MEDICAL PRACTICE

Occasional Survey

Non-healing Granulomata of the Upper Respiratory Tract

D. F. N. HARRISON

British Medical Journal, 1974, 4, 205-209

It is perhaps surprising that so much interest has been aroused, particularly by pathologists, in non-healing granulomata of the upper respiratory tract—a group of relatively unusual conditions. Yet despite numerous publications and many false trails it is only recently that confusion has been replaced by the "beginnings of order" and the real importance of these varied conditions appreciated.

The literature abounds with detailed descriptions of patients diagnosed as suffering from non-healing granuloma, malignant granuloma, lethal midline granuloma, Wegener's granulomatosis, and many other equally descriptive terms.[1]

Non-healing or Malignant Granuloma

Non-healing or malignant granuloma is a slowly progressing destructive ulceration of the tissues of the nose, sinuses, or occasionally pharynx. Soft tissues, bone, and cartilage are eventually destroyed by a chronic inflammatory process leading to severe mutilation. If the condition remains uncontrolled death from cachexia, haemorrhage, or intercurrent infection occurs sooner or later (see fig. 1). McBride[2] is usually credited with the first description of this condition though this seems to have been based primarily on the failure of a pathologist to find evidence of either syphilis or tuberculosis in tissue removed at a subsequent necropsy.

The first clear account was published by Robert Woods[3] in 1921 when he aptly described the lesion as a "wave of granulation tissue advancing irregularly into healthy parts, breaking down behind as it advanced in front, so that there was never any great depth of pathological growth present."

Institute of Laryngology and Otology, University of London
D. F. N. HARRISON, M.D., F.R.C.S., Professor of Laryngology and Otology

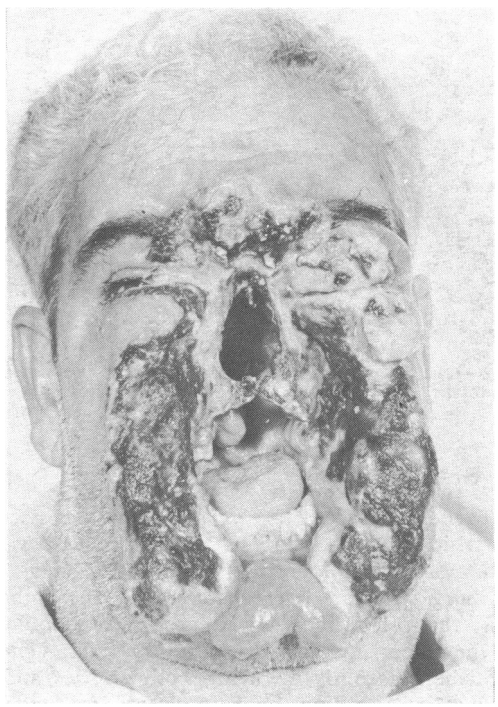

FIG. 1—Case 12. Patient with severe facial destruction from malignant granuloma.

The term "malignant granuloma" was suggested by his colleague Dr. O'Sullivan. In 1933 Stewart[4] published a detailed account of both clinical and histological features of the localized disease, but no better evaluation of the pathological features of granulomas can be found than that presented by Friedmann[5] in his Semon lecture of 1971. Nevertheless, persistent attempts to relate clinical manifestations to the histo-

logical appearances of often unrepresentative biopsy specimens have resulted in some degree of confusion ever since.

It is my own opinion, based on personal evaluation of 28 patients with non-healing granuloma or Wegener's granulomatosis, that where the lesion remains localized to the nose or pharynx, irrespective of the histological appearances, then this condition must be considered as a neoplasm, probably attenuated to a varying degree by the individual's own immunological defences. Since spontaneous resolution has not been reliably recorded the untreated patient probably always succumbs. Occasionally local destruction is slow and limited and the lesion eventually changes into a proved malignant lymphoma. (see fig. 2). Patients in whom this occurs may have a surprisingly good prognosis when treated with radiotherapy, and the slowness and limitation of the destruction may explain the dramatic effect of low-dosage radiotherapy in some patients with Stewart's type of nasal granuloma[6] and its ineffectiveness in other nasal granulomata.

