SPLENECTOMY IN THE TREATMENT OF RHEUMATOID ARTHRITIS*

A REPORT OF THREE CASES

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At a meeting of the Royal Medical and Chirurgical Society in 1896 Dr. George Still read a paper on "A Form of Chronic Joint Disease in Children." He described a form of chronic polyarthritism of childhood beginning before the second dentition, and characterised by chronic progressive enlargement of joints without bony change and by general enlargement of the glands and of the spleen.

In 1924 Dr. A. R. Felty published a paper in the Johns Hopkins Hospital Bulletin entitled "Chronic Arthritis in the Adult associated with Splenomegaly and Leukopenia." He described five middle-aged patients, three men and two women, suffering from chronic arthritis, with enlargement of the spleen, leukopenia and enlarged lymphatic glands. In every case a yellowish-brown pigmentation of the skin was noticed. All were undernourished and gave a history of marked loss of weight since the onset of symptoms. In every instance the arthritis was long-standing, and the spleen was palpably enlarged, firm but not tender. There was a slight anaemia and a leukopenia, the white cells varying between 1,000 and 4,000 per cubic millimetre. Two of the patients ran a low fever for some weeks. Dr. Felty appears to have been uncertain whether to classify these cases as an adult form of the syndrome described by Still, or as two separate entities—Banti's disease and chronic arthritis—occurring concurrently in the same individual. He presented them as examples of a distinct clinical entity of unknown origin.

In 1930 Dr. Paul Chevallier wrote in the Revue de Médecine an article on "La Maladie de Chauffard-Still et les Syndromes Voisins." He gave a detailed account of the aetiological and clinical aspects of this syndrome. He emphasised its similarity

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to "le rhumatisme bilaire" of Gilbert and Fournier and the arthritic manifestations of Hanot's "cirrhoses bilaires." He described the ineffectiveness of the various forms of medical treatment, and in his final paragraph noted that, as far as he knew, in no instance had the spleen been removed. "It might be worth trying. It is a known fact that in patients with splenic enlargement the associated symptoms often abate after removal of the spleen. Although such results of this kind would be incomprehensible at present, it is not impossible that the operation might bring about a regression of the arthropathies."

In 1932 Dr. Hanrahan and Dr. Miller reported from Baltimore the result of a splenectomy which they had performed on a patient presenting this clinical syndrome. Their patient was a woman of fifty years of age, suffering from a chronic arthritis, in whom a large spleen and liver, a slight secondary anaemia, and leukopenia of about 1,000 cells per cubic millimetre was noted. Following the removal of the spleen, they claimed that there was a marked improvement in the condition of the affected joints which became less painful and less stiff, and also the white cells rose to 10,000 per cu.mm. Five months after the operation this improvement was maintained. The spleen was found to weigh 525 grammes. Microscopically no specific changes were noted, although there was a great hyperplasia of the endothelial cell lining, dilated sinuses, and increased numbers of plasm cells in the pulp spaces.

In 1934 Dr. Erle Craven of Durham, North Carolina, presented a detailed report on a similar case. The patient was a woman of forty years of age, with a rheumatoid type of arthritis of five years' duration. The first clinical manifestations occurred some nine days after a normal pregnancy. Adenopathy and splenic enlargement were noted. There was anaemia with 3,000,000 red cells, 2,500 white cells and a low-grade pyrexia. Following removal of the spleen, there was a striking subjective improvement with increased mobility of the hands, elbows, knees, and ankles. When reviewed some eight months later, however, little permanent improvement was noted. The spleen weighed 620 grammes and revealed much the same histological picture as in the former case.

In 1935 Dr. Reginald Fitz presented at a clinical meeting at the Peter Bent Brigham Hospital, Boston, a man sixty-three years of age, who presented the clinical picture of Felty's syn-
drome. He was treated medically, but died soon after of a short illness suggesting a coronary thrombosis or pneumonia. While discussing this patient Fitz stated that both Hanrahan’s and Craven’s patients had died within eighteen months of the removal of their spleen.

