

REFRESHER COURSE FOR GENERAL PRACTITIONERS

RHEUMATOID ARTHRITIS

BY

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Rheumatoid arthritis is a general disease of unknown aetiology which is characterized clinically by a condition of non-suppurative polyarthritis. Pathologically the basic lesion is one of fibrinoid degeneration of the collagen component of the fibrous tissues. It is therefore an important member of what is often termed the collagen group of diseases.

Rheumatoid arthritis has been known under many names, which include atrophic arthritis, proliferative arthritis, arthritis deformans, and infective polyarthritis. When it occurs in children it is known as Still's disease. The disease may start at any age, but in the recent survey made by the Empire Rheumatism Council the age at onset in 532 patients was 41.5 years. Females are affected at least three times as frequently as males, and this preponderance is greater in the lower age groups. It was also established in the course of this survey that there is some familial tendency to develop the disease. It is thought that about 4% of the female population of this country are victims, and that the cost to the country is about one million pounds annually.

Aetiology

Although the aetiology of this disease is unknown, there are a number of factors which are far-reaching in their effects as predisposing or precipitating agents in certain patients. Amongst the intrinsic factors of this nature may be mentioned the patient's body-build (somatotype), abnormalities of the peripheral circulation, endocrine factors, metabolic and nutritional disorders, and response to stress. Of extrinsic factors such traditional entities as climate and environment, infection, and psychological upset or shock may be mentioned; while both pregnancy and jaundice will produce remissions of the established disease. In most cases the disease appears to result from the interplay of such factors, although future research may disclose some single aetiological factor.

Pathology

The pathological process as seen in the synovial membrane of the affected joints is inflammatory in nature. Later this spreads to the capsular, tendinous, and subchondral tissues, and the cartilage is invaded from beneath. Fibrous tissue later replaces these structures, and ankylosis will occur owing to the fusion of the layers of fibrous tissue on opposing joint surfaces. If untreated the affected joints will generally become immobilized in the position of flexion as the result of spasm of the surrounding muscles. The earliest radiographic appearance is osteoporosis of the bone ends. Later, marginal erosions and diminution in the affected joint spaces will be seen, and small cystic areas of degeneration are not unusual. In the latest stages joint disorganization and even bony ankylosis may occur.

In the active stage of rheumatoid arthritis the erythrocyte sedimentation rate is always raised, and progress can be followed by routine repetition of this simple test. Some degree of anaemia of the hypochromic type is also commonly found, and this generally fails to respond satisfactorily to the oral administration of iron. The serological tests formerly used to indicate the presence and degree of activity of the haemolytic streptococcus are not nowadays

used. The albumin/globulin ratio in the plasma is generally reversed in active cases, although the total protein content may be normal.

Clinical Features

A period of general ill-health which may be characterized by undue fatigue, pallor, loss of weight, paraesthesiae of the limbs, tachycardia, and muscular stiffness often precedes the onset of the articular phase of the disease. This may give rise to considerable diagnostic difficulty and uncertainty. When the condition starts acutely with pyrexia the clinical picture may resemble that of an infection, while in those cases in which the arthritis is of a fleeting nature the diagnosis of rheumatic fever may be suggested. Certain cases remain non-articular for weeks or even months, and tuberculous infection or trauma may then appear likely causes. In view of the great variation possible in the type of onset the following conditions, in addition to those already mentioned, may have to be distinguished from rheumatoid arthritis: gonococcal and acute suppurative arthritis, Reiter's syndrome, gout, osteoarthritis, disseminated lupus erythematosus, syphilitic arthritis, scleroderma and dermatomyositis, polyarteritis nodosa, and the joint symptoms of purpura or haemophilia.

In a classical case the small joints of the hands and feet will rapidly become swollen and painful, and the process will then progressively involve the larger joints, and sometimes even the spinal column and jaws, although remissions and exacerbations are to be expected at this stage. Morning stiffness is a prominent symptom, the patient often being almost helpless early in the morning, but regaining considerable freedom of movement later in the day. Persistent attempts on the part of the patient to "walk it off" will generally result in an increase in joint effusion, muscle spasm, and, later, flexion deformity and permanent impairment of function.