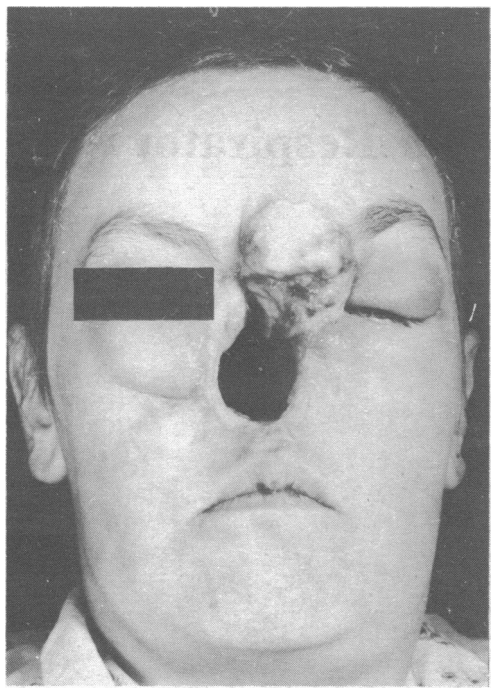

FIG. 2—Case 16. Young woman with malignant lymphoma after total rhinectomy for possible malignant granuloma.

Wegener's Granulomatosis

In 1939 Wegener[8] described three cases of another necrotizing granuloma which also affected the nose but which was associated with more lethal lesions in lung and kidneys. Goodman and Churg[7] 18 years later characterized the pathological features of this condition as: necrotizing granulomatous lesions in the upper and lower respiratory tract; generalized focal necrotizing vasculitis involving both arteries and veins, almost always in the lungs and more or less widely disseminated in other sites; glomerulitis characterized by necrosis and thrombosis of loops of the capillary tufts, capsular adhesion, and development as a granulomatous lesion.

There are quite clear clinical and histological differences between this condition and the localized non-healing granuloma. Onset of Wegener's granulomatosis is usually insidious with non-specific symptoms of infection in the respiratory tract. Constitutional upset is quite out of proportion to the severity of the local lesion, and the patient seeks advice initially because of malaise, fever, or weakness.[9] Until recently the course of the disease was rapid, progressing to death within six months from renal failure.[10 11] Pathologically the disease is characterized by giant-cell granulomas in the respiratory tract lesions, though these are not always easily found. Elsewhere there is widespread angiitis indistinguishable from polyarteritis nodosa, which is responsible for the renal and skin lesions. In the lung the lesions are areas of infarction undergoing necrosis and liquefaction with cavity formation (fig. 3). Even in uncontrolled cases the nasal lesions progress slowly and never become neoplastic or grossly destructive. It would of course be highly satisfactory to relate the aetiology of Wegener's granulomatosis and non-healing granuloma to a common sensitizing factor, such as autoimmunity, drug hypersensitivity, or viral infection. Until the late 1960s, when the prognosis for Wegener's granulomatosis was so dramatically altered, this was thought to be possible.

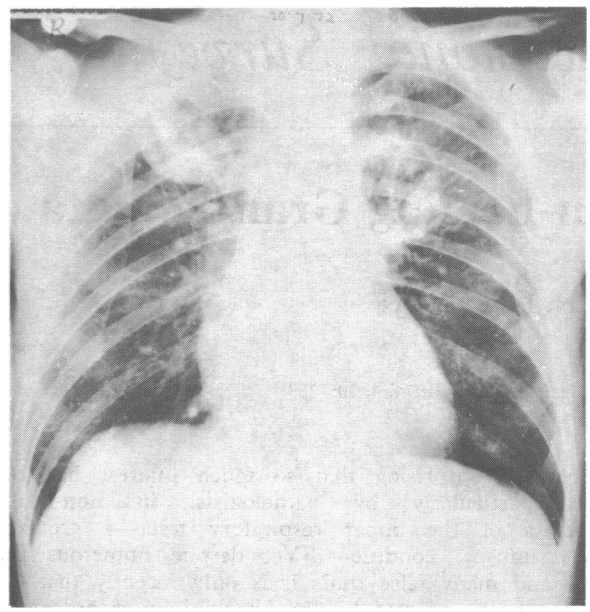

FIG. 3—Case 24. Chest *x*-ray picture of patient with Wegener's granulomatosis showing bilateral apical abscesses.