In 1937 Loeper, Lemaire and Patel reported in the Presse Médicale a case under their care at the St. Antoine Hospital, Paris. The patient was a woman twenty-eight years of age. She had an advanced rheumatoid type of arthritis of seven years’ duration. Splenic enlargement, a diffuse adenopathy, an anaemia with 3,480,000 red cells per cu.mm., and a leucocyte count of 6,800 per cu.mm. were noted. The patient was treated medically with drugs and blood transfusions without improvement. Finally the spleen was removed. There was an immediate marked subjective improvement with diminution of pain and swelling and increased joint movement. She continued to improve until, unfortunately, thirty-five days after the operation she developed a broncho-pneumonia and died. The spleen weighed 610 grammes, and the histological picture was similar to that in the previously recorded cases.

The authors state that “splenectomy transformed the patient’s pitiable condition within a few days.” There was a sudden and marked improvement in the general condition, and a gradual return to full function of the joints, the digital joints alone remaining deformed and a little stiff. They pointed out that in this disease one is probably concerned with diffuse mesenchymal reaction involving the synovial membrane, the capsule of the joints, the muscles, the spleen and the lymphatic glands characteristic of an infective disease. Although tuberculosis, syphilis and other infections had been held responsible for its aetiology, every laboratory investigation, biopsy of the synovial membrane, study of the articular fluid, and examination of the spleen had given negative results. They suggested that if the Chauffard-Still syndrome might be looked upon as being one of the “recticulo-endothelioses,” a vast framework to include the arthritic forms of Hanot’s disease and the primary splenomegalies with glandular enlargement or arthropathies, then, though the aetiology be unknown, a reason would be given for the clinical improvement following splenectomy. They suggest that if the spleen be regarded “as the essential site of the disease, and if the ‘arthropathising’ rôle (Alessandrini) is attributed to
its involvement, one might wonder if this organ liberates certain substances having a very weak action, but to which a previously allergic individual might react very strongly in certain preferred sites."

Later in 1937, Dr. Villaret and others presented a case at a meeting of La Société Médicale des Hôpitaux de Paris. The patient was a woman forty-two years of age with advanced rheumatoid arthritis of seven years' duration, slight splenic enlargement, a diffuse adenopathy, and anæmia with 3,800,000 red cells and 9,000 white cells. Intensive medical and physical treatment resulted in but little clinical improvement. The spleen was removed. On the day after the operation there was a marked decrease of pain and diminution of swelling in the affected joints, and there followed a gradual but marked improvement in the general condition of the patient. Immediately prior to the operation the white cell count was 21,000 per cu.mm.; ten days after the operation it was 15,000 per cu.mm.

We do not know the aetiology of the rheumatoid type of arthritis, nor are we prepared to conjecture as to the role of the spleen in this disease. In this paper we propose simply to report in some detail the case histories of three patients who during the last year have been under our care in the Rheumatic Unit at St. Stephen's Hospital (L.C.C.). They are all suffering from the rheumatoid type of arthritis. In each, after extensive but unsuccessful medical, physical, and in one case operative treatment, the spleen was removed.

CASE 1.—Rheumatoid type of arthritis—a young woman aged eighteen. Occupation none. Admitted to the Rheumatic Unit under our care on February 18, 1938.

Past History.—She is a twin whose brother is perfectly healthy. Until the age of nine she was well and won prizes at baby shows. When she was nine years old the joints of the fingers became swollen, and she began to lose weight rapidly and ran a temperature. She was admitted to St. Mary's Hospital, where a diagnosis of Still's disease was made. After a year's treatment she was quite well and running about. She went to school until the age of thirteen, when again she began to lose weight, had pain and swelling of the knees, feet and hands and a rash with fever.

She was readmitted to St. Mary's under the care of Professor Langmead, who has kindly given us a summary of her condition at that time: "Patient ill and anemic—swelling of the left wrist, which was hot, painful and limited in movement. Metacarpophalangeal joints of the left hand swollen and painful; movement in shoulders somewhat restricted; knees stiff. Considerable kyphosis. Spleen palpable one inch
below costal margin. Epitrochlear glands palpable. Few small soft glands in both anterior and posterior triangles of neck. Large soft glands in both axille and hard glands in the groins.

