AMERICAN RHEUMATISM ASSOCIATION

PROCEEDINGS OF THE ANNUAL MEETING, 1948

The Annual Meeting of the American Rheumatism Association was held in Chicago on June 19 and 20, 1948. The main points in The Presidential Address and reports of papers read at the meeting are given below.

Presidential Address

ROBERT M. STECHER

The American Rheumatism Association is a direct descendant of the American Committee for the Study and Control of Rheumatic Diseases appointed by Dr. Louis B. Wilson of the American Medical Association early in 1928 with Pemberton as chairman. This organization presented scientific exhibits at annual meetings of the American Medical Association in 1930, 1931, and 1932. It has held thirteen public meetings for the presentation of scientific programmes since 1932. One of its committees has published the "Primer on Rheumatism" in 1934 and the "Primer on Arthritis" in 1942. A third edition of this summary of accepted knowledge of rheumatism is now in preparation. Another committee developed the system of terminology for joint diseases which was incorporated in the 1942 edition of "Standard Nomenclature for Diseases and Operations".

The greatest contribution of this Association towards the understanding of joint diseases has been the publication of the *Rheumatism Reviews*, a comprehensive review with editorial comment of the literature of the English-speaking world on rheumatism and arthritis from 1932 to 1945. This accomplishment has been possible because of the energy and imagination of Philip S. Hench and his willing collaborators.

The American Rheumatism Association asserts its influence on pertinent matters in other ways. A committee headed by Steinbrook will present recommendations on Therapeutic Criteria. Lockie is chairman of a Committee on Affiliation with the Food and Drug Administration concerned with the approval and acceptance of drugs of interest and importance in the treatment of joint diseases. A committee headed by Crain is determining standards and criteria for the development of local rheumatism associations and the conditions under which such organizations may be affiliated with the American Rheumatism Association. Hench is chairman of a committee perfecting arrangements for the meeting in New York in 1949, when the American Rheumatism Association will act as host to the International League against Rheumatism.

The Committee on Research and Education, of which Holbrook is chairman, has undertaken important responsibilities. As part of this project, the American Rheumatism Foundation was incorporated in May to provide an organization for raising funds on a nationwide basis. There are estimated to be 7,500,000 cases of chronic rheumatism in the United States. Rheumatism in America causes twice as many disabled persons as does heart disease, five times as many as nervous and mental diseases, seven times as many as cancer, and ten times as many as tuberculosis. "Rheumatism has annually invalidated 147,000 persons, has cost 97,000,000 days lost from work, $200,000,000 in wages, and more than $100,000,000 for medical care."

Only a small proportion of the arthritics today have the benefit of adequate trial with the treatments which are now available. The present condition of many patients can be definitely improved, and the future prospects of patients with early cases can be bettered by proper therapy under the direction of informed and interested physicians. The American Rheumatism Association has already contributed substantially by dissemination of technical knowledge through official publications and committee reports—activities which will continue. The Association might properly describe and distribute data on the criteria for diagnosis and establish minimum standards for rheumatism clinics, rheumatism services, and rheumatism hospitals. Its influence will grow through an expanding membership and will be implemented at the city and county levels by increasing numbers of affiliated societies.

Improvement in medical care depends upon better understanding of the disease through research. The Association will support education and investigation in rheumatism. A fund-raising campaign is being organized. The exercise of free enterprise to solicit voluntary contributions for use in the study and control of a particular disease is one of the amazing phenomena of modern American culture. In 1947 the National Tuberculosis Association raised $18,224,786, The National Foundation for Infantile Paralysis raised $17,987,000, and the American Cancer Society raised $12,126,875. The rheumatism problem is just as important as these.

Competent men, adequate material, proper facilities,
and a congenial environment are also needed. Progress might be facilitated if men of experience would review the problems, define the issues, identify the crucial questions, and devise the investigation most likely to yield pertinent answers. A survey by the American Rheumatism Association should be made to discover the research facilities now available, to note the work now in progress, to point out duplication of effort, and to encourage activities in fields which are now neglected. Only in this way can a co-ordinated plan be developed.

