THE RHEUMATIC DISEASES

VISCERAL LESIONS ASSOCIATED WITH RHEUMATOID ARTHRITIS

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I. CRITERIA USED IN SELECTION OF CASES

In the study of the visceral lesions in rheumatoid arthritis, the records of 192 cases having a diagnosis of arthritis were examined. These cases were obtained from the autopsy files of the University of Minnesota Pathology Department and associated local hospitals. Out of this group there were 81 which were frank suppurative arthritis, 61 were rheumatoid arthritis, and 29 were osteo-arthritis. There were 8 with tuberculous arthritis; 7 had a simple, chronic, non-suppurative, non-specific arthritis of undetermined etiology and involving only one joint; five had an acute inflammatory, non-suppurative arthritis, type undetermined, and 1 had gonorrheal arthritis.

"Rheumatoid Arthritis" as discussed in this paper is the severe deforming type of chronic infectious arthritis. It is the atrophic, proliferative type of arthritis. The criteria used in selecting these cases of rheumatoid arthritis were as follows: The disease must have been chronic, being present a minimum of several months. It must involve two or more joints. It must have caused deformities of the joints and their adjacent structures, and finally, it must be of a non-suppurative type of involvement. That is, all cases which showed frank pus or definite etiological factors or trophic changes such as syphilis, trauma, syringomyelia, tuberculosis, gonorrhea, suppurative streptococcus and staphylococcus infections involving joints were immediately excluded. However, the differentiation and exclusion of osteo-arthritis or hypertrophic (degenerative) type of arthritis from the rheumatoid or atrophic (proliferative) type of arthritis was not so simple. Any cases which had mixed types of arthritis or different types of arthritis in different joints were not included. That is, if a case was found to have both proliferative and degenerative changes, it was omitted from the series. The distinction was made by the clinical, radiological, and pathological evidence available. On this basis, 61 cases of rheumatoid arthritis were obtained and were studied with regard to their visceral lesions.

II. TERMINOLOGY

Chronic arthritis was classified in 1905 by Richardson into two main types: (1) Proliferative and (2) degenerative. However, since then other terms have been introduced which have been used interchangeably with the above two. Proliferative arthritis is often named
atrophic or rheumatoid arthritis, and degenerative arthritis is often spoken of as hypertrophic or osteo-arthritis. The reason for the variability in terminology is that the clinician uses one classification, the pathologist another, and the roentgenologist yet another, and so on. For example, the terms "atrophic" and "hypertrophic" arthritis are primarily for the roentgenologist, who designates as atrophic that type which refers to bony atrophy, erosion, and destruction, and hypertrophic to eburnation and bone production with spur formation.

It might be added that it would be impossible to classify arthritis on an ætiological basis, since not all the ætiological factors are known and different ætiological agents appear to be able to give similar pathologic pictures—e.g., gonorrhoeal arthritis may simulate "non-specific" proliferative arthritis (Allison and Ghormley).

III. JOINT PATHOLOGY

In proliferative arthritis, as described by Richardson, Nichols, and others, there is proliferation of the synovial membrane and the perichondrium with the formation of a layer of granulation tissue over the joint surface as a thin, pannus-like layer. The pannus may cause a destruction of the articular cartilage, and as a result the joint space may disappear with the development of a fibrous or a bony ankylosis. At the same time, there may also be a proliferation of the connective tissue in the epiphyseal marrow spaces and proliferation of the endostium of the epiphysis. This process can also invade the articular cartilage from below, and thereby help destroy it.

In degenerative arthritis, the primary changes are a degeneration and fibrillation or splitting of the hyaline cartilage of the articular surfaces with erosion and exposure of the underlying bone, thus forming an irregular articular surface. Often there is a corresponding overgrowth of cartilage or bone on the opposite surface with spur formation. Due to the irregular surfaces, a pseudo-ankylosis from locking of the joint may occur, but never true ankylosis.

The anatomic changes in rheumatoid arthritis may be described briefly as follows: The disease may start out as an acute process with rapid destruction of the joints, or it may be very slowly progressive. The microscopic picture can vary from one showing neutrophilic infiltration to one showing round cell infiltration; or even fibrous scarred areas may be present.