"Pulse rate 100, B.P. 100/60. Soft apical systolic murmur. The patient suffered from rashes and a swinging temperature, often rising to 103. Duodenal catheterisation revealed a streptococcus from which a vaccine was made. No abnormality was found in the blood or stools. X-ray report showed no evidence of bony change nor reduction of cartilage spaces."

After six months she was sent to Margate Hospital, where the right leg was put in extension. At the end of a year she could walk, but with stiff knees.

Aged sixteen: She was at home and walking a little. The general health was good.

Aged seventeen: Two months before admission there was a severe relapse with fever and pain and increasing stiffness in all the joints, including the temporo-mandibular.

On Examination.—February 18, 1938. A pale, emaciated girl lying stiffly in bed. She was not in severe pain, and could only open her mouth a few degrees. T. 98.4° F., P. 100, R. 20. Weight 4 st. 3 lb. The spleen was not palpable and there was no adenitis. The range of movement in the hands, wrists, elbows, shoulders and neck was restricted to some 20 per cent. of the normal. The hips were fixed in flexion and the knees were flexed with less than 10 per cent. of normal movement.

Laboratory Investigations:

Blood count:
- R.B.C.: 4,120,000.
- Hb.: 58 per cent.
- C.I.: 0-7.
- W.B.C.: 12,200.
- Polymorphs: 89-5 per cent.
- Lymphocytes: 7-5 per cent.

Blood culture: Sterile.

Sedimentation rate: 53 mm. fall at end of first hour (Westergren).

Wassermann reaction: Negative.

Gonococcal fixation test: Negative.

Blood calcium: 9-7 mg. per 100 c.c.

Blood phosphorus: 3-6 mg. per 100 c.c.

Radiography.—All bones show generalised rarefaction. Marked cartilage destruction in all joints except the sacro-iliac joints where there was no evidence of fusion.

A diagnosis was made of the rheumatoid type of arthritis in an advanced and active phase.

Treatment.—A high caloric semi-solid diet was a necessity owing to the difficulty the patient had in opening her mouth. A course of neosalganal (Schering), calcium-gold-keratinate with 14 per cent. of gold, was begun with 0-01 gm. intramuscularly. After the second injection of 0-02 gm. there was a severe reaction. T. 103°, P. 140, and general malaise. The blood count showed a leucopenia of 2,000, polymorphs 74 per cent., lymphocytes 19 per cent. This leucopenia was treated with adrenaline subcutaneously, pentnucleotide intramuscularly and blood transfusions. Within six days the leucocytes had risen to 6,400, and after six weeks the pyrexia was lower and the general condition improving.
Two months later, with the object of relaxing the generalised muscular spasm, a posterior plaster shell was made including the head and supporting the body down as far as the knees. The patient remained in the plaster shell for six months, during which time she had physical treatment—general ultra-violet light, massage and gentle movements of the joints.

At the end of this period the general condition had improved and there was a gain of 10 lb. in weight, but there was very little improvement in the joint condition and the sedimentation rate remained at its previous high level.

It was decided to perform a splenectomy in the hope of arresting the disease.

October 25, 1938.—Mr. S. W. Holmes removed the spleen under spinal anaesthesia through a left paramedian incision. The spleen was found to be twice the normal size and to be bound down by avascular adhesions. There were no splenunculi.

Pathological Report.—The splenic tissue shows the changes of amyloid disease.

The post-operative course was uneventful. Gradually throughout the ten months following this period the general and local conditions have improved.

Eight months later the patient had improved sufficiently to go to a convalescent home for one month, and there could walk half a mile and climb a few stairs with the aid of crutches. Following this she was allowed to go home.

August 24, 1939.—Afebrile. Weight 5 st. 6 lb. No pain. The jaw movement was still restricted to 10 per cent. of normal. In the neck, shoulders, elbows, wrists, knees and ankles there was at least 50 per cent. of the normal range of movement and in the hips 20 per cent. of the normal.

Investigations:

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<tr>
<td>R.B.C.: 5,240,000.</td>
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<tr>
<td>Hb.: 80 per cent.</td>
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<tr>
<td>W.B.C.: 12,500.</td>
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<tr>
<td>Polymorphs: 58 per cent.</td>
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<td>Lymphocytes: 34 per cent.</td>
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Sedimentation rate: 32 mm. fall at the end of first hour.