The increased survival of patients with even advanced pulmonary and renal lesions when treated with cytotoxic and steroid drugs, however, and the relative lack of success when similar therapy is applied to patients with non-healing granuloma (see table) has widened the diagnostic and aetiological gap between these two conditions.

Treatment in the 1970s

Finding the true incidence of non-healing granuloma is complicated by the difficulties inherent in diagnosis, whether early or late. Confusion with syphilis, tuberculosis, neoplasia, and even local trauma is common and the diagnosis is often reached by a process of exclusion rather than inclusion. Since the histological findings are non-specific an additional complicating factor is the relative experience and enthusiasm of the examining pathologist, who may well possess little knowledge of either condition or the clinical history of the patient. Conversely, established Wegener's granulomatosis presents a clear clinical picture irrespective of the biopsy report so even relatively large series of "granulomas" contain a preponderance of this condition. Already there are abundant minutely detailed reports of the case histories of patients with some variant of nasal granuloma. Invariably individual series are small, preventing either writer or reader from gaining any

Data on 28 Patients with Non-healing Granulomata of Upper Respiratory Tract

Case No.	Age at Onset	Therapy	Survival (Months)	Condition March 1974
		Patients with Malignant Granuloma		
1	50	D.X.T., corticosteroids	48	Septal perforation, but well
2	10	D.X.T.	12 Years	Missing anterior septum and columella
3	80	D.X.T., intra-arterial methotrexate	18	Died of coronary occlusion
4	37	D.X.T.	48	Died of carcinoma of lung
5	20	D.X.T., corticosteroids	5½ Years	Well, but has headaches if steroids are reduced
6	69	D.X.T., corticosteroids	6½ Years	Well
7	34	D.X.T.	27	Well
8	52	Corticosteroids	48	Last seen 1967, palatal defect
9	31	Corticosteroids	30	Scarred palate and pharynx
10	87	Corticosteroids	6?	Lost to follow up
11	63	D.X.T.	24	Died of cachexia, massive facial destruction
12	52	Azathioprine, cyclophosphamide, corticosteroids	30	Died of gastric haemorrhage from steroids, minimal improvement
13	61	Intra-arterial methotrexate	18	Died of marrow failure, little improvement
14	64	Intra-arterial methotrexate	12	Lost to follow up, disease progressing
		Patients with Malignant Granuloma who developed Malignant Lymphoma		
15	32	D.X.T.	36	Malignant lymphoma diagnosed 1 year after onset of symptoms, well
16	30	250 kv	13 Years	Malignant lymphoma confirmed 2 years after onset of symptoms, well
17	48	D.X.T.	13	Malignant lymphoma diagnosed 2½ years after onset of symptoms, well
		Patients with Wegener's Granulomatosis		
18	33	Corticosteroids	18	Died of renal failure
19	56	Corticosteroids, cyclophosphamide	24	Died, cause unknown
20	64	Corticosteroids	8	Died of renal failure
21	57	Corticosteroids, methotrexate, cyclophosphamide	36	Died of renal failure
22	16	Azathioprine, corticosteroids, cyclophosphamide	36	Very well, blood urea normal
23	30	Azathioprine, corticosteroids	36	Well, blood urea 62 mg/100 ml
24	45	Azathioprine, corticosteroids	28	Well, blood urea normal
25	69	Azathioprine, corticosteroids	24	Died of adenocarcinoma of kidney
26	54	Aziathioprine, corticosteroids	24	Well, blood urea 43 mg/100 ml
27	58	Azathioprine, corticosteroids	16	Well, blood urea 60 mg 100 ml
28	31	Azathioprine, corticosteroids	10	Well, blood urea normal

D.X.T. = Deep *x*-ray therapy.

clear impression of natural history, clinical variations, or value of therapy.

It is not my intention to add to this confusion by detailing my own 28 patients but to describe briefly an illustrative case history for each of the clear clinical entities and then discuss these patients in relation to the whole series—for the time is ripe for a much needed reappraisal of these conditions.

Case 12

A 60-year-old Jordanian man was first seen in August 1972 with a two-year history of progressive facial destruction (fig. 1). Some minor debridements had been carried out abroad together with various non-specific treatments without any definite diagnosis being made. He had gross destruction of the middle third of the face with exposure of the symphysis of the mandible and necrotic maxillae. Active granulation tissue was present at the margins of the defect, biopsy showing the non-specific features of a Stewart's granuloma. Erythrocyte sedimentation rate (E.S.R.) was 90 mm in the first hour but there was no evidence of renal or pulmonary disease and the patient was surprisingly well, taking fluids intrapharyngeally through a straw.

