

support from the observations of Gould⁶ concerning the impairment of resources and of cerebral metabolism in infectious illnesses, which lead to imperfect psychiatric integration, finally resulting in post-infective debility.

Analysis of the present series reveals clearly the predominance of physical disorders in patients with significant tiredness; also, that such a complaint often heralds serious, but not necessarily irreversible, disease. Herein lies the practical application of this study, namely, that when a spontaneous complaint of tiredness, lassitude, lack of drive or exhaustion is made, careful inquiry and examination must be undertaken before consigning the case to what has been described as the clinical rubbish basket of neurotic ill-health.

SUMMARY

A survey of nearly 1200 consecutive cases of varied medical disorders has been made and 105 extracted in which the primary complaint was of tiredness. These have been analyzed and the relation of tiredness to specific conditions defined, particularly the predominance of tiredness as a symptom of physical rather than neurotic disorder. An attempt has been made to integrate the physiological and psychological processes which may take part in the production of this symptom, with particular reference to disorders of the endocrine, genitourinary and hæmopoietic systems in relation to specific processes of metabolism.

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RÉSUMÉ

La fatigue est plutôt un symptôme qu'une entité clinique. Dans certains cas elle peut être mesurée objectivement mais dans d'autres il faut se fier à la description subjective du malade. La plupart des auteurs s'accordent pour déclarer que sa cause principale dépend de l'état psychologique du sujet. Afin de déterminer le rôle que joue la fatigue dans la symptomatologie des cas de médecine courante, l'auteur a revu 1200 dossiers de malades qui se sont présentés à son cabinet de consultation accusant de la fatigue comme symptôme primaire ou secondaire. La fatigue causée par l'état d'angoisse se rencontre assez fréquemment de nos jours et ne peut être déterminée qu'à l'aide d'une anamnèse détaillée. La plupart des troubles endocriniens peuvent causer de la fatigue. L'auteur cite en exemple le diabète, le myxœdème, la maladie d'Addison, la myasthénie grave et la ménopause. On peut aussi impliquer les troubles du métabolisme qui se manifestent par de l'urémie, des pertes de sodium ou de potassium, un manque de vitamines ou un déséquilibre de l'eau et des électrolytes. Les affections rénales et hépatiques sont souvent en cause dans ces cas. L'anémie peut également engendrer de la fatigue par l'apport inadéquat d'oxygène aux tissus. Il convient d'ajouter que si les tissus ne sont pas en mesure d'employer l'oxygène ou si l'échange gazeux au niveau des alvéoles pulmonaires ne peut s'effectuer de façon satisfaisante le résultat est le même quel que soit le degré d'hémoglobine. Parmi les autres causes de fatigue, notons les néoplasmes et certaines infections chroniques.

ANKYLOSING SPONDYLITIS*

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DEFINITION AND ETIOLOGY

ANKYLOSING SPONDYLITIS is an inflammatory disorder of unknown etiology that involves not only the sacro-iliac and apophyseal joints of the spine, but also bony surfaces at sites of ligamentous, fascial or muscular attachments; synchondroses such as the manubrio-sternum, xiphi-sternum, symphysis pubis and intervertebral discs; frequently the costo-vertebral articulations, and at times, one or more extra-spinal or peripheral joints. Some degree of ankylosis of the affected joints, and calcification or ossification in the annulus fibrosus of intervertebral discs and in paravertebral tissues and ligaments, are commonly but not invariably present.

The relationship of ankylosing spondylitis to rheumatoid arthritis remains to be clarified but

the weight of evidence at present favours the concept that these two diseases are separate entities. The striking predominance among males; the consistently negative tests for serum rheumatoid factor; and the absence of that rheumatoid hallmark, the connective tissue necrobiotic nodule, in patients with ankylosing spondylitis are among the more impressive of the many fundamental differences between this disease and rheumatoid arthritis.¹

Ankylosing spondylitis begins characteristically in early adult life, between the ages of 18 and 35 years in 85% of patients. Males are affected nine to ten times as frequently as females.

ONSET

The onset is gradual and insidious in two-thirds of cases and more acute and abrupt in the remainder. In the majority, the earliest symptoms are referred to the low-back area but in 15 to 20% the disease begins as an acute inflammatory arthritis of one or more of the peripheral joints. Rarely, the initial pain and stiffness have a diffuse non-articular distribution in the thorax, the neck, or throughout the limbs.

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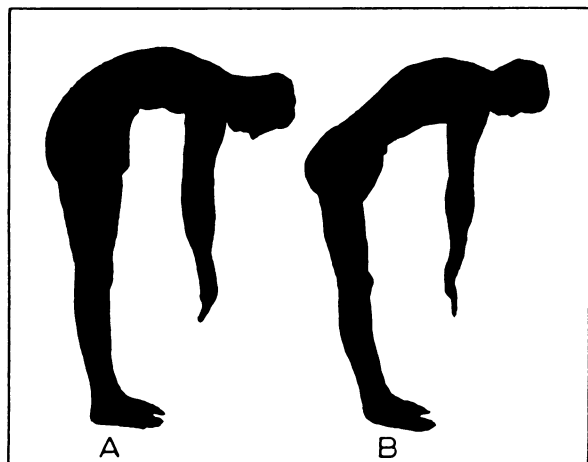


Fig. 1.—Silhouettes of (A) normal individual and (B) patient with ankylosing spondylitis, reaching toward the toes without flexing the knees. Note flattening and loss of flexibility of lower thoracic and lumbar spine of the spondylitic in contrast to the normal uniformly regular spinal curve.