The rheumatoid arthritis which we will discuss is the severe deforming advanced form of proliferative arthritis in which there are contractures, ankyloses, and atrophy of the extremities present.
IV. INCIDENCE

There are no figures available as to the exact incidence of rheumatoid arthritis. However, it is a common disease in the general population. The Ministry of Public Health in London states that in any 1,000 insured males of all ages there will be 1 case of proliferative arthritis, and that in any 1,000 insured females there will be 3 cases. This sex ratio of 3 to 1 is confirmed by other authors (Allison and Ghormley), but many do not find such a high proportion of females. In 110 cases studied by McCrae at Johns Hopkins Hospital, there was an equal distribution of females and males. In our series, we had a slight predominance of females, numbering 34 females and 27 males. However, the ratio of autopsies done on males to females at the University of Minnesota Pathology Department is approximately 2 males to 1 female. Thus, the normal distribution, females to males, as obtained from our series, would be 68 females to 27 males.

There is a wide variation in the age ranges. Our youngest patient was 10 years and the oldest 87 years of age. However, over three-fourths of the cases were between 40 and 80 years of age. The duration of the disease varied from 6 months to 35 years with the average duration being between 5 to 10 years. This age incidence is somewhat higher than that reported by other authors. Allison and Ghormley state that the average age of onset is 20 to 40 years. Others claim that it does become manifest before 35 years.

Our age group, from autopsy material, represents the time of death, which will be a later age than that reported by clinicians.

With regard to race, nothing remarkable was noted. There were 3 negroes in this series.

The effect of climate on chronic arthritis has not yet been determined (Hench et al.). In Europe, it is as common in northern Sweden as in Holland or Denmark. One does not see the striking geographical contrast in this disease that one sees in rheumatic fever, which is much more frequent in the north.

V. JOINTS INVOLVED

On analysis of the joints affected in rheumatoid arthritis, it was found that the knees were involved most commonly, 42 cases, being followed in frequency by the hands, 34 cases, feet 20, ankle 15, elbows 15, hips 12, wrists 10, shoulders 9, and spine 4. Allison and Ghormley list sites of involvement in the following order: first feet and hands, then wrists, ankles, elbows, knees, hips, shoulders, jaw, and spine. The distribution is usually symmetrical, however. This is in contrast to osteo-arthritis, which is rarely symmetrical.
VI. Cause of Death

The causes of death in this series were varied. The most common cause was bronchopneumonia, which occurred in 24 cases. The next most common cause was septicemia and pyemia, which occurred in 9. The other common causes of death in order of their occurrence were lobar pneumonia (8 cases), tuberculosis (7), carcinoma (3), amyloid disease (3), cardiac decompensation (3), and uremia (2).

VII. Cardiac Lesions

The cases having rheumatic heart disease were separated and analysed. Out of the total of 61 cases, 19 had rheumatic heart lesions. In other words, 31 per cent. of the patients were found to have fibrous adhesive pericarditis, aortic, mitral, or tricuspid valvular involvement and combinations thereof of a rheumatic nature. Most of these lesions were old healed valve defects of varying degrees of deformity with thickening and retraction of the leaflets, thickening and shortening of the chordae tendineae, and fusion of the commissures. The mitral valve was most commonly affected, with 16 out of 19 persons having rheumatic mitral valve lesions. One mitral valve had an acute rheumatic involvement, while the remainder had old deformed rheumatic defects. The aortic valve had lesions in 11, 2 of which were of the calcified nodular type. There was a fibrous adhesive pericarditis in 7. The myocardium in 2 patients showed an acute diffuse myocarditis, with many mononuclear cells present; 1 had several Aschoff nodules; 1 had tricuspid valvulitis together with a rheumatic mitral valve disease. There were 2 instances of superimposed terminal acute bacterial endocarditis, with one involving both the aortic and mitral valve, and the other affecting only the mitral valve (Chart I., p. 29).