This was a case of the rheumatoid type of arthritis occurring in a young girl. At its onset it fulfilled the criteria for a diagnosis of the Chauffard-Still disease.

Gold therapy had to be discontinued owing to the tendency to leucopenia, and other methods of treatment failed to improve the condition.

After splenectomy and removal of an amyloid spleen there was no dramatic change, but since that time improvement has been steady.

Case 2.—Rheumatoid type of arthritis. A young man aged eighteen, by occupation a clerk. Admitted to the Rheumatic Unit on April 10, 1938, under our care.

Past History.—On two occasions within the previous nine months he had had attacks of joint stiffness, once in the left shoulder and once in the knees, in each case lasting a few days and not causing him to leave work. He had had no sore throats before, and apart from measles and whooping-cough as a child had no illness. No history of venereal disease.
Present Illness.—One month before admission he had a sore throat and general malaise. The large joints became painful and swollen, and within two weeks he was unable to stand.

On Examination.—A pale, thin boy, lying in pain and unable to move. T. 100-4°, P. 100, R. 25. Soft discrete glands were palpable in the epitrochlear and inguinal regions. The spleen could not be felt. The skin was moist and atrophic and there was marked wasting of the limb muscles. There was gross periarticular swelling of the interphalangeal, wrist, elbow, knee and ankle joints. All movement was painful and limited by muscle spasm around the joints. The pharynx was injected—tonsils not enlarged—sounds normal. B.P. 130/85.

Laboratory Investigations: Throat swab—non-haemolytic streptococci.

Blood count:

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<th>Value</th>
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<tr>
<td>R.B.C.</td>
<td>3,920,000</td>
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<tr>
<td>Hb.</td>
<td>62 per cent.</td>
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<tr>
<td>C.I.</td>
<td>0.7</td>
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<td>W.B.C.</td>
<td>9,300</td>
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<tr>
<td>Polymorphs</td>
<td>67 per cent.</td>
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<tr>
<td>Lymphocytes</td>
<td>27 per cent.</td>
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Blood culture: Repeated several times yielded a growth of S. fecalis alkaligines on one occasion only.

Sedimentation rate: 66 mm. fall at end of first hour (Westergren).

Wassermann reaction: Negative.

 Gonococcal fixation test: Positive.

Urethral smear and prostatic bead (repeated): No pus; no organisms.

Electrocardiogram: No abnormalities.

Blood uric acid: 2 mgm per 100 c.c.

Radiography.—Generalised rarefaction of bone with commencing erosion of the articular cartilages of the wrist joints. No gross changes in the elbow or knee joints.

A diagnosis was made of the rheumatoid type of arthritis in an active phase.

Treatment.—Rest in bed. High caloric diet and six tablets of Multivite each day. (Vitamin A, 3,000; B, 50; C, 200; D, 600 units per tablet.) Sodium salicylate gr. xx, two-hourly by day, four-hourly by night for fourteen days. There was no improvement either in the joint pains or general condition.

At this stage light plaster shells were made to support the hands, wrists, knees, and ankles and to prevent deformity. Next iodoseptine (iodo-benzo-methyl-formin-42 per cent. iodine) was given intramuscularly, 10 c.c. each day for fourteen days. There was no improvement; the muscle wasting was increasing and the joint movement becoming increasingly restricted. Serial radiographs showed increasing erosion of cartilage.

May, 1938.—One month after admission a course of neosolganal was given by weekly intramuscular injections of 0·05 gm. After the sixth injection albuminuria was detected and the gold was stopped. The urine was sterile on culture and with an occasional granular and hyaline cast. Within ten days the urine was clear of albumen and no casts or cells were seen.

Following this, two fresh methods of treatment were tried—blood transfusions and arthrotomy and lavage of each knee.

June, 1938.—The patient was transfused with 300 c.c. of citrated blood, and this was repeated three weeks later. Iron therapy was continued and the blood picture improved.
July 8, 1938.—R.B.C.: 5,560,000, Hb.: 87 per cent., C.I.: 0-8, W.B.C.: 9,300.

May 27, 1938.—Arthrotomy and lavage performed on the left knee, and June 24 on the right knee by Mr. A. G. Timbrell Fisher. After each operation there was a fall of temperature for ten days. It then reverted to the former level of 99° to 101°.