It was decided to treat this man initially with immunosuppresive cytotoxic therapy since successful control would need to be followed by plastic surgery to provide some degree of rehabilitation. Previous radiotherapy might jeopardize these procedures and was therefore held in reserve, a decision which proved to be ill advised. Gross infection of the necrotic tissues had resulted in a low grade pyrexia which rapidly responded to cephalexin and treatment was then started with azathioprine and prednisone following the regimen used in patients with Wegener's granulomatosis. A daily dosage of 200 mg azathioprine and 30 mg prednisone was quickly reached with some obvious regression of visible granulation tissue and a cleansing of necrotic slough. Within two months the E.S.R. had fallen to 13 mm in the first hour and regression of granulations had shown gross destruction of the eyelids and exposure of the cornea. Reduction of the corticosteroid dosage, however, rapidly resulted in the appearance of fresh granulation tissue and only massive doses of prednisone, 120 mg/day, regained control. The E.S.R. rose to 70 mm in one hour.

Over subsequent months a variety of drugs was given in an attempt to produce lasting improvement—cyclophosphamide in intravenous doses of 40 mg/kg, methotrexate 2·5 mg/day by mouth, and short courses of high-dosage corticosteroids. The E.S.R. remained within the range 40-60 mm in the first hour and in January 1973 it was decided to begin a course of radiotherapy, which was never completed for the patient died on 10 January 1973 from a massive duodenal haemorrhage.

Necropsy.—(Professor Leslie Michaels) showed an obese jaundiced male with massive erosion of the whole of the anterior skull below and including lower eyelids. The nasal cartilages had been completely destroyed and there was some erosion of the nasal bones. The anterior surface of the maxilla and zygomatic arch was destroyed and the upper jaws together with hard and soft palate were absent, revealing the pharynx. Further morphological and histological examination showed multiple small duodenal ulcers with small bowel filled with blood. The left masseter muscle had been largely replaced by coagulation necrosis with lymphocytic and plasma cell infiltration and there was widespread centrilobular hepatic necrosis consistent with drug-induced cholestatic jaundice. The lungs showed widespread bronchopneumonia.

COMMENT

In many ways this patient exemplified the classical natural history of malignant granuloma, including the considerable delay in diagnosis but perhaps excluding the manner of his death.

Analysis of similar cases (see table) shows that the most effective means of treatment is radiotherapy. Dosage varies from 800-1,000 r given within six days to a full curative course of telecobalt. The former seems to be adequate for most patients and the larger dosage might well be reserved for those cases where biopsy eventually suggests a diagnosis of malignant lymphoma. It is doubtful if systemic corticosteroids are of any lasting value in this condition and if the concept of an immunologically controlled neoplasm is accepted such treatment might even be harmful. In this patient even very large doses of prednisone produced only temporary improvement and therapy was eventually responsible for his death.

My lack of success with cytotoxic drugs may well have been related to inadequate dosage. Von Leden and Schiff[12] perfused their patient via bilateral superficial temporal cannulae for four weeks, their total dosage of methotrexate being far greater than any that I gave. Whether this technique has any advantage over low-dose radiotherapy has yet to be proved. Systemic cytotoxic drugs alone are certainly far less effective than when used in Wegener's granulomatosis, which may be another indication of the differences between these two conditions.

Two of my patients, however, were completely controlled with corticosteroids alone. Both presented with severe oropharyngeal ulceration but without nasal involvement. The E.S.R. was raised and biopsy showed the histological features described by Friedmann[13] as being typical of the Stewart's type of granuloma. I believe that these lesions were in fact gross examples of aphthous ulceration, a condition which responds well to corticosteroids. Radiotherapy should not be used in this condition since subsequent deep penetration may result in a fatal haemorrhage. In such patients a trial of prednisone 30 mg/day should precede radiotherapy. Rapid improvement in both symptoms and appearance of the ulcers may indicate that this is in fact not a case of non-healing granuloma.

