OSTEO-ARTICULAR SITES OF BRUCELLOSIS

BY

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From 1927 to 1955 a series of 174 consecutive cases of brucellosis due to *Brucella melitensis* (sometimes called "Malta fever") was studied at the Barcelona University Medical Clinic of Prof. A. Pedro Pons. The duration and intensity of each case varied, but all showed or had shown a stage of acute brucellosis on which the clinical diagnosis was based. The laboratory diagnosis was based on the sero-agglutination, blood culture, intradermal reaction, and, in the latter cases, on the complement-fixation test and the test of incomplete antibodies.

Osteo-articular signs appeared in 148 cases (85 per cent.). This figure is about the same as that given by other writers who have studied this organism (Cantaloube, 1911; Ruiz Castañeda, 1954; Betoulères and Maléki, 1948; Rimbaud and Serre, 1947), whereas it is clearly above those obtained by writers studying brucellosis produced by *Br. suis* (Hardy, 1929, 1937; Harris, 1950), and far above those found by writers studying the disease produced by *Br. abortus* (Hardy, 1929; Dalrymple-Champneys, 1935, 1950; Sylvest, 1951).

Sex.—Our series comprised 130 men and 44 women. Osteo-articular signs appeared in 89 per cent. of the men and in only 67 per cent. of the women; this greater incidence in men was due to a greater incidence of vertebral lesions.

Age.—The locomotor system was more frequently affected in patients over 50 years of age, and the invasion of the spinal column was also more frequent in elderly people.

Site of Lesions

Muscle and Skin Tissue.—This is infrequent, and in general of little clinical importance, but an extraordinary variety of sites and symptoms has been observed:

1. Myalgia was noted in 5·7 per cent. of our cases.

2. No case of Primitive Brucellar Myositis was observed; the few cases published are rather unconvincing (Paviot, Martin, and Déchaume, 1930; Harris, 1950).

3. Subcutaneous Nodules.—These may be about the size of a bean, hard and painful under pressure (Bouchut and Barbier, 1924). A nodule found by us upon the front of the tibia of one patient was shown by biopsy to be formed of young connective tissue, with many round cells similar to those in the brucellar granuloma.

4. Cellulalgia was also found with pain under pressure in a wide area of the forearm.

5. Cellulitis as described by other writers was not found.

6. Suppurative Cellulitis was seen with multiple sites, and the Brucella was found in the pus collected in one case.

7. Bursitis was seen in the olecranon in two cases, and beside the great trochanter in one case. These lesions had an acute evolution and an area of cellulitis was formed round them. A biopsy from one of these showed a diffuse inflammation of the connective tissue with formation of microscopic abscesses.

8. Tendinous Synovitis was seen in the extensors of the fingers.

Thus, brucellosis may affect the various soft structures of the locomotor system and produce various manifestations that may be divided into three groups:

(i) Algias.

(ii) Inflammation with the formation of granulation tissue (subcutaneous nodule).

(iii) Formation of micro-abscesses with possible suppuration, of which an example may be found in the case of bursitis in which a biopsy was made, and in the case of suppurative cellulitis.

Peripheral Joints.—Osteophytes appeared in the peripheral joints in 86 of our series of 174 patients (about 50 per cent.). The articular pictures were of various types and did not appear in different cases, but often coincided in the same patient and even in one outbreak of the same illness. They have been classified into three clinical types:

1. Arthralgia.—The chief symptom is pain, with some stiffness in acute cases. It was found in 53 cases (30 per cent.). It appears more frequently in the first month (60 per cent.) and accompanies febrile outbreaks, but

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may also rise in afebrile periods, when it is a symptom of disease activity.

It may affect one or several joints. The intensity of pain is moderate, lasting only a few days in a given joint.

(2) Mild or Fugitive Arthritis.—This consists in an articular effusion shown by pain, synovial swelling, and an increase of local warmth; reddening of the skin is rare. The articular fluid is sero-fibrinous, and often shows the presence of the Brucella (Ruiz Castañeda, 1954; Jambon and Bertrand, 1953). It is not accompanied by radiological alterations, and lasts less than one week in 62 per cent. of cases and never more than 2 months. It leaves no anatomical or functional sequelae.

It was observed in 39 (22 per cent.) of our cases and appeared somewhat later than the arthralgia; 62 per cent. after the first and before the eighth month. It was mono-articular in fifteen cases, but in others several joints were affected. It has been termed "brucellar pseudorheumatism". Only in two cases was effusion the predominant symptom.