SYMPTOMS

The usual complaint is dull aching pain located in the low-back region in the early stages but tending to spread proximally up the spine as the disease progresses. As a rule the back pain is accompanied by a subjective sense of stiffness, often aggravated by cold, dampness, physical inactivity, or strenuous exertion and relieved temporarily by heat, salicylates and mild "limbering-up" exercise. Morning stiffness and "jelling" are common. Sharp stabbing pain may occur spontaneously but is brought on more often by sudden movements, jarring, coughing, sneezing or straining. Many patients describe a vague sense of weakness, tiredness and instability in the musculature of the affected regions. "Girdle-pain", a tight band-like feeling of constriction around the chest or abdomen, is a frequent complaint. In the presence of active arthritis of the cervical spine, pain may spread up the neck to the occiput and around the temporal, parietal and frontal areas of the cranium, resulting in severe headaches, spasmodic in occurrence but steady and non-throbbing in character, usually aggravated by sudden neck movements. Radiation of low back pain into the buttocks and thighs is a common symptom which may bear a superficial resemblance to sciatic pain due to herniation of an intervertebral disc or other lesion causing sciatic root compression. It differs from the latter, however, in that it usually varies from one side to the other, rarely extends below knee level, and is not accompanied by sensory, motor or reflex changes. Fatigue is often a prominent symptom and may be accompanied by loss of weight, malaise and general weakness in its more severe form.

PHYSICAL SIGNS

Occasionally, in the early stages of the disease, there may be no abnormal findings on physical examination. In the great majority, however, there

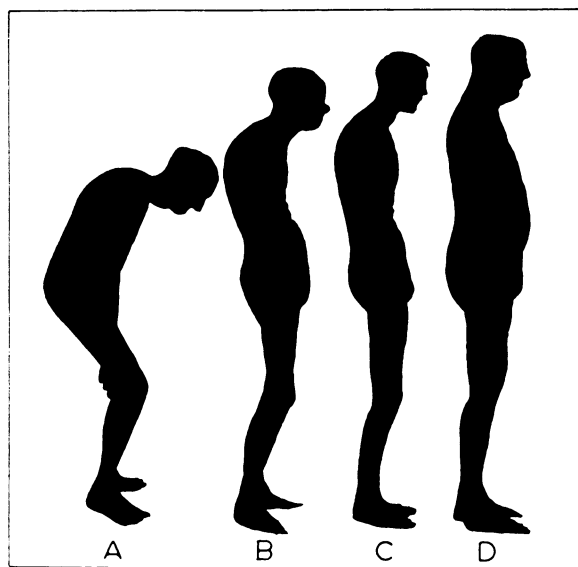


Fig. 2.—Silhouettes of four patients with ankylosing spondylitis illustrating varying degrees of static postural deformity. Note the forward thrust of head and neck, depression of chin toward the chest, the flattened "ironed-out" lumbar curve, upward tilt of pelvis and semi-flexion of hips and knees. Patient A illustrates severe degree of these abnormalities, while patient D has maintained almost normal posture.

is some reduction in spinal mobility, particularly in the lumbar region which characteristically reveals decreased flexibility and flattening when the patient attempts to stoop forward and reach toward his toes without flexing the knees (Fig. 1). In later stages of the disease, cervical mobility may also be reduced and in advanced cases the entire spine from occiput to sacrum may be ankylosed and rigid.

The typical postural abnormalities include a flattening and "ironing-out" of the lumbar curve, a smooth, rounded, thoracic kyphosis, forward protrusion of the head and neck with depression of the chin toward the chest, and less commonly, scoliosis. The pelvis may be tilted upward and the hips and knees semi-flexed, the over-all effect of these postural abnormalities producing a "simian" or ape-like posture. The extent and severity of deformity varies greatly from patient to patient (Fig. 2).

Decreased costovertebral movement and reduced chest expansion are frequently observed.

Spinal and sacro-iliac tenderness may be present during active stages of the disease, and spasm and atrophy of the paravertebral, abdominal, gluteal and thigh muscles are not uncommon.

Reduction in the range of hip and shoulder movement is demonstrable in about one-quarter of patients.

In 25 to 30%, one or more peripheral joints, particularly those of the lower limbs, exhibit evidence of an arthritis which is clinically and pathologically similar to rheumatoid arthritis.

The manubrio-sternal articulation is frequently involved, and less commonly the xiphi-sternum, acromio-clavicular, sterno-clavicular, costo-sternal and temporo-mandibular joints are the sites of painful, tender, inflammatory lesions.