Only 6 of the 19 patients showed signs of myocardial insufficiency with chronic passive congestion of the liver, ascites, and cedema; and cardiac decompensation was thought to be a primary cause of death in 3 cases.

In February, 1941, Baggenstoss and Rosenberg studied 25 cases of chronic infectious (i.e., rheumatoid) arthritis. All of their patients had progressive polyarticular inflammation. In these cases, 20 had associated cardiac damage. Lesions that were regarded as being identical with those produced by rheumatic fever were found in 14 of the 20; 5 of the 20 cases had non-rheumatic lesions. These 5 lesions were as follows: (1) Coronary sclerosis with thrombosis and acute and chronic infarction of the myocardium. (2) Non-specific subacute fibrinous pericarditis. (3) Cardiac hypertrophy with hypertension. (4) Coronary sclerosis with chronic infarction of the myocardium. (5) Hydropericardium. The remaining one had a fibrous obliteratorive pericarditis,
but the nature of this lesion could not be determined because neither
the heart nor the histologic sections were saved. In this series, cardiac
disease was considered a primary or important cause of death in 7 of
the 14 cases in which rheumatic lesions were found at autopsy.

Baggenstoss and Rosenberg believe that the high incidence of
rheumatic cardiac lesions suggested a relationship between chronic
infectious arthritis and rheumatic fever. They felt that the cardiac
lesions associated with chronic infectious arthritis are not quite as
severe or widespread as those lesions in hearts of young persons who
have rheumatic fever; however, the differences are of degree and not
of kind. Only 2 of the University of Minnesota series having cardiac
lesions had had episodes of rheumatic fever prior to developing de-
forming arthritis. Of the cases with valve deformities, only 7 of these
cases were described as having characteristic murmurs.

Examination of the blood pressure readings in the total series of
rheumatoid arthritis revealed that few of the patients had hypertension.
In fact, there seemed to be a tendency for them to have hypotension.
Only 1 case had a diastolic pressure over 100 mm. of mercury with a
systolic over 180 mm. of mercury. There were only 6 cases in which
the diastolic pressure was between 90 and 100 and the systolic between
150 and 180. The majority of the cases were between 150/90 to 110/70,
while there were 9 cases with pressures less than 110/70. The cases
with cardiac lesions seemed to follow the same proportionate grouping.

It must be remembered that most of these patients were bedridden
for some time before death and some of them were moribund; this may
explain the tendency toward hypotension.

Cardiac lesions have long been known to be associated with rheu-
matoid arthritis. Todd in 1853 was probably the first to mention the
relationship. Boas and Rifkin studied 80 cases of rheumatoid arthritis
at the Montefiore Hospital and found clinical signs of valvular heart
disease in 14 out of their 80 cases, or 17.5 per cent. Their criteria were
a diastolic murmur (aortic or mitral) or a systolic apical murmur with
cardiac enlargement, excluding hypertension and other causes.

Still, who described in 1896 the chronic joint disease in children
known as Still's disease, noted cardiac lesions. This disease he defined
as a chronic progressive enlargement of the joints associated with
generalized lymphadenopathy and splenomegaly. Actually it seems
to be a juvenile type of rheumatoid arthritis. He noted an adherent
pericardium in 3 out of 12 cases which came to autopsy, and that 1 had
a thickened mitral valve.

In 1924, T. W. Froggatt studied 50 patients having chronic in-
fected arthritis to determine how many had physical signs of heart
disease. On the basis of heart murmurs, dilatation of the heart, and
symptoms, he found 14 of them to have cardiac abnormalities.