The most frequent sites were the shoulder, knees, ankles, elbows, hips, the interphalanges of the hands and wrists, and the metatarsal-phalange of the big toe.

Scapulo-humeral periarthritis was observed in nine cases out of eighteen with osteophytes in the shoulder. It consisted in a pain and limitation of mobility lasting from 2 to 4 months.

We have no data of the pathological anatomy of these forms of arthritis. From the clinical and radiological studies it is inferred that it must be a capsulo-synovitis with which the joint reacts to the presence of the Brucella.

(3) Severe or Destructive Arthritis.—This is arthritis of an acute or subacute type, lasting from 2 to 8 months. It is accompanied by marked radiological alterations similar to those seen in infective arthritis. The articular fluid has a tendency to become suppurative, though it does not fistulate to the surface. When the process abates, it often leaves grave anatomical or functional sequelae.

Eight serious attacks of arthritis were seen in seven patients (4 per cent.). The hip was affected in six cases, the knee in one, and the metatarsal-phalangeal joint of the big toe in one.

The pathological anatomy has only been studied in one case (Michel-Bechet, Puig, and Charvet, 1939); there was intense capsulitis and pericapsulitis, the bone being affected slightly or not at all.

It appears that the process is similar to that of the mild or fugitive arthritis, but perhaps because of the anatomical conformation of the hip joint, the Brucella seemed more persistent, causing suppuration in the synovial membrane and destruction of the articular cartilage. Further histological examinations are desirable to confirm this theory.

Relations of Brucellosis with Other Forms of Chronic Rheumatism

Rheumatoid Arthritis.—No case was observed which evolved towards progressive chronic poly-arthritis, nor did any factor appear to relate to the two diseases.

On the other hand, it is thought possible that the joints that have suffered a destructive melitococcic arthritis may later develop degenerative arthritic changes. These may be styled secondary or post-melitococcic arthroses (osteo-arthrosis) but not "melitococcic arthroses" as has been stated by some writers (Harris, 1950).

Melitococcic Sacro-Iliitis.—In our series 65 cases presented with melitococcic sacro-iliitis (37 per cent.) and in eight cases this sacro-iliitis was the only articular manifestation.

It appeared twice as frequently in men (43 per cent.) as in women (20 per cent.), and was observed with greater frequency in young than in older persons.

The time of onset was usually the first month of illness. No cases were found after the seventh month.

The clinical picture varied in intensity from mild arthralgia with lameness of the lower limb lasting a few days, to acute arthritis which made the patient bed-ridden, and prevented all movement. The evolution rarely lasted more than 3 months and the patients were cured without clinical sequelae. It was unilateral in 36 cases and bilateral in 29; the two contralateral joints may be affected simultaneously or successively.

The appearance of radiological alterations begins between the 10th and 15th days. These consist in a widening of the articular interline, the disappearance of the lines marking the osteo-cartilaginoid limit, and alterations in the periarticular osseous density, either by osteoporosis or osteosclerosis. Less frequently seen are the "pseudosequestrative" form, simple osteoporosis, and articular fusion. Only very rarely did any radiological alterations persist when the clinical symptoms were cured.

Spondylitis.—This was observed in 93 cases (53 per cent.); it appeared in 60 per cent. of men (79 cases) and in only 31 per cent. of women (fourteen cases), and unlike other forms of brucellosis was more common in elderly patients.

It was seen in only one vertebral region in 43 cases, and in several regions in fifty cases. The lumbar region was affected in 79 cases, the dorsal in 22, and the cervical in seventeen.

The clinical picture consisted of pain, generally more severe than in Pott's disease and located in two or three or more vertebrae, contracture of the paravertebral muscles, and rigidity. Gross deformities were rare.
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Evolution.—This may be divided into three phases:
(1) Acute.—The patient is obliged to remain in bed for from 2 weeks to 2 or 3 months.
(2) Subacute.—The pain diminishes, and the patient may rise, although walking is very difficult. This stage lasts from a few months to over a year, and may only be considered as finished when all signs of inflammatory spondylitis have disappeared.
(3) Residual or Metabacillary.—Vertebral pain of a static type may last for many years.