The time has come when this association must establish a journal of its own. Business of the organization is complex, important decisions must be made, and an adequate medium of communication to the membership is essential. Publication of editorials, presentation of individual views from various officers, and preliminary explanation of controversial matters will inform the members so they will be better able to make intelligent decisions at the regular business meetings. The Rheumatism Reviews, the Proceedings of our meetings, programmes with informative abstracts of the papers to be presented, and news items concerning the Foundation and affiliated rheumatism associations provide adequate material for an excellent journal. In contrast to the United States, England has two current rheumatism journals and formerly had a third. There are two French journals, a Spanish journal, and one from the Argentine. Of particular interest is the Annals of the Rheumatic Diseases published in London by the British Medical Association, affiliated to the Empire Rheumatism Council, the Heberden Society, and the International League Against Rheumatism. The editors have been cordial to the American Rheumatism Association by including three Americans among the list of associate editors and soliciting scientific articles from our members. The Annals is not the official journal of the American Rheumatism Association but your officers have recommended this journal to you and have accepted your order and subscription payment along with your dues if you so order it.

Alterations in Synovial Fluid with Variations in Severity of Joint Disease

MARIAN W. ROPES
Boston, Massachusetts

Synovial fluid has been found to reflect the severity of inflammation of synovial tissues. In the mildest inflammation, that due to trauma, the changes in the synovial fluid are never marked. The leucocyte count averages 1,080 cells per c.cm. The sugar level is the same as in serum. Mild cases of infectious arthritis or of rheumatoid arthritis compare with traumatic conditions. Severe rheumatoid arthritis have an average sugar level of 55 mg. and globulin of 4-1 g. Synovial fluid has diagnostic value in differentiating various types of infectious arthritis and rheumatoid arthritis from joint diseases that are traumatic in origin. In infectious arthritis the fluid findings are of prognostic value.

Discussion

DR. CURRIER McEWEN (New York): Synovial fluids of different patients with the same type of disease can vary, especially as to the cellular components, more strikingly or just as strikingly as fluids from patients with different diseases. Therefore one cannot take a single examination of a fluid and draw full diagnostic conclusions from it any more than one could from most other individual studies that might be made in this group of diseases. When one examines the synovial fluids of large numbers of patients one finds these trends which Dr. Bauer has reported in the different types of joint disease. However, findings in individual patients at different stages of disease vary so widely that study of synovial fluids is of comparatively little diagnostic value in many instances except as the results are weighed in relation to other findings.

DR. J. ALBERT KEY (St. Louis, Mo.): I thought that joint sugar and blood sugar were about parallel, and the same with other substances that diffuse through the synovial surface. I think the sugar is low because the leucocytes consume the sugar.

DR. DAVID H. Klings (Los Angeles): Dr. McEwen is right in pointing out the limitations of the analysis of synovial effusions. Nevertheless, this is a very useful and direct approach to an understanding of joint pathology; and it is to be regretted that, except in a few clinics, hardly any systematic examination of joint effusions is carried out.

In our experience, effusions in rheumatoid arthritis are turbid and have a low viscosity and a high cell count, with prevalence of polynuclear leucocytes. These characteristics are present as long as the rheumatoid process is active. Effusions occur in osteo-arthritis. They are almost clear, have a high viscosity, a low cell count, with prevalence of mononuclear cells, lymphocytes, and synovial-lining cells. If effusions of this character are aspirated in a case of longstanding rheumatoid arthritis, this is a sign that the rheumatoid process has burned out and a secondary osteo-arthritis is the source of the effusion.

I have for many years stressed the importance of mucin and its variations in the synovial fluid, and am happy that Dr. Ropes has arrived at similar conclusions.

DR. HUGO A. FREUND (Detroit): We have studied the globulin content by electrophoresis in two cases where enough fluid could be withdrawn from the joints, and found that the γ globulin is increased exactly as the γ globulin is increased in the serum. The same, I think, has been reported elsewhere.

I disagree that osteoarthritic processes occur only in elderly individuals. Recently I have seen two patients past 60—one of 64 and one of 67—who had pure rheumatoid arthritis, with globulin changes in the electrophoretic curve, the γ globulin increased. They had no osteo-arthritic changes.

DR. WALTER BAUER (closing): Dr. McEwen is right. In mild cases of infectious arthritis or mild cases of rheumatoid arthritis the changes in synovial fluid are slight, such as those found in traumatic effusions (Group I fluids). With increasing severity of disease the changes in the fluid are much greater.
We use the following working rule: if a fluid is cloudy, clots, has a cell count over 5,000 per c.mm. with over 50 per cent. polymorphonuclears, a protein concentration above 5-5 g. per 100 c.c.m., a serum-fluid sugar difference above 20 mg. per 100 c.c.m., and a poor precipitate of mucin with acetic acid, one can say with relative certainty that the joint disease is not traumatic in origin.