Muscle wasting is often a prominent feature of these cases, and in the hands this may result in ulnar deviation and subluxation of the metacarpo-phalangeal joints. Abduction and rotation of the shoulders is generally much restricted, particularly in patients who are confined to their bed or a chair. Flexion of the knees as the result of powerful spasm of the hamstring muscles will generally occur in cases inadequately treated, and constitutes a serious and disabling deformity. Even when the active phase of the disease subsides, pain and disability are likely to persist in such cases as the result of residual joint damage. In the later stages of the disease, in addition to permanent deformity of the joints, there may be profound emaciation and anaemia, and the patient may die of intercurrent infection. Psoriasis is not infrequently associated with rheumatoid arthritis, and the association of these conditions is thought by some authorities to increase the gravity of the prognosis.

Prognosis

It is a matter of the greatest difficulty to forecast the course that the disease will run in any particular patient. The type of onset gives no clue to its subsequent behaviour. The average case runs a course in which exacerbations and remissions may alternate over many years. It is thought that if a group of average well-treated patients were followed over a period of ten years, at the end of that time 45% would be stationary, 50% would be in remission or improved

to some extent, while the rest would be crippled in varying degrees. As Davidson has said, "The attitude of the physician should be one of cheerful optimism, as in about half his patients this will be justified by results, and in the other half much can be done to conserve function and prevent deformity."

General Management

There is no specific curative agent known which is uniformly effective in the treatment of rheumatoid arthritis. The application of more scientific and critical methods of assessment in the past few years has destroyed the claims made on behalf of a number of remedies previously believed to be effective. Nothing will be lost by the patient being aware of this, since the hope of a magical cure will militate against acceptance of methods of treatment which may require life-long application and co-operation. In many cases the patient must be taught and helped to "live with his disease." The enlightened application of methods of treatment aimed at maintaining or restoring a reasonable level of function, together with the relief of symptoms, notably pain, will retain the patient's active co-operation and produce improvement or remission in at least half our patients.

In the early stages, when constitutional symptoms are severe and the affected joints are swollen and painful, there should be no alternative to rest in bed. It is at this stage, and not at the stage of crippledness, that such patients can most profitably be admitted to hospital. During this period the affected joints should be immobilized for most of the time by means of plaster-of-Paris splints, which can easily be moulded to the limbs. The physical condition of the body will, however, deteriorate if the rest is too complete, and if this occurs subsequent rehabilitation may be retarded. A compromise must therefore be adopted whereby the benefit of this rest is combined with the performance of general bodily exercises which are designed to maintain the functional integrity of the main muscle groups in the gluteal, lumbar, and thoracic regions, as well as those controlling the limbs. These exercises are known to all well-trained physiotherapists.

The position of the patient in bed must also be regulated so that the spine is not maintained in a position of flexion, with consequent restriction of thoracic movement. The knees must not be helped into contraction by allowing a supporting pillow, and the feet must not be allowed to drop as the result of pressure by the bedclothes. The bad reputation of rest in bed in this disease arose purely as the result of failure to recognize the importance of these simple, but fundamental, principles. In addition, such factors as a nourishing mixed diet, good nursing, and cheerful surroundings will help to forward the physical and mental regeneration of the patient.

Most patients suffering from this disease are underweight, and in such cases it is important to secure an adequate intake of protein, together with an ample supply of vitamins and minerals, such as are indicated in all patients who are suffering from a chronic wasting disease. Extra fat is also indicated in the form of milk, cream, eggs, and butter.

Relief of Pain, Sleeplessness, and Anaemia

It is important to prescribe both hypnotics and analgesics in adequate regular dosage during the acute phase of the disease, since lack of sleep and the endurance of needless pain will produce very rapid deterioration in the patient's condition. Aspirin in one of its forms is the most readily acceptable analgesic in doses of 10 to 15 gr. (0.65 to 1 g.) every four hours. This can be alternated with tab. codein. co. (B.P.) two tablets after each meal. As a hypnotic, in cases in which sleep is disturbed, this may be reinforced with one of the barbiturate preparations, taken with a hot drink last thing at night.

A common feature of rheumatoid arthritis is anaemia, and iron should therefore be administered as a routine in the form of the ferrous salt. If this proves ineffective the intra-

venous route should be substituted for the oral. A reliable preparation can be injected twice a week on four or five occasions with advantage. Toxic symptoms practically never result from this procedure, but the subjective improvement manifested by the patient as the blood improves is often rapid and considerable. Blood transfusion, on one or more occasions, is also a useful supporting measure and probably merits more frequent use in this disease.