Since that time several authors have noted a relationship between
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Fibrous Adhesive Pericarditis</th>
<th>Aortic Valve Lesion</th>
<th>Mitral Valve Lesion</th>
<th>Tricuspid Valve Lesion</th>
<th>Myocardial Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Present</td>
<td>Old valve defect, superimposed bacterial endocarditis</td>
<td>Old valve defect, superimposed bacterial endocarditis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td>Old valve defect</td>
<td>Old valve defect</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Present</td>
<td></td>
<td>Acute bacterial endocarditis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>Old valve defect</td>
<td>Old valve defect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Present</td>
<td>Ditto</td>
<td>Ditto</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Present</td>
<td>Ditto</td>
<td>Acute rheumatic endocarditis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td>Old valve defect; mitral stenosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
<td>Old valve defect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Present</td>
<td>Ditto</td>
<td>Ditto</td>
<td></td>
<td></td>
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<tr>
<td>10</td>
<td></td>
<td>Ditto</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
<td></td>
<td>Old valve defect; mitral stenosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td>Old valve defect; stenosis and insufficiency</td>
<td>Old valve defect; stenosis and insufficiency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td></td>
<td>Old valve defect</td>
<td>Old valve defect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td></td>
<td></td>
<td>Ditto</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td></td>
<td></td>
<td>Ditto</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td></td>
<td>Calcified nodular</td>
<td>Ditto</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td></td>
<td>Old valve defect; stenosis and insufficiency</td>
<td></td>
<td></td>
<td>Acute diffuse myocarditis with Aschoff nodules</td>
</tr>
<tr>
<td>18</td>
<td>Present</td>
<td></td>
<td>Ditto</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Present</td>
<td>Calcified nodular</td>
<td>Ditto</td>
<td></td>
<td>Acute diffuse myocarditis</td>
</tr>
</tbody>
</table>
chronic infectious or rheumatoid arthritis and acute rheumatic fever. M. H. Dawson made a comparative study of the subcutaneous nodules in rheumatic fever and rheumatoid arthritis and found the nodules presented striking similarities; and he advanced the hypothesis that the lesions are manifestations of the same fundamental pathological processes. In frequency the subcutaneous nodules occur in acute rheumatic fever in 10 to 50 per cent. of cases, while in infectious arthritis, Clawson and Wetherby have found that the nodules were present in over 25 per cent. of 800 cases. Both types of lesions have focal necrosis and inflammatory cell infiltration in the early stages. Later the collagen fibres in the centre of the nodules swell and form a central hyaline fibrinoid material. Dawson stated that the size of these nodules is proportionate roughly to the length of the disease. Usually, in acute rheumatic fever, the nodules are about 5 mm. in diameter, while in rheumatoid arthritis they vary between 1 to 2 cm. in diameter. The appearance of these nodules is generally associated with a severe form of their respective diseases, especially in acute rheumatic fever, in which the presence of nodules is indicative of cardiac damage (Dawson).

**VIII. Laboratory Data**

An analysis of the laboratory data in this group of 61 arthritics revealed that some of them had anemia. The hæmoglobin varied between 50 and 100 per cent., with the average between 70 and 80 per cent. The erythrocyte count was reduced accordingly.

**Chart II.—Hæmoglobin**

<table>
<thead>
<tr>
<th>Hæmoglobin Percentage</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>100-90%</td>
<td>5</td>
</tr>
<tr>
<td>90-80%</td>
<td>8</td>
</tr>
<tr>
<td>80-70%</td>
<td>15</td>
</tr>
<tr>
<td>70-60%</td>
<td>7</td>
</tr>
<tr>
<td>60-50%</td>
<td>7</td>
</tr>
<tr>
<td>50-40%</td>
<td>3</td>
</tr>
</tbody>
</table>

The urine from 28 of the patients contained albumin, leucocytes, and erythrocytes; however, 13 of these had only a faint trace of albumin.

**Chart III.—Urinalyses**

<table>
<thead>
<tr>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Albumin—faint trace</td>
</tr>
<tr>
<td>2 Albumin—1+</td>
</tr>
<tr>
<td>3 Albumin—2+</td>
</tr>
<tr>
<td>4 Albumin—3 to 4+</td>
</tr>
</tbody>
</table>

The kidneys at autopsy showed no marked abnormalities grossly. The combined weights ranged from 150 to 350 grammes, with the largest
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group (17) having their total weight between 200 and 250 grammes. Grossly only 19 cases had a uniform type of abnormality, that is, granular pitted surfaces with adherent capsules. Microscopically the kidneys from 8 patients showed glomerulitis with moderate to marked increase in endothelial nuclei; 2 of these had had clinical signs of glomerulonephritis. Most of the patients in this group had some sort of concomitant infection such as decubital ulcers (18 cases), pneumonia (31 cases), and septicemia (9 cases).