Complications.—The following complications were observed:
(1) Vertebral Ossifluent Abscesses.—These occurred in eleven (12 per cent.) of the spondylitic cases; only five reached the surface of the body where they fistulized or were punctured, the other six being seen radiologically. In every case the fistulae closed in a few weeks or months.
   It was only possible to cultivate the Brucella in one out of ten complete examinations of the pus undertaken in four cases; this shows that the absence of Brucella from the pus of an ossifluent abscess does not rule out the diagnosis of Malta fever.
(2) Neurobrucellar Alterations.—Certain changes, by reason of their site and time of onset, have a possible relation with spondylitis:
   (a) Cervical meningomyelitis (tetrapareses or paraplegias), three cases; dorsolumbar (parapareses or paraplegias), two cases.
   (b) Pure myelitis, two cases.
   (c) Meningeal radiculitis in the form of monopareses, monoplegias, or diplegias, five cases; radicular sciatica only, three cases.
   (d) Latent meningeal reactions were observed in ten cases out of fourteen in which a lumbar puncture was performed.

In two of the meningeal cases, myelitis was verified. A subarachnoid block on the level of one of the principal spondylitic foci, precisely coincided with the level of the neurological segment in which the transverse myelitis was sited, so that there existed a transverse syndrome of the dorsal spine affecting all its elements: vertebrae, meninges, and spinal cord.

Radiology.—The radiological picture may not be altered in cases lasting less than 3 to 5 weeks, or in mild cases of “frustrated” or “congestive” spondylitis.

The radiological lesions are varied; they generally consist in focal lesions of the vertebral body appearing in several vertebrae. Destructive lesions of the epiphyseal angles are frequent and highly characteristic. Erosions of the front and lateral surfaces of the vertebral bodies are also frequent. In some cases intraspongy geodes are visible. The disks in the centre of the process are nearly always diminished in height; the contiguous disks may be swollen, and their height greater than normal. The destructive process progresses rapidly, but it is also rapidly limited by the first signs of osseous reconstruction, such as osseous sclerosis, osseous bridges (synesmophytes), and proliferations of the periostuem.

The osteophytes and other degenerative radiological signs that may be found in such cases appear to be early alterations unrelated to the brucellar osteomyelitis, or developing in the metabacillary phase after the activity of the spondylitic focus has died out.

Pathological Anatomy.—A study was made of post mortem specimens from the spinal column of four patients who had suffered from brucellosis either just before death or at an earlier stage in life.

Case 1, a man aged 73, with brucellosis, in whom dorsal and lumbar spondylitis appeared at the beginning of the evolution. The blood culture was positive. He died 5 months after the onset with cirrhosis and renal insufficiency with haematuria and uraemia.

A specimen from the spinal column from D11 to L5 studied histologically showed an inflammatory granuloma which had formed upon the vertebral body in the vicinity of the disk; starting from the osseous marrow it had destroyed the osseous trabeculae, giving rise to the formation of intraspongoid geodes. The intervertebral disk was destroyed secondarily. An osseous bridge studied histologically turned out to be a reconstructive enchondral ossification of the ligaments.

Case 2, a man aged 65, contracted brucellosis at the age of 59, and lumbar and cervical spondylitis developed 3 months later. Positive sero-agglutination titre 1:680. A remission occurred 5 months later. The patient died 6 years later with aplastic anaemia and renal sclerosis.

A specimen from D6 to L5, studied macroscopically, showed that once the active phase of the spondylitis had passed, the lesions were confined and appeared as osteosclerotic reactions around the intraspongoid geodes, the established osseous destruction being only partially restored. The destruction of the disks persisted and developed until the osseous bridges round the destroyed disks and epiphyses were completed at many points.

Case 3, a man aged 57, contracted brucellosis with lumbar spondylitis and sacro-iliitis. Positive sero-agglutination titre 1:1,280. The patient developed a psychosis and committed suicide by throwing himself under a train after 4½ months of illness.

A specimen from the spinal column from D11 to the coccyx, studied histologically, showed incipient destruction of the intervertebral disks.

Case 4, a man aged 71, who contracted brucellosis, never suffered from lumbar pain, but a lumbar spondylitis was observed radiologically. He died 10 months after the onset with cirrhosis and intense ascites.
A specimen of the spinal column from D12 to L5, studied histologically, showed that in this case the vertebral degenerative alterations were not due to brucellosis but to a co-existent process.