Case 16

Early in 1961 a 30-year-old woman complained of persistent nasal obstruction. Examination by an ear, nose, and throat surgeon showed ulceration and crusting of the anterior part of the nasal

septum and the skin of the columella. Biopsy suggested a possible neoplasm and she was given superficial radiotherapy which resulted in gross deformity and destruction of the nasal and septal cartilages. About one year later her symptoms returned and the remaining septum was found to be thickened. The results of biopsy were equivocal but the remaining nasal septum was removed. Within a few months swelling of the nasal tissues had appeared together with necrosis of overlying skin. In March 1963 the nose was removed surgically but the skin edges never healed and by August of that year a swelling had appeared over the centre of the forehead (fig. 2). The patient was referred to me for cytotoxic therapy. Opinion as to the probable diagnosis varied between a reticulum cell sarcoma and histiocytic nasal granuloma. Treatment with high dose intravenous cyclophosphamide (40 mg/kg) was started after surgical removal of both lateral walls of the remaining nasal passages. By November 1963 a hard lymph node had appeared beneath the angle of the right mandible and biopsy of the forehead mass now substantiated a diagnosis of lymphosarcoma.

On 28 January 1964, three years after her initial symptoms, she began a course of 250 kv to the forehead and neck, receiving 4,250 r in 37 days to the forehead and 2,180 r in 21 days to the neck. There was rapid and complete resolution of the tumour and she remained completely well, being last seen in December 1973.

COMMENT

The difficulties of differentiating between nasal malignant lymphomata and the histiocytic type of non-healing granulomata from small and often infected biopsy specimens is well known. It has been reported on several occasions since 1949 that patients with Stewart's nasal granuloma may eventually die with dissemmated malignant lymphoma. Walton[14] elaborated on this complication, describing five patients all of whom eventually developed a reticulum cell sarcoma of the nose or palate. The real incidence of malignant lymphoma in a previously existing non-healing nasal granuloma is unknown, the time delay is certainly variable (see table), and possibly such neoplastic changes may be related to the immunological competence of the patient or even ill-advised treatment with systemic immunosuppressives.

Whether radiotherapy even in low doses early in the disease prevents frank neoplastic change in cases of non-healing granulomata is a matter for conjecture. A patient reported by Ardouin,[15] however, who received 600 r for this condition developed a local reticulum cell sarcoma within three months of completing therapy. Kassal *et al.*[16] suggested that non-healing granuloma should be regarded as a form of malignant midline reticulosis. the disease usually remaining localized but eventually overcoming immunological control with possible visceral dissemination.

My own studies of the available evidence and experience of a group of such patients substantiates the view of Kassal *et al.*[16] Provided diagnosis is early the prognosis of patients with such a "neoplastic change" remains better than when a malignant lymphoma occurs de novo in the nose. All nine patients reported by Eichel[17] in 1966 survived at least five years after curative radiotherapy, and my own three patients all showed a favourable response. Perhaps this indicates a considerable degree of immunological competence on the part of the patient though none had evidence of systemic metastasis. The term "malignant granuloma" may be more apt than has hitherto been suspected.

Case 24

A 45-year-old man first complained of malaise, generalized muscular pains, and night sweats in the autumn of 1971. Chest *x*-ray appearances suggested a lung cancer and he was admitted to a chest unit for diagnostic bronchoscopy. Bronchoscopy showed abscess cavities in the apices of both lungs and shortly after his discharge in May 1972 he developed a painless haematuria and epistaxis.

Nasal examination showed appreciable crusting and ulceration of the nasal septum and a provisional diagnosis of Wegener's granulomatosis was made. On admission to this hospital in July 1972, he was found to be extremely ill with a pyrexia of 37·8 °C, productive cough, and a weight loss of more than 12 kg. A chest *x*-ray picture (fig. 3) showed bilateral cavitation. There were large numbers of red cells and casts in the urine and a blood urea of 69 mg/100 ml with an E.S.R. of 188 mm in one hour. Treatment was started with azathiopine 50 mg twice daily, which was increased to 200 mg/day. This was supplemented with prednisone 10 mg three times a day, and on this regimen the E.S.R. fell to normal (fig. 4) within five weeks. Both red cells and casts almost completely disappeared from the urine, and the blood urea in September 1972 was 34 mg/100 ml with a creatinine clearance in January 1974 of 110 ml/hr. The chest *x*-ray picture cleared completely after expectoration of large quantities of purulent material and the temperature then returned to normal.