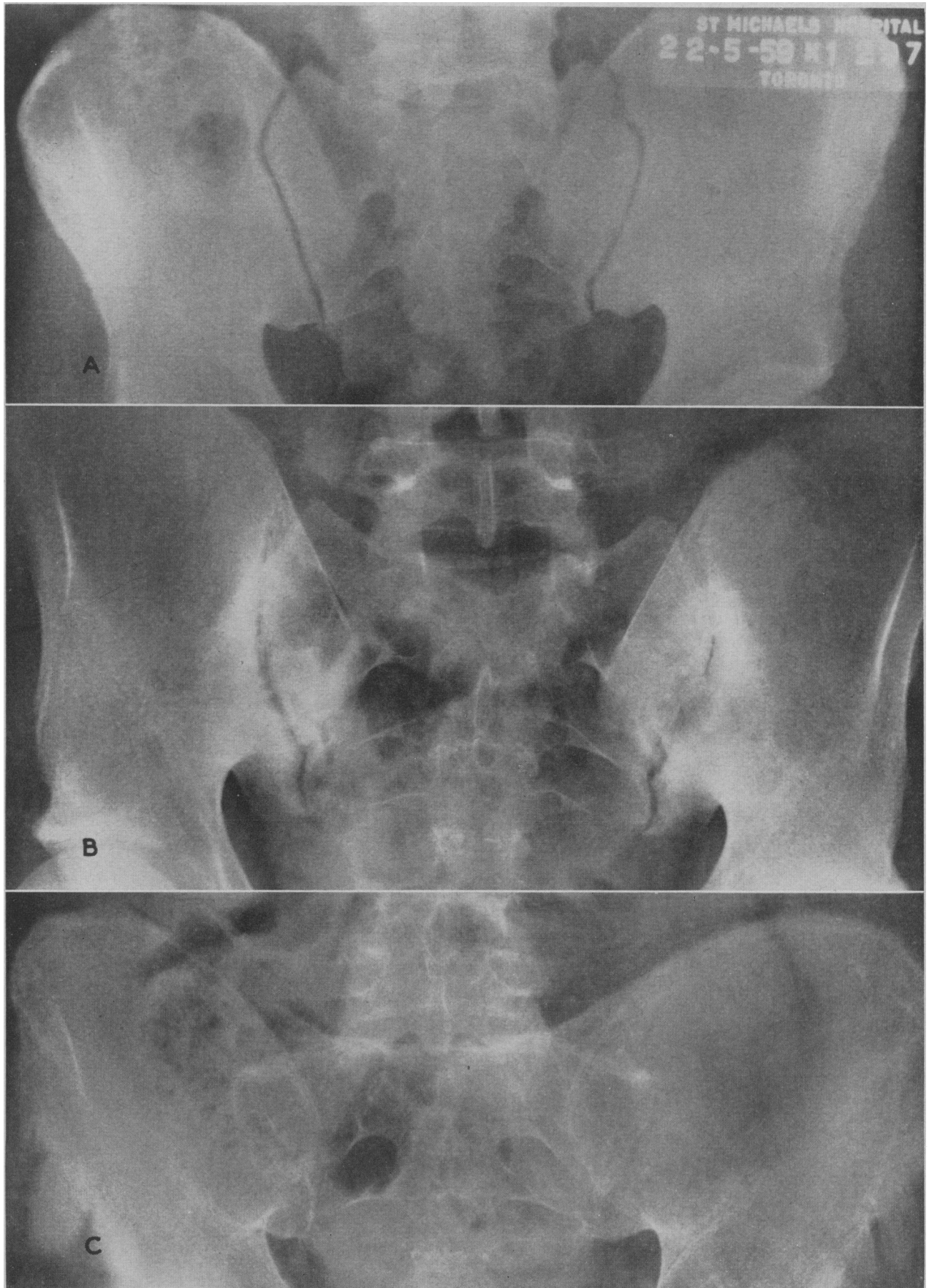


Fig. 3—(A) Radiographic appearance of normal sacro-iliac joints with uniformly regular articular space, well-defined clear-cut margins, and even density of adjacent bone. (B) Early sacro-iliac changes in ankylosing spondylitis. Joint outlines are hazy and blurred, the articular space appears unevenly widened, and its margins reveal erosions with patchy sclerosis of adjacent subchondral bone. (C) Late sacro-iliac changes are seen. The joint spaces have been obliterated by bony fusion. As arkylosis has progressed, the subchondral sclerosis has faded and the bone structure of the sacrum and ilium is of less than normal density.