**Macroscopic Lesions.**—These have been classified according to their behaviour in face of the osseous trabeculae:

(a) **Destructive Lesions.**—These are produced by a granulation tissue starting from the osseous marrow and destroying the surrounding osseous trabeculae, and secondarily invading and destroying the intervertebral disk. These predominate in the acute stage of the illness. They comprise intraspongy geodes, destructions in the epiphyseal angles, erosions of the anterior and lateral faces of the vertebral body, and lessening of the thickness and density of the osseous trabeculae.

(b) **Reconstructive Lesions.**—These do not develop until the subacute phase of the spondylitis is reached and they often continue during the residual or metabrucellar stage after the activity of the inflammatory-infectious process is over. They comprise an increase in the number and thickness of the osseous trabeculae surrounding the intraspongy geodes, a thickening of vertebral bodies, and the formation of osseous bridges.

(c) **Degenerative Lesions.**—These affect the vertebral bodies and disks; they may develop in the residual or metabrucellar stage, or may have begun before the onset of the brucellar spondylitis.

**Histological Lesions.**—These are characterized by the formation of granulation tissue initiated by interstitial oedema and the infiltration of large and small mononuclear cells. In some areas, accumulations of these cells give rise to granulomata similar to those seen in other organs affected by brucellosis. They are characterized by round mononuclear cells with an abundant eosinophil cytoplasm and large round nuclei (Lowbeer, 1949).

In some zones, where the granulation tissue is dense it provokes a partial or total reabsorption of the osseous trabeculae. In some cases, nodules of granulation tissue are formed, in the centre of which appear zones of necrosis which may become caseous and suppurate.

The development of granulation tissue and the corresponding osseous destruction takes place rapidly in a period of about 3 or 4 months, but at the same time a process of limitation and reconstruction begins; the connective tissue proliferates round the brucellar nodules, new osseous trabeculae form and the thickness of the existing ones increases, new bone starts to form from the vertebral periosteum, and osseous bridges appear. All these bone-forming processes are of a reparative nature, independent of the brucellar inflammation, and they are apparently caused by the increased mechanical load on the remaining vital structures of the vertebrae and disks which have undergone destruction. This explains why the reconstructive processes attain their maximum development in the residual or metabrucellar stage of the spondylitis, i.e. when the patient has already got out of bed and is able to take up a certain activity.

The intervertebral disks are secondarily destroyed by the granulation tissue both by direct erosion of the cartilaginous disk starting from the subchondral bone, and by holes produced in the disk by pre-existent intraspondyly hernias (Schmorl's nodules).

Finally, there exists an extraordinary disproportion between the extent of the histological lesions and the radiological changes which show only the macroscopic lesions.

**Spondylo-Arthritis (Ankylosing Spondylitis).**—No case was found evolving towards ankylosing spondylitis nor was anything seen to support the notion of an aetiological relation between the two diseases. Some resemblances were observed in the sites preferred (bilateral sacro-ilitis, lumbar spine), which suggests the existence of some common pathogenic mechanism leading to invasion of the spinal column. The agents of both diseases would reach the column through the pelvic-vertebral system of Batson, and the mechanism of formation of the osseous bridges would be similar in both cases.

**Osteomyelitis.**—Extravertebral brucellar osteomyelitis is very rare. We have only had two cases with costal osteitis out of a series of 174 patients, and one more case, not included in this series, with osteomyelitis of the lower metaphysis of the femur which developed the clinical and radiological picture of an osseous abscess of Brodie.

We have also collected 24 cases from the literature (Brault, 1910; Cantaloube, 1911; Cazeneuve, 1913; Brun and Brunet, 1924; Favre, 1931; Salan, 1932; Hamant and Rothant, 1933; Kulowski, 1936; Mazzini and Carman, 1940; Steindler, 1940; Hardy, Jordan, and Borts, 1936; Gardner, Girdlestone, and Gillespie, 1932; Horstman, 1937; Lowe and Lipscomb, 1947; Harris, 1950; Lowbeer, 1949; Antocci, 1948).

The brucellar osteomyelitis appears to have affected one site in seventeen of these 27 cases and more than one site in the remaining ten (six cases with two sites affected and four with three sites affected). The site most frequently affected was the anterior surface of the ribs (seventeen cases) and the femur (seven cases), especially in its lower metaphysis. Then come the cranium (four cases), the tibia (three cases), the humerus (two cases), and the iliac bones, ischium, and coracoid process (one case each). In the long bones the metaphysis was
generally affected, but some cases had diffuse lesions of the diaphysis.