In normal joints the synovial fluid sugar parallels the blood sugar, as Dr. Key has stated. In moderately severe and severe infectious arthritis and rheumatoid arthritis, low synovial fluid glucose levels are found; in some instances no sugar can be detected. The low sugar concentrations are not due solely to the increase in leukocytes.

The answer to Dr. Cecil’s question is yes. If the fluid clots, the cell count is lowered appreciably. This can be avoided by collecting a small amount of fluid in a test tube containing an anticoagulant; in addition, one should always use normal saline as the diluent.

We have done electrophoretic studies on both blood and synovial fluid for about eight years and agree that the $\gamma$ globulin which is increased in the serum is likewise increased in the synovial fluid. In some cases a higher concentration of $\gamma$ globulin has been found in the fluid than in the serum, suggesting the possibility either of increased difficulty in removal of this protein fraction, or of local formation of protein by tissue breakdown or by activity of the surrounding cells.

It is important for us to remember that rheumatoid arthritis can occur at any age, from childhood to senility.

The Use of Curare in Rheumatoid Spondylitis

ELI BAUMAN, EDWARD B. SCHLESINGER, and CHARLES RAGAN

New York

Spasm of erector spinae muscles is a characteristic finding of rheumatoid spondylitis. Curare is a potent relaxant. Seven patients with proven rheumatoid spondylitis were studied. All were given 1-0 c.c.m. of $d$-tubocurarine in oil and wax on at least three successive days and continued thereafter once or twice weekly for variable periods. Six showed increase in mobility of spine and reduction in pain by the third day of curare administration. One patient with extensive ligamentous calcification showed no response. The study suggests that spasm of the erector spinae muscles is an important factor in the early stages of this disease.

Discussion

Dr. W. H. Kammerer (New York): I have observed a small group of cases treated at a Veterans Hospital in New York City. There were seven patients in the group, five of whom were suffering from rheumatoid spondylitis, the other two having other forms of rheumatic disease. The patients were hospitalized for periods up to eight months, the minimum being three months. They were given larger doses of curare than Dr. Bauman suggested. We pushed the dose up to the point of toxicity, and then held it there or dropped it back a little and held it there, so that many of them were getting 1-4 to 1-6 c.cm. of curare. They received injections three times a week after the initial course of three daily injections. That was continued for a period of two or three weeks or longer.

Our results in these patients were disappointing. Two patients showed objective evidence of improvement in increased mobility of the spine. Only one patient would admit to subjective improvement. These cases differed in two respects from Dr. Bauman’s group in that they all showed x-ray changes characteristic of rheumatoid spondylitis. We felt that was important, because we believed there should not be any question but that the stiff back was due to demonstrable organic disease. Secondly, they were veterans and some were drawing disability compensation. It is notorious that where compensation is involved, therapeutic effects are less easy to attain.

Dr. Charles W. Wainwright (Baltimore): We have been able to use curare in three instances of Marie-Strümpell arthritis, and in all these the mobility was increased. One man had had the disease for four years and had not been able to cross his knees for two. Immediately following the administration of curare he was able to cross his knees with comparative ease. It was our observation, too, as one would expect, that the pain was diminished as well as the movement increased.

Dr. Philip S. Hench (Rochester, Minnesota): In the last two years we have discussed neostigmine, procaine given intravenously, and now curare for the relief of muscular pain. All of this work represents a laudable attempt to do something about a condition we have not tackled before.

Dr. Bauman, did you have any control studies? Can you tell us how the effect of curare compares with the presumed effect of neostigmine or procaine administered intravenously, or of the simple procedures of physical therapy and aspirin? Is curare a remedy useful for the "long pull" in rheumatoid spondylitis or is it merely useful for the painful, acute muscular spasms, and the acute exacerbations which these patients have now and then? Will you tell us a little about the supposed physiology of this drug? Dr. Howard Polley used curare in a few cases of rheumatoid spondylitis and was disappointed in the results. He understood that ocular relaxation occurred before relaxation of skeletal muscles. He did not obtain much in the way of relaxation of either the spinal or ocular muscles. Is one supposed to obtain the latter in the successful use of curare?

Dr. Eli Bauman (closing): We do not have any control studies with prostigmine or any of the other muscle relaxants in this disease.