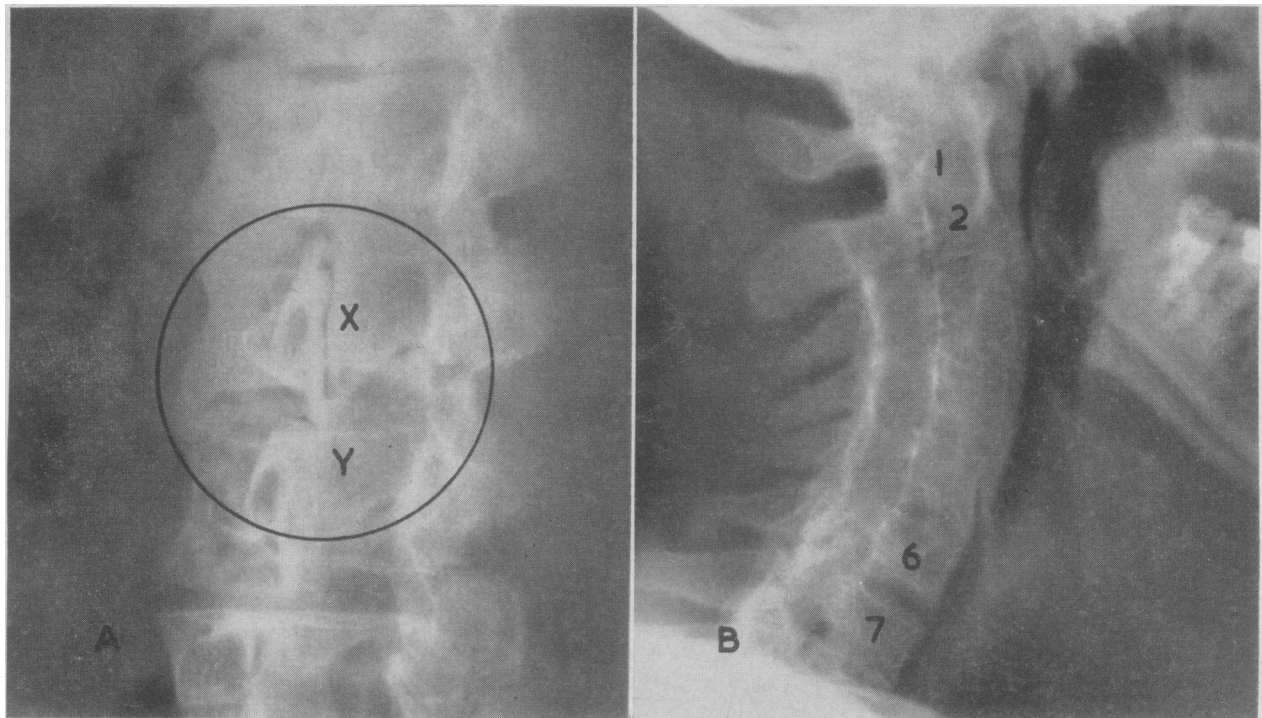


Fig. 4.—(A) Oblique radiograph of lumbar spine demonstrating the intervertebral apophyseal facets of a patient with ankylosing spondylitis. Apophyseal joint —X— reveals irregularity of articular space, erosions of its margins, and sclerosis of adjacent subchondral bone. Apophyseal joint —Y— has been obliterated by uniform bony ankylosis. (B) Lateral radiograph of cervical spine showing bony fusion of the apophyseal facets from C1 to C6 level. The facet at C6-C7 reveals a remnant of its joint space with well-marked sclerosis of the marginal bone.

About 10% of patients exhibit tenderness of the heels, over the plantar or posterior aspects of the calcanei, with or without calcaneal spur formation.

LABORATORY FINDINGS

The sedimentation rate may show little or no elevation in as many as 20% of patients, but is usually moderately increased and in severe cases may be grossly elevated.

Slight to moderate "secondary" anaemia and leukocytosis are not uncommon.

The serological reactions for rheumatoid factor, using the sensitized sheep cell agglutination, F-II latex fixation and bentonite flocculation tests, are characteristically negative.¹

RADIOGRAPHIC CHARACTERISTICS

The earliest x-ray abnormalities nearly always involve the sacro-iliac joints in the form of blurring and haziness of their outlines, pseudo-widening of the joint space, irregular punched-out erosions of their margins and sclerosis of the adjacent subchondral bone. These changes may progress to bony ankylosis and finally to complete obliteration of the joint spaces (Fig. 3).

Similar radiological changes involve the intervertebral apophyseal joints, with an irregular distribution; the process tends to progress proxi-

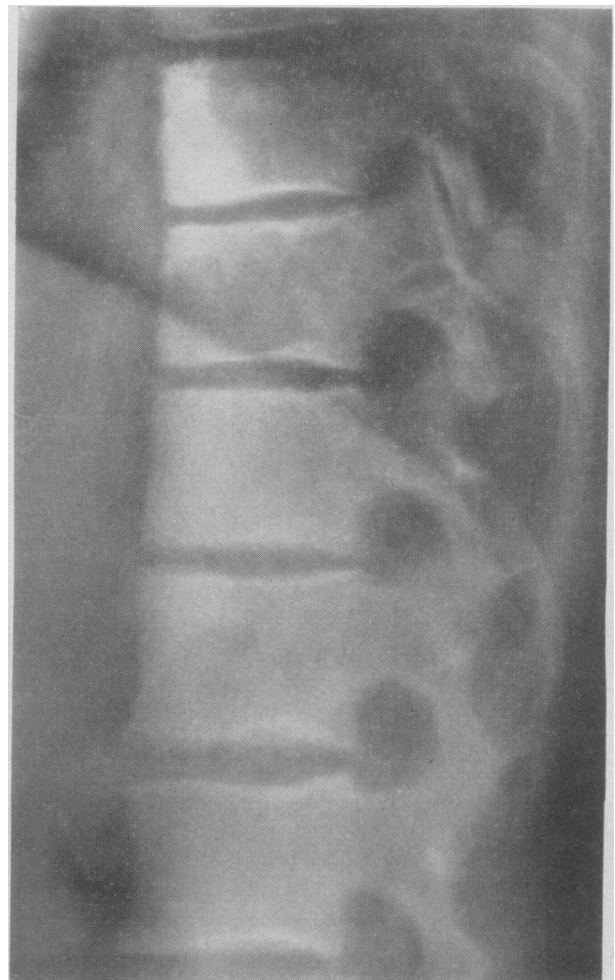


Fig. 5.—Lateral radiograph of the thoracic spine illustrating the "squaring-off" phenomenon. The corners of the upper three vertebral bodies are practically right-angled and their anterior borders are straightened out. In contrast, the lower vertebral body has a normally concave anterior border and its anterior corners have normal angles of less than 90°.