Two clinical types were observed:

(1) Acute.—This was accompanied by fever and systemic involvement;

(2) Chronic.—This type is more characteristic of brucellosis, with only local lesions; it has a low virulence and evolves gradually over a long period. The diagnosis may be difficult because the sero-agglutination titres are only in the upper limit of normal, and only the intradermal reaction to melitine is intensely positive.

Diagnosis

The appearance of the locomotor system may suggest the diagnosis of brucellosis. In Spain, an acute spondylitis, sacro-iliitis or coxitis will always suggest brucellosis, but more frequently the osteo-articular signs are not characteristic. In such cases, the fact that lesions appear at various sites in the locomotor system, a peculiar condition of brucellosis, is sometimes suggestive. The radiological appearance is only characteristic of spondylitis. Effusions or purulent abscesses may allow the Brucella to be cultivated, but the finding of sterile fluids does not discount a diagnosis of brucellosis.

The data supplied by the study of the general clinical picture are of greater value. A history of exposure to contagion is frequently found; 78 per cent. of our cases came from rural areas, where brucellosis is endemic, and most of them had drunk goat’s milk, worked as shepherds or butchers, kept goats at home, or frequented goat-yards.

Such systemic symptoms as recurrent fever, asthenia, abundant perspiration, orchitis, and splenomegaly often give definite indications of brucellosis, and must therefore be investigated.

Various laboratory techniques gave the following results:

(1) The blood culture was positive in 58 per cent. of the cases in which it was employed.

(2) The sero-agglutination test was positive in 98 per cent. of the cases. This test gives the highest titres during the first 6 months of the disease.

(3) The complement-fixation test was positive in 94 per cent. of the cases investigated.*

(4) The Coombs test for incomplete antibodies has lately proved to be specific.*

(5) Intradermal reaction to melitine was used only secondarily when the other tests were negative or doubtful but it is of great value in very prolonged or chronic cases, in which the sero-agglutination, complement-fixation, and incomplete antibodies tend to give titres that are low or in the higher limits of normal.

None of these tests are 100 per cent. specific, but if they are used systematically, like a battery, with their correct techniques, a positive diagnosis can be made in practically every case.

The erythrocyte sedimentation rate has no value at all for diagnosis; it was normal in twelve out of the 75 cases investigated. In the cases where it was raised, however, its variations in successive tests formed a good index of the activity of the brucellar inflammation.

Therapy

(A) General Treatment of Brucellar Infection.

This must be the same as in cases without localizations in the locomotor system. We use as a basic treatment insoluble terramycin (Ruiz Castañeda, 1954; Magriñá and Foz, 1954) at the rate of one injection weekly for from 6 to 10 weeks.

In the acute phases, especially if the blood culture is positive, soluble terramycin or dihydrostreptomycin with sulphaguanidine may be given for 5-day periods in small doses.

If symptoms of brucellar activity persist after the third or fourth week of treatment with terramycin, intravenous vaccine therapy may be added.

(B) Local Treatment of the Joints

This has recently been modified because the treatment of the brucellar infection is now more efficacious.

Arthralgia and mild arthritis do not require local treatment. Patients with mild sacro-iliitis and spondylitis without radiological alterations must have complete rest on a hard bed (with a board under the mattress). They must not get out of bed until the pain has disappeared altogether, and must then wear an orthopaedic corset for 3 to 4 months. In cases of medium or serious spondylitis with radiological alterations, we apply a plaster corset which must be worn for from 3 to 6 months.

Cases of very serious spondylitis, with large vertebral destructions or abscesses, and also aged or exhausted patients, must be nursed on a plaster bed.

In treating the hip joint, modern antibiotic therapy renders complete rest on a hard bed sufficient. Continued traction of the lower limb for contorted attitudes in flexion is rarely necessary. From the time when the pain stops, exercises for the functional recovery of the joint must be started with the patient lying down.

Semipenetrating radiotherapy has been found useful in some cases with recalcitrant pain.

* These two tests tend to give higher titres than the sero-agglutination test after the first 6 months of illness.
ANNALS OF THE RHEUMATIC DISEASES

Summary

1. A series of 174 consecutive cases of brucellosis due to Brucella melitensis has been studied.

2. Lesions of the locomotor system were found in 148 cases (85 per cent.).

3. The sites of these lesions may be classified as follows:
   (a) Muscle and skin (myalgia, myositis, subcutaneous nodules, cellulitis, bursitis, tendinous synovitis),
   (b) Peripheral joints (arthralgia, mild or fugitive arthritis, severe or destructive arthritis),
   (c) Sacro-iliac joints (sacro-iliitis),
   (d) Spine (spondylitis),
   (e) Bone marrow (osteomyelitis).