Operation findings were similar in each knee. The joint was full of necrotic fibrinoid material of which about 8 oz. could be easily expressed. The synovial membrane was congested and oedematous. Beyond early pannus encroaching on to the edges, no change was seen in the articular cartilages. The joints were irrigated with Dakin’s solution and closed without drainage.

July 8, 1938.—Prontosil 0·5 gm. in tablet form was given four-hourly for ten days. There was no change in the clinical condition, nor was the pyrexia diminished.

By this time, two and a half months after admission and three and a half months since the onset of the illness, the condition of the patient was gradually becoming worse. There was persistent pyrexia (99° to 100·4°), extreme muscle-wasting and restriction of movement in all joints. The range of movement in the elbows, wrists, knees and ankles was less than 10 per cent. of normal. The blood sedimentation rate remained raised.

All forms of therapy tried (salicylates, Iodoseptine, gold, arthrotomy, and lavage, transfusions, and prontosil) had failed to arrest the progress of the disease. It is felt that there was insufficient or no evidence to suggest that Streptococcus fecalis alkaligines or the gonococcus played an aetiological rôle.

In order to relieve the pain and spasm around the joints it was decided to try the effect of splenectomy.

August 16, 1938.—The operation was performed by Mr. S. W. Holmes, under general anaesthesia. The spleen was found to be twice the normal size. There was no perisplenitis.

Pathological Report.—Moderate oedema and congestion and slight excess of leucocytes in the spleen.

The post-operative course was uneventful. Fourteen days after the operation the fever tended to lessen. There was no marked improvement following splenectomy, and two months later the boy’s father insisted on taking him home against advice.

June, 1939.—The boy was visited in his home by one of us (O. S.) and examined. Though the general condition was extremely poor, it was no worse than when he left hospital, and there were clinical signs that the rheumatoid arthritis had become quiescent. There was no fever nor peripheral sweating and no pain at rest or on movement. In the fingers, wrists, elbows, shoulders, hips and ankles the movement was 10 per cent. of normal. There was none in the knees.

It is probable that had this boy been able to have continued orthopaedic and physical treatment while the disease was becoming quiescent, the result would have improved. Even with partial ankylosis the joints are in the optimum position owing to early splinting.

Case 3.—Rheumatoid type of arthritis. A young woman aged twenty-nine years. Occupation, children’s nurse. Admitted to Rheumatic Unit under our care on April 21, 1938.
Past History.—Eight years ago: The right hand suddenly became swollen and painful. This subsided after three days but recurred later. Within two years all the large joints had become affected and she was getting about only with difficulty. She came under the care of one of us (F. J. B.) at the St. John Clinic, when a diagnosis of the rheumatoid type of arthritis was made. She was treated with intra-pelvic diathermy and the joints improved, but she was not able to go back to work.

Five years ago: Admitted to the Westminster Hospital for six months. Tonsillectomy was performed, the hands were supported with plaster shells and physical treatment given. The left leg was stiffened at the knee and a caliper worn for some months.

Three and a half years ago: Readmitted to the Westminster Hospital. At that time radiography showed no sign of anylosis, and the joint spaces were reported as being “fairly good.”

One year ago: A course of gold injections was given, and this resulted in some improvement until after two months she developed a rash on the face, with a yellow nasal discharge, and the gold was stopped.

A second course was started some months later, but this was terminated after four months, as the pains were worse.

Four months ago: Admitted to Lewisham Hospital where a course of prontosil was given.

During her illness, apart from the joint pains, she had felt well, and there had been only slight loss of weight. The menses had been irregular ever since the onset.

On Examination.—A well-nourished girl lying in constant pain. T. 98.4°, P. 82, R. 22. There was cyanosis of the cheeks, lips, fingers, and toes, and the hands and feet were moist. There were no enlarged lymph glands nor was the spleen palpable. Movement in all joints was limited: in the wrists to 10 per cent., and in the elbows, shoulders, right knee, and ankles to 30 per cent. of the normal. The left knee was stiff. The most marked feature was the degree of muscle spasm which resulted from passive movement of any joint, especially those of the lower limbs. There were also painful involuntary attacks of spasm in the quadriceps muscles.