The leucocyte count showed a wide range of variation. There were 3 with counts of less than 4,000, one of them being 1,400; 6 cases were below 5,000. There were 22 cases whose counts were between 4,000 and 10,000, and there were 20 cases which were above 10,000, with 6 of these between 20,000 and 30,000. (See Chart IV below.)

<table>
<thead>
<tr>
<th>Cases</th>
<th>Leucocyte Counts</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>1,000-4,000</td>
</tr>
<tr>
<td>3</td>
<td>4,000-5,000</td>
</tr>
<tr>
<td>2</td>
<td>5,000-6,000</td>
</tr>
<tr>
<td>9</td>
<td>6,000-7,000</td>
</tr>
<tr>
<td>3</td>
<td>7,000-8,000</td>
</tr>
<tr>
<td>1</td>
<td>8,000-9,000</td>
</tr>
<tr>
<td>4</td>
<td>9,000-10,000</td>
</tr>
<tr>
<td>11</td>
<td>10,000-15,000</td>
</tr>
<tr>
<td>2</td>
<td>15,000-20,000</td>
</tr>
<tr>
<td>6</td>
<td>20,000-30,000</td>
</tr>
<tr>
<td>1</td>
<td>Over 30,000</td>
</tr>
</tbody>
</table>

The patients who had high leucocyte counts invariably had some other infectious process present such as a septicemia or pneumonia. Of the patients who had leucopenia, 2 had Felty's syndrome.

IX. SPLENIC LESIONS

In 1924, Felty described 5 cases which were strikingly similar in that they all had chronic arthritis, splenomegaly, and leucopenia. In 3 of the 5 there was brownish pigmentation of the skin and generalised lymphadenopathy. These features are usually included in the syndrome.

Felty's syndrome as a disease entity has been subject to some question in recent years. In 1940, Curtis and Pollard compared the tissue changes in Felty's syndrome with other forms of rheumatoid arthritis. They believed rheumatoid arthritis to be a generalised disease which affects other tissues such as the skin, muscle, spleen, liver, lymph-nodes, and bone marrow, as well as the joints. They stated that Felty's syndrome is merely one particular symptom complex of the disease and not a clinical entity, and that it occurred merely as a matter of chance. These men had 11 arthritics which were divided into three groups. Group I consisted of 4 cases that had all
the cardinal symptoms as described by Felty. Group II was a controlled group that had arthritis and splenomegaly; however, it had a leucocytosis instead of a leucopenia. Group III had rheumatoid arthritis but no palpable spleen or leucopenia.

Biopsies of the skin and muscles of the calf were made and compared in these patients. All of the groups were the same, and one could not be distinguished from the other microscopically. In general the biopsies showed atrophy of the epithelium, fibrosis of the corium, increase in interstitial nuclei of the muscle fibres, and small peri-vascular infiltration through the corium and muscle. These men felt that splenomegaly and leucopenia were two of the multiple findings that may occur with chronic infectious arthritis. They saw no justification for the separation of those cases having arthritis, splenomegaly, and leucopenia into a specific syndrome. Since it was merely a matter of chance, they thought that the use of the term "Felty's syndrome" should be discontinued.

In our series of 61 patients, 3 had Felty's syndrome. However, there were 6 other cases which had splenomegaly along with the arthritis deformans but who did not have leucopenia. The weight of the spleens in most of our cases varied from 75 to 300 grammes, the majority of them (32) being between 100 and 200 grammes. Nine weighed over 300 grammes and 4 of them over 500 grammes.