The frequency and characteristics of each type are described.

4. No cases of progressive chronic polyarthritis (rheumatoid arthritis) nor of ankylosing spondylitis were observed.

5. Diagnosis and treatment are discussed.

REFERENCES


Localisations ostéo-articulaires de la brucellose

RÉSUMÉ

1. On étudia une série de 174 cas consécutifs de brucellose due à Brucella melitensis.

2. On trouva des lésions du système locomoteur dans 148 cas (85%).

3. On peut classer la localisation de ces lésions de la manière suivante:
   (a) Muscle et peau (myalgie, myosite, nodules souscutanés, cellulite, bursite, téno-synovite).
   (b) Articulations périphériques (arthralgie, arthrite bénigne ou fugitive, arthrite sévère ou destructrice).
   (c) Articulations sacro-iliaques.
   (d) Colonne vertébrale.
   (e) Moelle osseuse.

On décrit la fréquence et les caractères cliniques, radiologiques et anatomopathologiques de chaque type.

4. On n'observa aucun cas de polyarthrite chronique évolutive (arthrite rhumatismale) ni de spondylarthrite ankylosante.

5. On discute les méthodes diagnostiques et thérapeutiques.

Localizaciones osteo-articulares de la brucelosis

SUMARIO

1. Se estudió una serie de 174 casos consecutivos de brucelosis debida a Brucella melitensis.

2. Lesiones del sistema locomotor encontrarseon en 148 casos (85%).

3. La localización de estas lesiones se puede clasificar de la manera siguiente:
   (a) Músculo y piel (mialgia, miositis, nódulos subcutáneos, celulitis, bursitis y tenosinovitis).
   (b) Articulaciones periféricas (arthralgia, artritis benigna o fugaz, artritis severa o destructiva).
   (c) Articulaciones sacro-iliaicas.
   (d) Columna vertebral.
   (e) Medula ossea.

Se describen la frecuencia y los caracteres de cada tipo.

4. No se observó caso alguno de poliartritis crónica evolutiva (artritis reumatoide) ni de espondilartritis anquilosante.

5. Se discuten los métodos diagnósticos y terapéuticos.
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the adrenal ascorbic acid levels were high and depletion under stress was reduced, the depletion effect of histamine being greater than that of corticotrophin, suggesting some changes at both the pituitary and adrenocortical levels.

After discussing the various mechanisms involved in these reactions, the authors conclude that the reversible stage of cirrhosis is associated with normally functioning adrenal glands, or glands which can still respond by showing further activity when exposed to stress. Irreversible cirrhosis is associated with functionally damaged adrenal glands.

In the second part of this study albino rats were given carbon tetrachloride as above. From the 8th week onwards batches of six rats were isolated each week and given no more carbon tetrachloride, but instead each received a daily intramuscular injection of cortisone acetate as follows: 5 mg. per day for 6 days, 10 mg. per day for 3 days, and finally 5 mg. per day for 2 days; 3 days after completion of these injections the experimental animals were killed and they and the control animals examined as in the first part of the study. The results showed that cortisone assists in the regression of hepatic cirrhosis only during the period in which the condition is naturally reversible, but that the hormone has no effect on the later irreversible stages once "mature fibrous tissue" has been laid down. B. G. Maegraith.

A 49-year-old woman with lupus erythematosus disseminatus treated with ACTH presented pronounced retinal changes similar to thrombosis of the central retinal vein. In a 38-year-old woman with a similar disease receiving similar drugs, the blood-pressure rose and she showed increasing fundus changes of a hypertensive character and myopia. A 43-year-old woman with chronic polyarthritis suffered a retinal haemorrhage and slight increase in myopia during treatment with ACTH. A 70-year-old woman with polyarthritis showed macular oedema during such treatment. G. von Bahr.


Corrigendum
In the article by Dr. J. Rotés-Querol entitled "Osteo-articular Sites of Brucellosis", which appeared in the March issue of the Annals (1957), 16, 63, col. 2, line 33, for 'Osteophytes' read 'Osteo-articular sites'.

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