Gold

It is generally recognized, although it has not been scientifically proved, that the employment of gold salts by intramuscular injection will have a beneficial effect upon the course of active rheumatoid arthritis in most cases. It is also generally believed that the maximum therapeutic response to gold is likely to occur during or following the first course of injections, although this is not invariably so. The toxic reactions which may follow the injection of gold salts have probably received more than their fair share of publicity, since they are serious enough to cause treatment to be withheld in only 4 to 5% of cases. Toxic reactions include irritation of the skin, which may be followed by an erythema or a morbilliform rash, and if treatment is not stopped this may progress to the stage of severe exfoliative dermatitis, which will necessitate special treatment with dimercaprol. Such patients should never receive gold again. Less serious complications of this method of treatment are stomatitis, transient albuminuria, and very occasionally a toxic nephritis or hepatitis. Agranulocytosis has been reported on one or two occasions.

Gold should never be the only form of treatment used, since it will do nothing to prevent deformity; nor should it be used as a last resort in a severely crippled patient. Its only function is to lessen the activity of the unknown disease-process in the blood stream.

There are several preparations of gold salts on the market. Preference should be given to the water-soluble salts which are given by intramuscular injection. Colloidal preparations are believed to be less effective. Injections are generally given at intervals of a week. The first two or three should be very small (0.01 g.), in order to test the patient's sensitivity. If no contraindication has arisen this dosage can then be doubled, and after a further few injections raised to 0.05 g. and continued at this level until a total of 0.5-1 g. has been administered. If improvement occurs after or during this course of treatment a further similar course may be embarked upon after an interval of four to six months, or at the first sign of renewed activity of the disease. Some authorities prefer the alternative of a fortnightly maintenance dose of 0.05 g. for a few weeks after the termination of the complete course, after which the time interval can be lengthened to once a month, and maintained in this way for six to twelve months.

It is important to question the patient for early signs of toxicity at each visit, otherwise such early toxic signs as a metallic taste, itching of the skin, or purpuric spots might be ignored. It is wise also to examine the urine for albumin on each occasion, and an occasional blood count should be made during a long course of treatment. Should any abnormality be noticed gold should be stopped until it has disappeared. Gold is contraindicated in old patients or in cases in which there is evidence of disease of the kidneys, liver, or bone marrow, and also in cases of severe skin disease other than psoriasis.

Other Remedies

Copper salts have recently been introduced as an alternative to gold in cases in which the latter for any reason is not well tolerated. Experience of them in this country does not seem to have been encouraging, however. Bismuth has also been recommended for the same reason, but no appreciable benefit is generally observed as the result of its use.

Claims have been made in the past for numerous remedies for rheumatoid arthritis. These are too numerous to mention in detail, but it can be said with some confidence that few, if any, of these if subjected to controlled clinical assessment could be shown to have more than a placebo value. The list would include such diverse entities as iodine locketts, bee venom, vitamin D in enormous dosage, cobra venom, guaiacol, chaulmoogra oil, sulphur (both internally or sprinkled in one's shoes), and celery salt with every meal.

Focal Infection

The belief that rheumatoid arthritis is caused by obscure focal infection is no longer widely held in this country or America. The removal of teeth and tonsils or the surgical approach to nasal sinuses on suspicion alone is therefore not generally encouraged. Obvious infection in any site should naturally be approached in a rational spirit owing to its secondary deleterious effect on chronic disease of this type. Vaccines are not now often thought to be indicated in the treatment of rheumatoid arthritis in which no specific infection can be demonstrated.

Care of the Joints

In cases in which muscle spasm is pulling the joints into a position of flexion a plaster-of-Paris splint should be applied, so as to immobilize them in their best position for a few days. Spasm and pain will be abolished by this procedure, and after a few days the splint can be removed and the joint put gently through full movement in order to prevent adhesions forming. Another plaster can then be applied, and it will generally be found that on this second occasion it will be possible to fix the joint in full extension. After a week this also should be removed and the posterior portion retained for use as a gutter splint. The affected limb should be bandaged into this for most of the day, being removed only for gentle movement once daily.