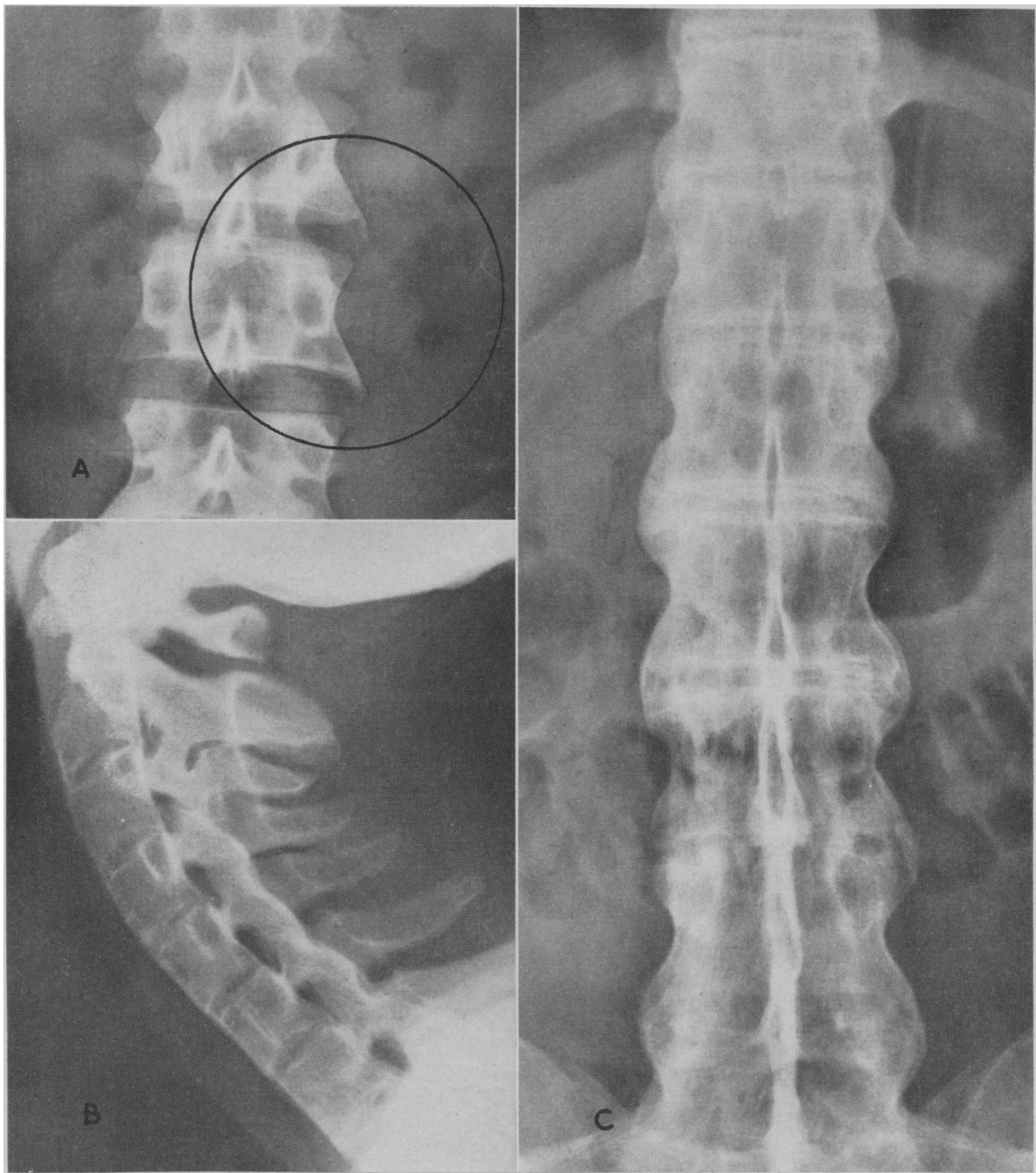


Fig. 6.—(A) Antero-posterior radiograph of upper lumbar spine showing early paravertebral ossification. Delicate linear spicules of new bone project from the infero-lateral angles of the bodies of the 2nd and 3rd lumbar vertebrae along the outer margins of the intervertebral discs and inner aspect of the paravertebral ligaments. (B) Lateral radiograph of cervical spine showing continuous intervertebral bony bridging due to ossification along both anterior and posterior spinal ligaments. (C) Antero-posterior radiograph of lower thoracic and lumbar spine showing extensive intervertebral bony bridging due to ossification along the paravertebral ligaments and disc margins. Ossification is also evident along the interspinous ligament in the mid-line of the lumbar (so-called "bamboo-spine").

mally for a variable extent through the lumbar spine, and in more advanced cases extends through the thoracic and later the cervical regions (Fig. 4).

Comparatively early in the disease, the thoracic and lumbar vertebral bodies frequently show a straightening out of their normally slightly concave surfaces, giving them a "squared-off" appearance (Fig. 5).

Calcification or ossification occurs at first in the annulus fibrosus of the intervertebral discs and

later along the paravertebral and ilio-lumbar ligaments. Such paravertebral ossification usually begins in the lower thoracic and upper lumbar regions and gradually extends to involve other levels. In severe cases it may progress to complete intervertebral bony bridging throughout the entire spinal column, producing a rigid "bamboo-spine" (Fig. 6). At times, similar calcification or ossification may involve other ligaments including those of the extremities as well as the spine (Fig. 7).



Fig. 7.—Ligamentous ossification at other less common sites in patients with ankylosing spondylitis. A.—Ossified lumbo-costal ligament between L1 transverse process and neck of 12th rib. B.—Uniform ossification of coraco-clavicular ligament at the shoulder. C.—Ossification of the fibular capitular ligaments traversing the anterior and posterior aspects of the proximal tibio-fibular articulation at the knee.