We do not have enough evidence at this point to say whether curare should be used at all in the treatment of Marie-Strümpell spondylitis. We do feel that the best results are obtained in either the initial acute stage of this disease or the acute exacerbation, but whether or not it should be used therapeutically we will have to wait several years to determine.
We have had very few reactions to curare. The rare cases of diplopia and dizziness have been transitory and not troublesome.

**Dr. Charles Ragan (closing):** I would like to answer some of Dr. Hench's questions. We have a control series of patients with peripheral joint rheumatoid arthritis treated with neostigmine which in our hands was completely ineffective. Two years ago we reported on peripheral joint rheumatoid arthritis with curare. Where the flexion contracture is of brief duration we hope to achieve some benefit from curare.

For treatment over a long period of time this is a tedious process, which requires much supervision to avoid toxic reactions, and we do not present it as a therapeutic agent. We presented this report primarily to demonstrate a factor of importance in the mechanism of the disease.

With long-acting curare preparations such as we use—d-tubocurarine in oil and wax—we do not expect to achieve muscle paralysis. We only wish to depress the myoneural junction to the point where aberrant impulses do not come through.

It has long been known that curare affects the small muscles first. If the patient complains of diplopia we decrease the dose.

**Long-Range Evaluation of Radiotherapy in Rheumatoid Spondylitis**

**William D. Robinson and Isadore Lampe**

Ann Arbor, Michigan

Fifty-five patients with rheumatoid spondylitis have been followed by clinical, laboratory, and x-ray examinations for 5 to 9 years after the initiation of radiotherapy. Of 13 subjects with x-ray evidence of involvement of the entire spine at the time treatment was started, 3 showed objective clinical improvement which was maintained, 3 had no significant objective change, and 7 had clinical progression during the period of observation; radiographs showed progression in all 13. Of 17 patients with x-ray changes in the sacral, lumbar, and dorsal spine, 8 maintained objective improvement, and 9 progressed clinically; radiographs showed progression in 15. Of 7 who originally had x-ray changes restricted to the sacro-iliac joints and lumbar spine, 2 maintained objective improvement, and 5 progressed; progression of x-ray findings occurred in 6. Of 17 with x-ray abnormalities in the sacro-iliac joints only, but clinical evidence of lumbo-dorsal involvement, 12 have maintained significant objective improvement, and 5 have progressed clinically; progression by x-ray was seen in 12. One patient had x-ray and clinical evidence of sacro-iliac involvement only; after a complete remission lasting five years, clinical and x-ray involvement of the lumbo-dorsal spine developed.

**Discussion**

**Dr. Richard H. Freyberg (New York):** I am interested in this report because some of these patients are those we observed in our earlier studies and reported in regard to initial results of radiotherapy. At the onset we were using 200 roentgen units, repeated three times, a total of 600 units in each course of treatment. Later some of these patients were treated with smaller amounts of roentgen therapy, usually 150 r times 3. Was there any difference in the long-term response in these patients depending upon differences in techniques?

**Dr. Frank P. Foster (Boston):** I think it is apparent that x-ray treatment helps to handle these cases of rheumatoid arthritis of the spine. Gillespie and I have just completed a review of 92 cases treated in the last ten years. The method of treatment was much the same as has been reported by Drs. Robinson and Lampe, the total dosage being perhaps a little less. The duration of the disease was approximately nine years up to the time of our seeing the patient; the follow-up was on the average a little better than 7½ years.

Sixty per cent. of our patients indicated they felt better; 25 per cent. felt worse; 15 per cent. were the same. Objectively, 5 per cent. had complete relief over the period of follow-up; 28 per cent. had no evidence of progression of the disease demonstrable by laboratory or physical test, but there had been one or more recurrences of pain. Fifty per cent. of the group had had only recurrence of pain but the disease had progressed, and 13 per cent. had had neither relief of pain nor cessation of the progress of the disease. Thus about 30 per cent. were either relieved completely of pain and progression or else showed no progression.

Steinbrocker has reported that 50 per cent. of patients may expect to go back to light work. We therefore tried to find out what the patients were doing at present. As would be expected in New England, 40 per cent. were at shop or housework. Thirty-one per cent. were doing heavy manual work, and 26 per cent. were doing office work. Of the total group, 87 per cent. were at full-time occupation, 9 per cent. at part-time occupation, and 4 per cent. were disabled, of whom one patient was blind.

**Dr. Wallace Graham (Toronto):** I have seen two patients with ankylosing spondylitis treated by x-ray therapy who developed fatal leukaemia presumably as a result of the therapy.