He was maintained on a regimen of azathioprine 200 mg/day and prednisone 30 mg/day, and in February 1974 was found to be extremely well except for a small area of consolidation in the right mid-zone of the lung. The E.S.R. was 15 mm in the first hour, and the nose was free from crusting or obvious disease, only a small area of scarring remaining on the nasal septum.

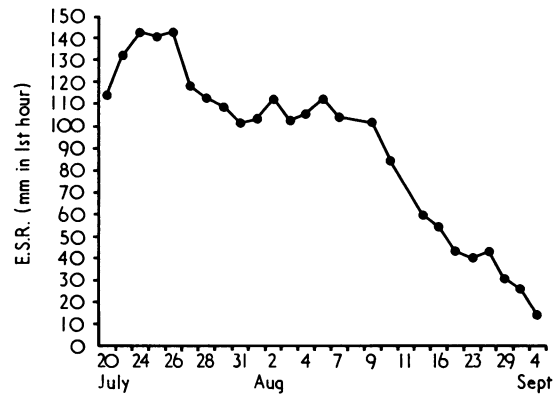

FIG. 4—Case 24. Fall of E.S.R. to normal during treatment with azathioprine and prednisone.

COMMENT

This brief account of a patient suffering from classical Wegener's granulomatosis serves to emphasize several important points. Even in the early stages of the condition the patient is often surprisingly ill, which together with minimal physical signs may delay diagnosis. Once the lungs or kidneys become obviously involved progression is usually rapid, and untreated most patients die within six months —usually of renal failure.

The introduction of cytotoxic therapy has dramatically altered the immediate prognosis (see table). Complete reversal of both pulmonary and renal conditions to a near normal state is possible though this obviously depends on the extent of the initial damage. Repair is by fibrosis and the renal tissue left may be inadequate for normal function.

It is therefore vital that a diagnosis should be made and that therapy should be implemented without delay thus offering the patient expectation of a greatly improved prognosis. Whether it is ever possible to diagnose this condition on a nasal biopsy alone is extremely doubtful. There will always be extranasal disease and if the diagnosis of Wegner's granulomatosis cannot be substantiated by examination of lungs, urine, muscle biopsy, skin examination, etc. then despite the histopathological evidence it might be more sensible to treat the nasal lesion as a non-healing granuloma. Such lesions heal rapidly with radiotherapy but response is poor if the underlying lesion is a Wegner's granulomatosis, which responds rapidly to cytotoxic therapy. During this period of "mismanagement" other lesions will usually appear elsewhere, which will tend to confirm the diagnosis of Wegner's granulomatosis.

Discussion

Though early diagnosis and treatment of the conditions under discussion should result in a reasonably optimistic prognosis virtually no substantial evidence is yet available to explain their aetiology. The list of suggested causes is comprehensive but even such sophisticated immunological investigations as reported by Shillitoe *et al.*[18] do no more than suggest future lines of inquiry, and when dealing with conditions of

such rarity adequate prospective studies may take many years. Undoubtedly clear differentiation between these various clinical entities is essential for effective management. In the case of non-healing granuloma, malignant lymphoma, and the confusing idiopathic pharyngopalatal ulceration, management presents minimal problems. Control of Wegener's granulomatosis, however, may necessitate a life time of cytotoxic and immunosuppresive therapy.

The dramatic improvement in outlook for patients with Wegener's granulomatosis occasioned by the addition of cytotoxic drugs to the more conventional corticosteroids is not simply because of their increased immunosuppression or their anti-inflammatory effect. Possibly the two types of drugs act at different points in the immune reaction (if this is significant), but a more likely explanation is that the cytotoxic agents act in their own special way. Published reports indicate that both alkylating agents and antimetabolites are equally effective and on occasions I have combined drugs from both groups.