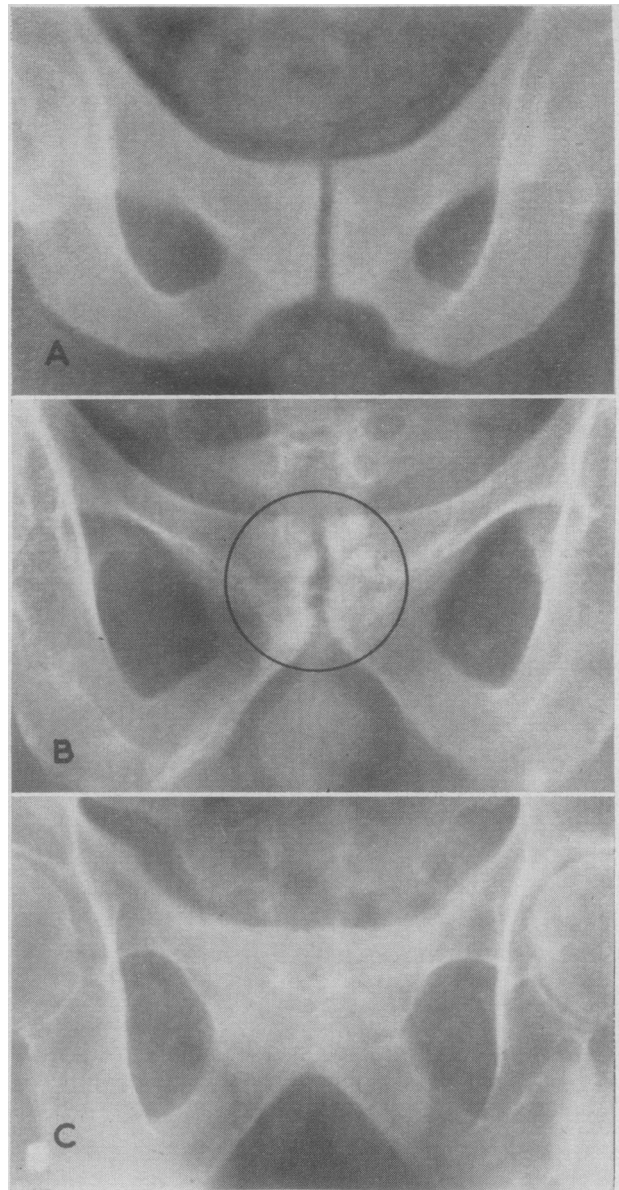


Fig. 8.—A. Normal symphysis pubis with regular interpubic space, clear-cut margins and uniform density of adjacent bone. B.—Early changes in pubic symphysis in ankylosing spondylitis. The margins are hazy in outline with irregular erosions and patchy sclerosis of adjacent bone. C.—Late changes in pubic symphysis in ankylosing spondylitis. The synchondrosis has been obliterated by uniform bony fusion. The evolution of these changes in the pubic symphysis is strikingly similar to that observed in the sacro-iliac and apophyseal joints and in the manubrio-sternal synchondrosis.

Synchondroses such as the symphysis pubis, manubrio-sternum, and xiphi-sternum may reveal irregular erosions of their margins which occasionally progress to bony fusion (Figs. 8 and 9).

Irregular surface erosions and new bone formation frequently occur at sites of fascial, ligamentous or muscular attachments, notably over the ischial tuberosities, the lateral surfaces of the iliac bones, the inferior aspects of the calcanei in the form of calcaneal spurs, the femoral trochanters, and occasionally at other locations in the extremities (Figs. 10 and 11).

The extent of these radiological changes varies greatly from patient to patient. Not uncommonly,

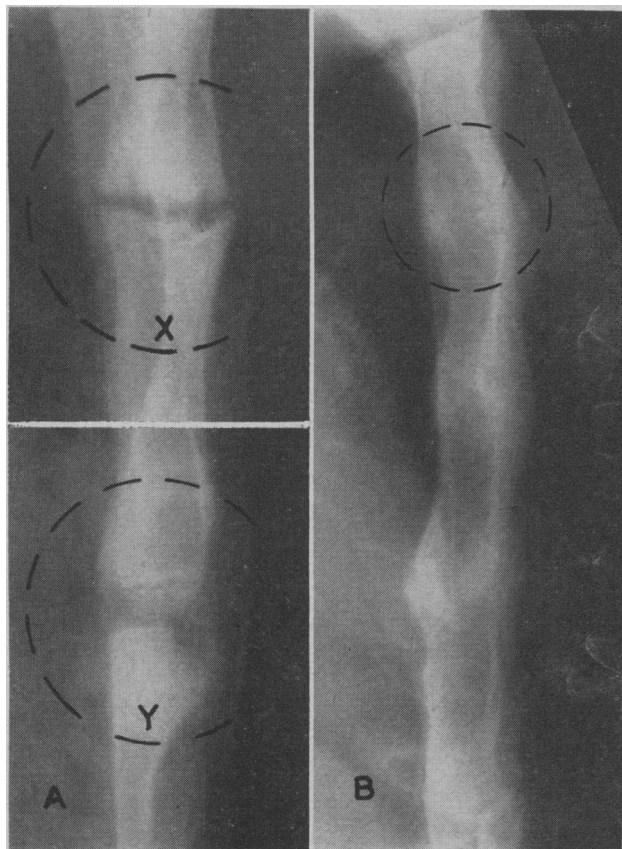


Fig. 9.—(A) Lateral radiograph of sternum illustrating irregular erosions of the margins of the manubrio-sternal synchondrosis —X—; and the xiphi-sternal articulation —Y—. (B) Lateral radiograph of sternum illustrating late stage of manubrio-sternal involvement with uniform bony fusion of this synchondrosis.

x-ray abnormalities remain confined to the sacroiliac joints, no other spinal or extra-spinal changes being demonstrable. In other instances the various x-ray findings described above occur in a great variety of combinations and degrees. X-ray changes in peripheral joints, when present, may resemble those of rheumatoid arthritis.

COMPLICATIONS

Recurring attacks of iritis or uveitis are the most common complication of ankylosing spondylitis, increasing in prevalence with increasing duration of the disease. These attacks of ocular inflammation usually subside completely with no residua but occasionally, after repeated recurrences, synechia, visual impairment or blindness may ensue.