**Dr. William D. Robinson (closing):** I believe we have tended to use smaller doses of x rays in the last few years. At the present time, in the first series of treatment, total dosage will average about 450 r per course, and two or three courses will be given.

Dr. Boland and his associates have reported on the importance of physical therapy and postural exercises. We are now making a definite effort to instruct the patients in postural exercises, usually after they have had symptomatic improvement from radiotherapy. It is useless to instruct them in postural exercises while they are still having pain and muscle spasm.

We have seen only temporary harm from radiotherapy; the usual picture of x-ray sickness, with loss of appetite, vomiting, and at times diarrhoea. They have been less frequent with the smaller doses, and are transient. We
have had no patients in whom there has followed any blood disease which could be attributed to the x-ray therapy. As far as I know, the two cases noted today are the first to be reported. Certainly it is a theoretical danger and one that we may have to look out for.

We have not followed the effect of fertility in men. Some women who have had treatment over the sacroiliac joint have had temporary suppression of menses; in two cases I believe menopause has been induced by radiotherapy. However, we have in three patients a total of four normal pregnancies following temporary suppression of the menses by radiotherapy in this area. It is a serious problem and one that I do not think we have answered at the present time.

Some patients have had hip-joint involvement during the period of observation. There are others who have had treatment over the hip joints with radiotherapy and appear to have had some subjective improvement. In some there has been later progression of the hip-joint disease. In others it has appeared to stay relatively stationary.

I am grateful to have the report on the results of the study in Boston. The information that progression occurs in as high as 50 per cent. of the patients after radiotherapy indicates that it is by no means the final answer in this disease.

Treatment of So-called Palindromic Rheumatism with Gold Compounds

EDWARD W. BOLAND and NATHAN E. HEADLEY

Los Angeles

"Palindromic rheumatism", as described by Hench and Rosenberg, is characterized by (1) multiple afebrile attacks of acute arthritis with pain, swelling, tenderness, varying degrees of redness, and increased local heat; (2) frequent recurrences (88 per cent. of cases averaging 23 attacks per year) at irregular intervals (few hours to two weeks in most cases); (3) short attacks (80 per cent. lasting a few hours to three days); (4) attacks usually affecting a single joint (90 per cent. of cases); (5) disability often considerable with temporary loss of function of the involved part; (6) complete restitution of joint appearance and function following attacks; (7) para-arthritis consisting of red, tender swellings near a joint (in 30 per cent. of cases) and frequent involvement of finger pads; (8) absence of general constitutional signs and symptoms; (9) absence of chronic arthritis when the disease has persisted for years; (10) intracutaneous or subcutaneous nodules (in 9 per cent. of cases); (11) essentially normal laboratory tests including erythrocyte sedimentation rates, blood uric acid determinations, and radiographs of involved joints; (12) adults of either sex affected equally.

Various types of medication have been tried but the results have been either negative or equivocal. No report on the use of gold compounds has appeared in the literature.

Three patients were treated with soluble gold compounds (gold thioglucose). Striking improvement occurred in each case. Maintenance doses of gold salts were continued after an initial course had been completed. One case averaged 73.4 attacks per year prior to chrysotherapy and with treatment had only one attack in an eighteen-month period; another averaged 228 attacks per year before treatment and four attacks per year with treatment; a third averaged 83-3 attacks before treatment and had no attack during a six-month follow-up period.

If further trials with chrysotherapy substantiate these favourable results, some weight may be added to the contention that the syndrome of so-called palindromic rheumatism may merely represent an atypical form of rheumatoid arthritis.

Discussion

DR. DAVID E. MARKSON (Chicago): One of the palindromic patients that Dr. Hench reported in his original series died in the Evanston Hospital from rheumatic heart disease. I saw, in consultation with Dr. Howard Alt, a middle-aged school teacher, who met all the requirements listed on Dr. Boland's chart for the diagnosis of palindromic arthritis. She died about six years later. The anatomical diagnosis at necropsy was lupus erythematosus. I have a school-teacher with a typical palindromic syndrome who had from twenty to thirty attacks each year. We found haemolytic streptococci in her throat culture. A vaccine was made from the culture in a dilution of one million per c.c.m. Her attacks after treatment with this vaccine have been reduced to probably one or two in the past two years. I wonder whether Dr. Boland has had any such experience with this method of treatment?

