granulomatous reactions as well as neoplasm. There are possibly several histological types or variations of malignant granuloma of the nose. The most common type appears to be a pleomorphocellular granulation tissue as described in this case. In other cases one or more of the following morphological features have predominated: (1) histiocytes, (2) foreign-body giant cells, (3) extensive necrosis. One particular variety, the giant-cell granuloma, is frequently associated with necrotizing vascular disease resembling polyarteritis nodosa. The case here described appears to belong to the classical type as there was no sign of systemic vascular complications."

In spite of treatment with sulphonamides and penicillin, pieces of necrotic bone were daily extruded from the depths of the cavity, and later the palatal mucosa gave way. The patient was referred to Dr. M. Lederman, radiotherapist at the Royal Marsden Hospital, for irradiation, but after consultation it was decided not to risk a form of treatment which might itself cause bone necrosis. Large doses of potassium iodide together with a course of calciferol were given and the ulcer became cleaner and showed signs of healing. The horrible fetor disappeared and the steady necrosis and sloughing ceased. However, the improvement

was only temporary, and a few months later the condition again became noticeably active. Dr. Lederman then consented, with some misgivings, to try a course of deep x rays, and the very small dose of 300 r was administered between December 19, 1949, and January 21, 1950. A dramatic change followed. The margins of the ulcer became clean and a healthy skin-mucosal junction formed. The mucosal junction between the oral and nasal surfaces of the palate also healed. By April 12 there was no further evidence of activity, and the vast, hideous cavity gradually became lined with pink mucosa.

As the ulcer remained soundly healed, Mr. J. P. Reidy, early in 1952, began the difficult plastic reconstruction which is still in progress. In spite of four operations on the tissues of the nose and face, there has been no evidence of any return of the disease.

Comment

The natural history of malignant granuloma of the nose has not been precisely identified, and the histological picture itself has not been clearly established as a specific entity. Stewart's exhaustive review of the cases described up to 1930 was accompanied by a composite clinical description based on these records, but it is more than possible that some of them would not now be accepted as true cases of the disease. The lesion usually begins as an intranasal ulcerative process which soon appears on the face after having eroded the lateral wall of the nose or the anterior wall of the antrum. The facial tissues are progressively destroyed and bone necrosis with sequestration is a marked feature. The spread towards the pharynx is slower. Death usually results from cachexia, in anything from one to three years. The case reported here has followed the classical course, except for the end-result.

However, there is occasionally another type of case in which the necrotizing reaction remains confined within the nasal cavities and spreads over the surface of the mucosa. One such case has recently come under my care.

Case 2

A man aged 48 was first seen on October 26, 1954, complaining of pain in the nose for about four months. This pain followed a thyroidectomy. The teeth were thought to be the cause of the pain and had been extracted, but without relief. The right nasal cavity contained pus and crusts, and pus was found on antral lavage. On November 11 a granular area was noticed on the septum and a portion was removed for biopsy. This revealed a non-specific type of granulation tissue covered with a thick stratified squamous epithelium. The granular area increased in extent and a large ulcer appeared on the septum and also on the middle turbinal. On December 15 the patient was admitted and the antrum opened and inspected by the Caldwell-Luc approach. Macroscopically it appeared normal, and pieces

of tissue for biopsy were taken from the antral mucosa, the right middle turbinal, and the septum. The antral mucosa was normal, but (Fig. 4) "the nasal mucosa is densely infiltrated by large lymphocytes and histiocytes showing considerable irregularity of nuclear size and shape. There are numerous plasma-cytes present, and frequent mitoses

FIG. 4.—Case 2. Showing the similar pleomorphic reaction, but with an excess of histiocytes and plasmacytes. ($\times 750$.)

are seen. The cartilage of the nasal septum has been eroded by the process" (Dr. I. Friedmann). Dr. L. W. Pagel concurred with this description, and both pathologists agree that this is a case of malignant granuloma. The distinctive feature of predominance of histiocytes and plasmacytes is a variation to which Dr. Friedmann has already drawn attention.

By January 8, 1955, destruction of the septum had occurred, but the process, although spreading rapidly within the nasal cavity, still shows no sign of involving the skin.

Discussion

Although it is possible that these two differing clinical pictures are associated with certain variations in the histological picture (Friedmann, 1955), the ultimate prognosis has hitherto been fatal in both types of case. Case 2 has been treated in a similar manner to Case 1, but it is as yet too early to say what will happen.

No rationale is claimed for the treatment given in Case 1, much less for the dramatic success with which it was attended. It was frankly a shot in the dark, entirely on an empirical basis of trial and error. The patient is apparently cured, presumably by the irradiation, as resolution followed immediately after it was given, and the disease had previously resisted, or relapsed after, other methods of treatment. The reluctance in trying irradiation naturally follows the knowledge that irradiation can itself cause, especially in bone, a similar necrotizing type of lesion. The end-result indicates that an almost absurdly small dose was the treatment of choice in this particular case, and would be well worth trying in other similar cases. In fact, at a meeting of the Section of Laryngology of the Royal Society of Medicine on December 3, 1954, Mr. Gilroy Glass reported two cases which were treated similarly and which have responded similarly. They had remained healed for about a year, up to the time of his report.

Summary

A case of malignant granuloma of the nose is described which has been cured by a very small dose of deep x rays. This is the first genuine case recorded in which the patient has not died of the disease.

In addition to the classical type of case with sloughing of the facial tissues there is another type which remains confined within the nasal cavities, spreading superficially in the mucosa.

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The third pamphlet in a series on Food Hygiene has just been published by the Central Council for Health Education. This leaflet deals with refrigerator storage. It describes how the refrigerator should be used and cleaned, and what foods should have priority in it. A previous leaflet advised on food storage without a refrigerator, and another presented a "Shopping Quiz" for housewives, drawing attention to poor hygiene standards in food shops.