A small number of patients exhibit an unusual cardiovascular lesion involving mainly the aortic valve and proximal aorta, which appears to be specific for this disease. Its major clinical manifestations are aortic regurgitation and prolonged atrio-ventricular conduction, and less commonly pericarditis. This "spondylitic heart disease" usually runs a prolonged course, but in time may eventuate in cardiac failure which may be the cause of death.²

Secondary amyloidosis, affecting the kidneys predominantly, is a rare complication which may

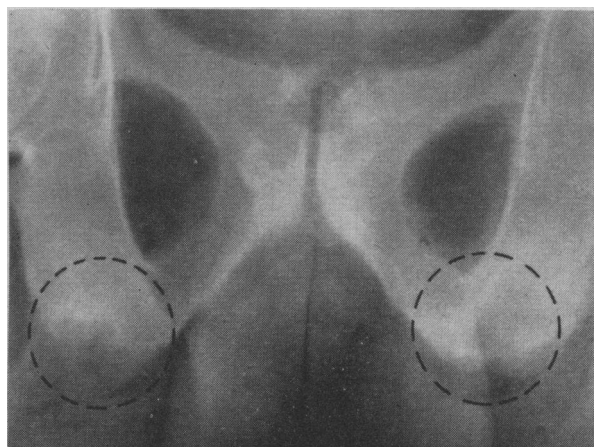


Fig. 10—Irregular osteolytic erosions of the ischial tuberosities. Such lytic lesions usually precede the production of irregular new bone illustrated in Fig. 11.

result in a nephrotic syndrome, gradual failure of renal function and death.

TREATMENT

The following general measures constitute the fundamental principles of care of the spondylitic patient: (1) The provision of adequate rest. This does not necessarily entail cessation of work except for the small proportion of patients who are badly disabled by severe, active disease. In some cases, a physically strenuous occupation may require modification or a change to lighter employment within the patient's limitations, but commensurate with his abilities, skills and training. (2) The use of a firm, non-sagging sleeping surface with boards under the mattress. (3) Daily physical therapy procedures involving the application of suitable forms of local heat followed by a specific program of therapeutic exercises, including deep breathing exercises and constant observance of proper postural habits. Most patients require encouragement, explanation and repeated instruction regarding these techniques and their importance in maintaining functional ability and preventing or minimizing deformity. (4) Maintenance of optimum nutrition with a full, well-balanced diet. (5) When required for relief of pain and stiffness, the regular administration of salicylates in adequate doses which may amount to as much as four, or occasionally five, grams daily.

This program, modified to meet the needs of each patient, should be observed faithfully whether or not other so-called "specific" forms of treatment are employed. Many patients do quite well on this regimen alone.

If pain and spasm persist and result in significant disability, phenylbutazone has proved particularly useful in doses of 100 mg., three to four times daily, and sometimes in smaller doses. While beneficial to many patients, its effects may, however, be disappointing to some and precautions must be observed to avoid its well-known toxic effects.

Deep x-ray therapy also may be followed by relief of pain and spasm during active phases of