<table>
<thead>
<tr>
<th>Grammes</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-100</td>
<td>8</td>
</tr>
<tr>
<td>100-150</td>
<td>16</td>
</tr>
<tr>
<td>150-200</td>
<td>16</td>
</tr>
<tr>
<td>200-250</td>
<td>2</td>
</tr>
<tr>
<td>250-300</td>
<td>5</td>
</tr>
<tr>
<td>300-350</td>
<td>3</td>
</tr>
<tr>
<td>350-400</td>
<td>2</td>
</tr>
<tr>
<td>Over 400 (520, 775, 700, 1,475)</td>
<td>4</td>
</tr>
</tbody>
</table>

As far as actual pathology in the spleen itself was concerned, there was nothing remarkable to note: 8 cases showed hyaline perisplenitis; a few were congested; 11 of the spleens had amyloid in them in association with amyloid deposits in other organs of the body, and 2 of these were over 300 grammes. Amyloidosis will be discussed later.

X. BACTERIOLOGIC FINDINGS

Bacteriologic findings also seem to point to some relationship between rheumatoid arthritis and rheumatic fever. Dr. Clawson has cultured the subcutaneous nodules seen in rheumatoid arthritis and has shown that the macerated nodules yielded organisms which were the same as those from the blood of patients having rheumatic fever. He
also noted that structurally the nodules seemed to be similar to those found in acute rheumatic fever and to those produced in animals by injecting streptococci.

In 1936 Singer and Levy reported 2 cases of Felty’s syndrome in which they isolated *Streptococcus viridans* from blood culture. They felt that Felty’s syndrome was due to chronic, low-grade sepsis, probably streptococcic. Their 2 cases were described in detail, especially the microscopic examination. They thought that the anatomic changes represented the effects of a long-standing low-grade infection, and they felt that they were typical of the alterations observed in sepsis lenta. These changes included activation of the endothelium, noted especially in the spleen and lymph-nodes and indicated by swelling, increase in number, and desquamation of the endothelial cells. They also noted erythrophagocytosis, increased plasma cells in the spleen and lymph-nodes, and particularly in the bone marrow. They also observed a decrease in the bone marrow elements, notably the granulocytes.

Microscopic examination from the skin of the thigh showed a great deal of iron pigment in the cutis. There were iron-containing cells particularly evident about the sweat glands which were in the form of heavy coats. The adventitial cells of the cutaneous capillaries were engorged also with iron granules. The melanin in the basal layers of the epidermis was not increased, however. This change probably accounts for the pigmentation.

Also noted were the microscopic findings of subacute glomerulonephritis and evidence of myocarditis. The glomeruli of the kidneys were cellular and the basal membranes were slightly thickened. Occasional fibrous crescents were seen and some of the glomeruli were partially hyalinized. Many of the tubules were filled with blood or hyaline casts, and the tubular epithelium was swollen and granular in places. The myocardium had increased amounts of connective tissue around the larger vessels, and it was loose and oedematous. It contained many swollen fibrocytes and loosely scattered lymphocytes and plasma cells. The muscle fibres were free of fat and the cross striations were indistinct. One of the cases showed typical Aschoff bodies in the myocardium. The authors state, as Dr. Clawson pointed out, that although the Aschoff nodule is characteristically noted in rheumatic fever, it is not limited to that disease.

From the evidence obtained in these cases, Singer and Levy state that Felty’s and related syndromes are special forms of sepsis lenta. They believe that the underlying sepsis affects not only the joints but also the haematopoietic system—that is, the spleen, liver, bone marrow, and the lymph-nodes. The variable response of the different tissues of the host determines the symptomatology and accounts for the different clinical pictures observed. The aetiologic agent is believed
to be a streptococcus of the viridans type. It is likely that other bacteria can occasionally produce Felty's and allied syndromes.

Some of our evidence could be readily applied in support of the hypothesis advanced by these authors, since we have found a variable picture in all of our cases of rheumatoid arthritis. That is, some had leucopenia and others did not; some had splenomegaly and others did not, etc. This evidence also seems to support the idea of Curtis and Pollard that Felty's syndrome is not a disease entity.