Apart from the joints no clinical abnormality was found. B.P. 120/75.

Laboratory Investigations:

Blood count:

- Hb.: 64 per cent.
- C.I.: 0-6.

- W.B.C.: 8,700.
- Polymorphs 52 per cent.
- Lymphocytes 32 per cent.

Sedimentation rate: 57 mm. fall at end of first hour (Westergren).

Spectroscopic examination of blood: Sulphemoglobinæmia.

Wassermann reaction: Negative.

Gonococcal fixation test: Negative.

Blood uric acid: 1-9 mgm. per 100 c.c.

Test meal: Achlorhydria.

Radiography.—Partial ankylosis of the carpal joints, some destruction of the heads of the metacarpals. Other joints show narrowed joint spaces and cartilage erosion.

A diagnosis was made of the rheumatoid type of arthritis in an advanced and active phase.
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Treatment.—Complete rest, a high caloric diet and analgesics for the pain. Light plaster supports were made for the hands and right leg.

May, 1938.—Ten million T.A.B. was given intravenously, resulting in a fever of 104° F. The peripheral sweating was much reduced after this and the joints were looser for five days only. This was followed by ionisation with histamine to the hands and feet and gentle movements of the joints, but no improvement resulted and there was still as much pain.

June 24, 1938.—In the hope of relieving the painful spasms and increasing the joint movement, bilateral lumbar sympathectomy was performed by Mr. Holmes. The spasm was relieved to some extent, but there was still great pain on any movement.

July, 1938.—A course of solganal B was given by weekly intramuscular injections until 1.76 gm. had been given. At the same time, on the advice of Mr. Philips, the consulting gynaecologist, endocrine therapy with progeston and menformon was begun. During this time the general condition improved, but there was no change in the joint function nor relief of pain.

Eight months after admission and following treatment by protein shock, gold, physical methods and sympathectomy, there was little improvement and the sedimentation rate remained high.

It was decided to try splenectomy in the hope of relieving the pain and improving the joint condition.

December 12, 1938.—Under general anaesthesia, Mr. K. F. D. Waters removed the spleen, which was enlarged to twice the normal size and was bound down with dense adhesions.

Pathological Report.—The spleen shows the changes of amyloid disease.

The post-operative course was uneventful. Since splenectomy there has been a very slow but sustained improvement. Eight months later she was able to walk 100 yards with little pain and was sent for a month's convalescence, during which she improved considerably. Following this, she had been admitted to a training school in order to learn needlework so that she may earn her living again.

September, 1939.—She can walk several hundred yards and climb a few stairs without pain. She can use her fingers well, and there is an increased range of movement in the wrists, elbows, shoulders and right knee to 50 per cent. of the normal range. Peripheral sweating is absent and the involuntary muscle spasms are very occasional.

Laboratory Investigation:

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<tr>
<td>Hb.: 96 per cent.</td>
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<td>C.I.: 0.9.</td>
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Sedimentation rate: 28 mm. at end of first hour.

It is well known that surgical intervention such as tonsillectomy or cholecystotomy for the removal of possible foci of infection in patients suffering from the rheumatoid type of arthritis may be followed by transient clinical improvement. Some temporary diminution of pain and joint deformity may occur. Whether this is due to the removal of a specific causative factor, or to the
production of non-specific protein shock with stimulation of the reticulo-endothelial system, or to the period of rest and controlled dieting that follows an operation, we do not know. In our opinion the improvement in the clinical picture which may follow splenectomy is of quite another character and is probably not explainable along these lines. Although we may offer certain reasons for the clinical improvement, we do not feel that as yet they are sufficiently well defined to be included in this description of our cases.

SUMMARY.—Three cases are described in which splenectomy was performed for the rheumatoid type of arthritis; in two cases amyloid change was found. They have been followed for a period of over nine months in each case. In two of the cases marked clinical improvement has followed the operation, and in the other, although there is no clinical improvement, the disease appears to have become quiescent. The literature on the subject has been reviewed.

We are indebted to Sir Frederick Menzies, Chief Medical Officer to the London County Council, for permission to publish the case reports.

REFERENCES