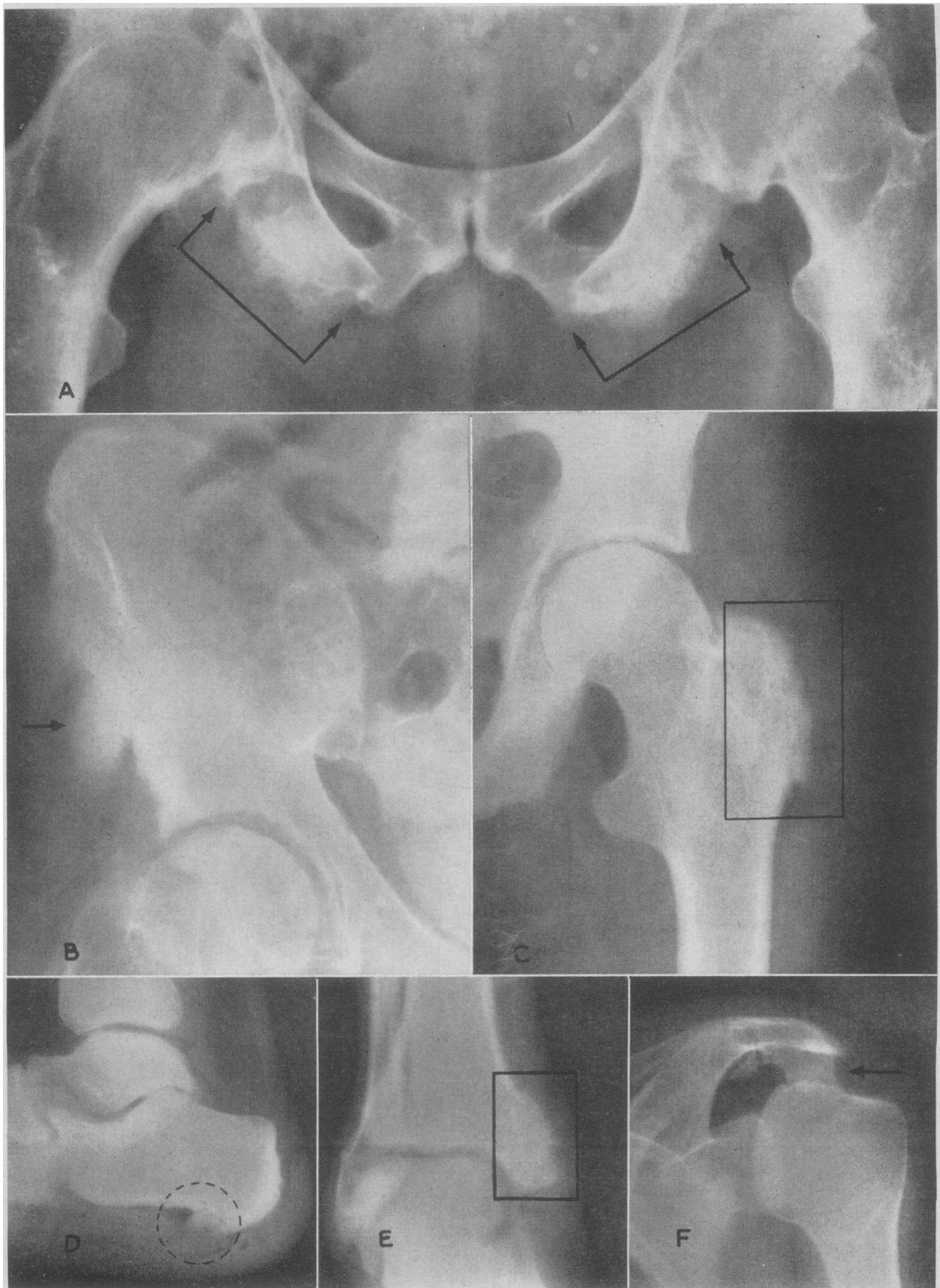


Fig. 11.—Irregular new bone formation at sites of muscular ligamentous and fascial attachments to bony surfaces.—(A) Over the ischial tuberosities.—(B) Over the lateral aspect of the ilium.—(C) Over the greater trochanter of femur.—(D) Over the plantar surface of the calcaneus in the form of a calcaneal spur.—(E) Over the medial malleolus of the tibia.—(F) Bar of new bone extending from the interior surface of the acromion.

the disease in some, but not all, cases. There is no convincing evidence that it halts progression of the disease or results in permanent remission. The development of leukæmia several years after roentgen therapy is now well documented and while it occurs in only a small proportion of patients, this potential hazard must be recognized and weighed against the probability of concrete benefit to the majority of patients so treated.³

Cortisone or other corticosteroid analogues may assist in the rehabilitation of some who have not responded satisfactorily to other measures, but these hormones are not required or indicated for the majority of patients and their prolonged administration may result in undesirable and occasionally serious effects.

Mr. Arthur Smialowski and the Department of Photography, St. Michael's Hospital, Toronto, provided valuable assistance in the preparation of illustrations.

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RÉSUMÉ

La spondylose rhizomélique ou spondylarthrite ankylosante est un trouble inflammatoire d'origine inconnue affectant les articulations sacro-iliaques et apophysaires de la colonne vertébrale, les surfaces osseuses au point d'attache des ligaments, muscles et aponévroses et les synchondroses. En dépit de ressemblance entre elles, la spondylarthrite et la polyarthrite chronique évolutive

semblent deux entités distinctes. Dans les deux tiers des cas le début est lent et insidieux. La majorité des symptômes se rapportent à la région dorso-lombaire sous forme de douleurs sourdes avec extension ascendante le long de la colonne à mesure que l'affection progresse. Le malade accuse de la rigidité augmentée par le froid, l'humidité, et la grande activité physique et soulagée par la chaleur, les salicylates et des exercices modérés. Le malade se plaint de fatigue et d'une sensation de constriction de la poitrine et de l'abdomen. L'examen clinique révèle une diminution dans la flexibilité de la colonne surtout dans la région lombaire. La posture est affectée par le redressement de la courbure lombaire et le malade prend une apparence simiesque. Des spasmes musculaires sont observés. Les épreuves de laboratoire peuvent montrer une vitesse de sédimentation élevée ainsi qu'une certaine anémie et une leucocytose. A la radiographie l'articulation sacro-iliaque perd de sa netteté et l'os adjacent montre de la sclérose. Les corps vertébraux thoraciques et lombaires revêtent une apparence de bloc comme le montre la Fig. 5. On découvre aussi une ossification para-vertébrale avec syndesmophytes qui débute habituellement dans la région dorso-lombaire et qui s'étend par la suite dans les deux directions. La colonne évoque alors l'aspect d'une tige de bambou. Parmi les complications notons l'iritis et l'uvéite qui peuvent quelquefois créer des synéchies et même causer la cécité. On peut aussi trouver des atteintes à la valvule aortique et même une péricardite. L'amylose secondaire ne se manifeste que rarement. Le malade atteint de spondylose doit pouvoir se reposer sans nécessairement interrompre toute activité physique. Il couchera sur une surface ferme et recevra des applications de chaleur locale suivies d'un programme d'exercices thérapeutiques comprenant des exercices respiratoires. La nutrition doit être maintenue à son niveau optimum grâce à un régime bien équilibré. La douleur et la rigidité peuvent répondre à l'administration de salicylate. Dans les cas rebelles l'administration de phénylbutazone a déjà donné des résultats intéressants. Lorsque l'affection est en phase d'activité la radiothérapie peut soulager la douleur et le spasme sans nécessairement interrompre l'évolution de la maladie. On peut aussi avoir recours à la cortisone et aux autres stéroïdes.

CASE REPORT

FUNGOUS GRANULOMA OF THE LOWER LEG DUE TO TRICHOPHYTON MENTAGROPHYTES

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NUMEROUS REPORTS have appeared in the North American literature on mycotic granulomas of the leg due to *Trichophyton rubrum*.¹⁻³ Some European articles⁴⁻⁶ indicate that rarely *Trichophyton mentagrophytes* may be the cause.

Mrs. H.S., aged 36, was referred to me by her family doctor* for diagnosis and treatment of a non-healing "sore" on her right anterior lower leg. The "sore" appeared in November 1958. There was no known exposure to animals with ringworm.

*Dr. Donald Robertson of Morrisburg, Ontario.



Fig. 1.—Scaly dermatitis on anterior lower leg (from 35 mm. colour transparency).