XI. Pleuræ, Lungs, and Liver

Examination of the pleurae, lungs, and liver gave the following findings in our series. There was a marked fibrous or completely obliteratorive pleuritis in 23 instances. There were 24 that had bronchopneumonia and 8 cases that had lobar pneumonia. Active pulmonary tuberculosis occurred in 7 cases. With regard to the liver, 6 cases had chronic passive congestion and 14 showed fatty metamorphosis.

XII. Amyloid Disease

An interesting finding which came out in this study was the high incidence of amyloid disease in our series of rheumatoid arthritis. Out of 61 cases there were 13, or 21 per cent., with amyloidosis. The organs involved were the liver, spleen, kidneys, adrenals, pancreas, and thyroid gland. The spleen was most commonly involved, being affected in 11 cases. The kidneys contained amyloid in 9 cases, the liver in 9 cases, and the adrenals in 8 cases; the pancreas and thyroid gland each in 1 case. (See Chart VI, p. 35.) It should be added that in 3 of these there was also active pulmonary tuberculosis, and this may have been a contributory aetiologic factor in the development of the amyloidosis.

It is well recognised that amyloid disease is a sequel to chronic suppuration and that it may also follow chronic, non-suppurative inflammations, yet the frequent association of amyloidosis with chronic arthritis is not mentioned in the literature. A few isolated case reports are available, however. A. Imrie in 1939 described an instance of amyloidosis in a young girl having Still's disease, and H. Reiman found amyloidosis in an adult arthritic.

It is of interest to note that amyloid disease has also been found in association with acute rheumatism. Thus Beattie recorded four instances of amyloid degeneration following repeated attacks of acute rheumatism where all other causes were definitely excluded (Brit. Med. Journ., 1896, 1444).

XIII. Scleromalacia Perforans

A rare condition occurred in two instances in our series. This condition is called "scleromalacia perforans." This was first described by van der Hoeve in 1934. It is a disease in which the principal
finding is the appearance of defects in the sclerae which can coalesce so that the sclerae show large gaps in which the uvea lies either covered by the conjunctiva or bare. Some men believe the process to be a degenerative one, while others say it is inflammatory. Verhoeff and King reviewed the literature in 1938 and found 14 instances of scleromalacia perforans, 10 of which had an associated chronic rheumatoid arthritis. They noted that the microscopic findings in the sclerae markedly resembled the structure of the subcutaneous nodules found in arthritis.

One of our cases showed signs of chronic inflammatory disease having an exudate of leucocytes, and plasma cells in the sclera and episcleral tissue. This did not extend beyond the equator of the eyeball. It is possible that this condition is more common than believed, but either it is not recorded or else it is probably not recognised. Whether or not it is commonly related to chronic rheumatoid arthritis is still a matter of speculation.

**XIV. CONCLUSION**

1. The clinical records and available pathologic material from 61 patients having died with chronic rheumatoid arthritis have been examined.

2. Lesions indistinguishable from those found in the rheumatic heart were encountered in 19 cases (31 per cent.).

3. Six of the cases with rheumatic heart lesions had congestive heart failure as evidenced by chronic passive congestion of the liver.

* Also thyroid and pancreas.
4. Only 3 persons in the entire group had "Felty's syndrome."
5. Amyloidosis involving one or several organs was found in 13 patients (21 per cent.).
6. Glomerulitis was found in 8, 6 of which were in early subclinical stages, and the remaining 2 had clinical evidences of glomerulitis.

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REFERENCES
BLOOD CULTURES IN RHEUMATOID ARTHRITIS
(HISTORICAL AND PERSONAL OBSERVATIONS)
BY THOMAS N. FRASER

The problem of microbial infection in relation to the etiology of rheumatoid arthritis has led to much discussion and experiment. Evidence of infection, particularly by streptococci, has been sought for both directly by blood cultures and indirectly by the study of immunity reactions of different kinds. The result of all this body of work remains entirely inconclusive, and it may seem redundant to burden the literature with further negative and inconclusive results.

While carrying out intensive observations on a group of cases of rheumatoid arthritis, however, a good opportunity was presented of repeating previous observations on blood cultures on this disease, and these have been contrasted in Table I with the results of the majority of previous workers in this field. The observations on blood cultures which have undoubtedly