PROBLEMS OF LONG-TERM THERAPY

Azathioprine has been widely used in transplant surgery, skin diseases, and other conditions, and there is much information on dosage and side effects. It is an imidazolyl derivative of mercaptopurine and by interfering with purine metabolism affects both RNA and DNA. The toxic effects include bone marrow hypoplasia, hepatotoxicity, and reduced resistance to infection, but even in the large doses used in Wegener's granulomatosis these have as yet presented few problems. It is usually necessary to achieve a daily dosage of 200 mg and then add prednisone until the E.S.R. has returned to normal limits. Since the toxic effects of both drugs are largely dose related every effort is made to reduce therapy as soon as the patient's condition is controlled. In practice this presents considerable difficulties since the most reliable guide to dosage seems to be the E.S.R. Increase in this value, it is hoped, will precede any recurrence of nasal, pulmonary, or renal disease, and certainly reduction in dosage in many patients is followed by an increase in the E.S.R. As yet no patient has been left on this reduced dosage to test the significance of this finding for there is no guarantee that control will be possible on a second occasion.

The dangers inherent in long-term cytotoxic and corticosteroid therapy are well known and need no comment (case 12). Even the risk of sterility or genetic damage to children born of our younger patients cannot be ignored. Yet we can now increase the survival period of these patients from six months to many years, though with only their general condition and E.S.R. to guide us in determining dosage. Even when it is possible to reduce therapy to minimal levels the risk of a sudden uncontrollable relapse remains and as yet this is a risk I am not prepared to take. It seems therefore that until satisfactory evidence of the action of these drugs is available and the means by which we can reliably monitor this action each patient must be maintained on the dosage just sufficient to keep the E.S.R. within normal limits and the clinical state as normal as possible. Awareness of the potential dangers of both the cytotoxic drug and corticosteroids used and the means to remedy any side effects are vital, and these patients need to be under the care of people experienced in the management of such problems.

References

1 Burston, H. H., *Laryngoscope*, 1959, **69**, 1.
2 McBride, P., *Journal of Laryngology and Otology*, 1897, **12**, 64.
3 Woods, R., *British Medical Journal*, 1921, **2**, 65.
4 Stewart, J. P., *Journal of Laryngology and Otology*, 1933, **48**, 657.
5 Friedmann, I., *Journal of Laryngology and Otology*, 1971, **85**, 631.
6 Butler, D. J., and Thompson, H., *British Journal of Oral Surgery*, 1972, **9**, 208.
7 Godman, G. C., and Churg, J., *Archives of Pathology*, 1954, **58**, 533.
8 Wegener, F., *Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie*, 1939, **102**, 36.
9 Mills, C. P., *Hospital Medicine*, 1967, **2**, 183.
10 Walton, E. W., *British Medical Journal*, 1958, **2**, 265.
11 Singh, M. M., *et al.*, *Lancet*, 1958, **1**, 401.
12 Von Leden, H., and Schiff, M., *Archives of Otolaryngology*, 1964, **80**, 460.
13 Friedmann, I., *Proceedings of the Royal Society of Medicine*, 1964, **57**, 289.
14 Walton, E. W., *Journal of Clinical Pathology*, 1960, **13**, 279.
15 Ardouin, A. P., *Proceedings of the Royal Society of Medicine*, 1964, **57**, 299.
16 Kassell, S. H., Echevarria, R. A., and Guzzo, F. P., *Cancer*, 1969, **23**, 920.
17 Eichel, B. S., *et al.*, *American Journal of Surgery*, 1966, **112**, 597.
18 Shillitoe, E. J., *et al.*, *Lancet*, 1974, **1**, 281.

Hospital Topics

Lesions of the Symphysis Pubis in Women

N. H. HARRIS

British Medical Journal, 1974, **4**, 209-211

Changes at the symphysis pubis due to repeated minor trauma have been reported in athletes.[1] Thirteen women seen with similar changes, resembling osteitis pubis, have been described,[2] while there were 27 women in a series of 45 patients with osteitis pubis.[3] In three of the last symptoms had begun during or shortly after pregnancy; eight had had pelvic surgery, in four of whom infection developed postoperatively.

St. Mary's Group Hospitals London W2 1NY
N. H. HARRIS, M.B., F.R.C.S., Consultant Orthopaedic Surgeon

This paper reports the details of three women who presented with a long history of disabling pain in the pubic region. In many respects the symptoms and radiological changes were similar to those observed in athletes.[1]

Case Reports

Case 1.—A 33-year-old woman presented with a nine months' history of pain in the pubic region radiating to the thigh, aggravated by bending, rising from a sitting position, and turning over in bed. She could not go for long walks, do her housework, or gardening. A particular feature was an unpleasant clicking over the pubis with all movements. She had two children aged 2 and 3,