Later, further measures will be required to restore active function and stability of the affected joints: these will involve the re-education of the muscles which should control these joints. Premature weight-bearing in the absence of such control must be avoided, since it will lead only to a recurrence of pain and effusion, and so to further muscle-wasting. This stage of muscle re-education consists in skilfully graduated resisted exercises and physiotherapy, which may lead on to the use of the stationary bicycle or rowing machine before actual walking is allowed with or without the help of crutches or sticks. It is important that the patient shall understand that full restoration of function ultimately depends upon his own efforts, which are supplemented, controlled, and directed by the doctor and the physiotherapist in consultation. Pain can be relieved with the help of heat in various forms, which may vary according to circumstances from poultices to short-wave diathermy, but massage is seldom indicated in active rheumatoid arthritis.

In the later stages of rehabilitation purposeful activity in the form of occupational therapy may supersede routine exercises in re-educating the patient in the use of his limbs and in restoring manual skill and dexterity. It will also restore the power of concentration, which often tends to be lost as the result of chronic illness.

In patients who become severely crippled in spite of adequate medical treatment certain orthopaedic measures may become necessary, and skilled surgical intervention if necessary need no longer be delayed on account of the disease being in an active stage.

Cortisone and A.C.T.H.

Three years ago Hench and his colleagues announced that they had been able to suppress the symptoms of rheumatoid arthritis by the administration of Kendall's compound E—now called cortisone—and of A.C.T.H. (adrenocorticotrophic hormone). This claim has subsequently been amply con-

firmed. It is important to realize, however, that it is *suppression* and not *cure* of the disease which is achieved by the use of these hormones, and thus relapse is usual soon after their administration is stopped. They are difficult to procure and expensive, and their prolonged use, which is necessary in a chronic disease such as rheumatoid arthritis, is apt to produce undesirable side-effects. Until these disadvantages have been overcome the use of cortisone and A.C.T.H. cannot be recommended as a routine procedure in a busy general practice, as much time and trouble are demanded by their successful use.

Their clinical suppressive effect is remarkable, and improvement generally occurs in the following sequence. First, stiffness is relieved, and then pain, tenderness, and swelling of the affected joints. Fever, if present, disappears, and the patient's appetite and weight increase. All this is accompanied by a sense of well-being which will often amount to euphoria. Cases in which the joint changes are potentially reversible will become practically symptom-free in seven to ten days, although some will continue to manifest minor signs of activity of the disease. The E.S.R. falls and the anaemia tends to revert to normal, as do the plasma proteins.

The dosage of cortisone originally recommended was 300 mg. on the first day, 200 mg. on the second day, and subsequently 100 mg. daily. Recent workers tend to adopt a lower scale and endeavour to maintain the patient on the lowest possible dosage consistent with reasonable comfort, since in this way the risk of side-effects is lessened. Some patients can be maintained on a daily dosage as low as 50 mg. or less with reasonable efficiency. Cortisone can be given either by injection or, in slightly higher dosage, by mouth. A.C.T.H. has to be given by injection every six hours; 40 mg. of A.C.T.H. is roughly equivalent to 100 mg. of cortisone.

The chief side-effects produced by these hormones are the result of their excessive physiological action, and consist principally in sodium retention (oedema), potassium excretion (muscle weakness), excess of sex-hormone production (acne, hirsutism, etc.), abnormalities of carbohydrate metabolism (diabetes), and cerebral stimulation (psychosis). Hyperadrenalism in the form of Cushing's syndrome may also occur. Other somewhat less important side-effects will include pigmentation, alteration in the facies, striae, rise in the blood pressure, tachycardia, and irregularity of the monthly periods. Wound healing may also be delayed, and the symptoms of the onset of acute inflammatory disease such as appendicitis may be masked. The chief contraindications to the use of cortisone and A.C.T.H. are incipient heart failure from any cause, thrombosis, diabetes, hyperpiesis, renal or tuberculous disease, and an unstable personality.

The mode of action of these hormones is completely unknown. With further experience of their use, together with technical improvements, which should result in a prolongation of their action and the elimination of side-effects, they will take their place as a very valuable medical treatment in selected cases. It is unlikely, however, that their use will ever entirely eliminate the need for the use of the other less specific types of treatment which have been briefly described above.

Next Refresher Course Article.—"Fractures in the Aged," by Mr. Richard H. Metcalfe.

The International Hospital Federation has chosen the week immediately preceding the Coronation for the Eighth International Hospital Congress—the first to be held in Great Britain. It will take place in London from May 25 to 30, 1953, and 1,000 delegates from some 30 countries are expected to attend. The meetings will be held at Church House, Westminster, where the Houses of Parliament met during the war years. A Hospitals Exhibition will be held in conjunction with the congress.