DR. RICHARD T. SMITH (Philadelphia): A 34-year-old woman who had four years of palindromic rheumatism had an average of 106 attacks a year. During that time, the longest interval between attacks was two weeks. For approximately a year the diagnosis has been established, but her physician failed to follow the recommendations. Finally he accepted the diagnosis and decided to use chrysotherapy. Instead of following the outline of treatment, he gave 5 mg. doses for eight weeks, then 10 mg. doses for thirteen weeks, without any change in the patient's condition. Finally he agreed to follow the programme as outlined. She then received two 25 mg. doses, one a week, and then 50 mg. doses. After she had received eleven of the 50 mg. doses, she ceased to have attacks. At that time she had received 770 mg. of gold. She was continued at 50 mg. a week until she had received a total of 1,020 mg., and was then placed on a maintenance dose of 50 mg. every two weeks for three doses, and then 50 mg. every three weeks until she received a total of 1,420 mg., or about sixty weeks of treatment. She has received no treatment for the past
thirteen weeks and over a period of nine months has had no further attacks of her palindromic rheumatism.

Dr. Ernest Stengel (New York): Dr. Boland suggests that this condition is related to rheumatoid arthritis or is a variation of it. I had occasion to see five patients with palindromic rheumatism. When I saw the first two cases, I also had the feeling that this condition was related to rheumatoid arthritis; and therefore I established a treatment which had previously been helpful in cases of rheumatoid arthritis; it includes gold treatment. After a certain time of treatment for rheumatoid arthritis we usually can tell whether we can expect good results from further treatment. When using our arrangement of treatment for rheumatoid arthritis in our cases of palindromic rheumatism we could not see any benefit. We therefore gave this treatment up, and I do not believe any longer that those two conditions are identical or related to each other. We changed to antihistamine treatment and a course of multiple, combined streptococcus vaccine; thereafter the condition improved rapidly and markedly.

One of our cases we could follow up for longer than a year and a half. Once the clinical picture of palindromic rheumatism disappeared it did not reappear. The patient was free from any attacks for a period of at least one year after the last treatment. We therefore believe that palindromic rheumatism is not related to rheumatoid arthritis.

Dr. Russell L. Cecil (New York): A case of palindromic rheumatism has been under observation for three and a half years. It is interesting how very sensitive this patient is to emotional upset. The attacks were very frequent before she was started on gold treatment. She herself claims—and I believe rightly—that she has been very much benefited by gold therapy. Like the case reported, she is now on maintenance doses and has had only one attack since the first of the year, and that was when her mother-in-law came to visit. As soon as the mother-in-law departed, she recovered.

Dr. Philip S. Hench (Rochester, Minnesota): About fourteen papers on this subject have appeared since Dr. Rosenberg and I presented the original paper in 1940. In the discussion, at the time of this presentation, some thought we might be describing atypical rheumatic fever, atypical rheumatoid arthritis, or atypical gout. Others considered it a separate entity. The consensus then was that if the condition was not a clinical entity it might be rheumatic fever. Since then, the tendency of those who believe palindromic rheumatism is not an entity has been toward the idea that it is an atypical form of rheumatoid arthritis. Walter Bauer and his colleagues have presented that idea several times.

Except for Cecil's brief comment on one case, no one who has written on palindromic rheumatism has discussed chrysotherapy. Those of us who first described this condition were struck by the similarity between this and what we thought "allergic arthritis" should be, if there were any such a condition. We first studied that possibility with unconvincing results.

I believe our original work has brought into much clearer focus the clinical variations of rheumatoid arthritis. I am not convinced that palindromic rheumatism is a variant of rheumatoid arthritis. For one thing, I have not seen rheumatoid arthritis affect finger pads, as may occur in palindromic rheumatism. Up to the time of our report there were no reports of the presence of "purulent" or "semi-purulent" synovial fluid or acute polymorphonuclear reactions in the synovial tissues in rheumatoid arthritis. But this is what we saw in a few of our marked cases of palindromic rheumatism.

In my opinion and by my criteria, many of the cases of so-called palindromic rheumatism reported since our series were not cases of palindromic rheumatism but were cases of "episodic rheumatoid arthritis" which I believe can be differentiated from palindromic rheumatism by the criteria which I recently outlined. By my criteria palindromic rheumatism is still rare. I certainly am delighted to know that gold is apparently effective. We are doing exactly what we have to do, namely, studying the condition further.

Dr. Currier McEwen (New York): I am not sure that palindromic rheumatism is the same thing as rheumatoid arthritis. Even if it is, it is so distinct in the way it behaves that it would still be a service to have it described. I would urge caution in assuming that because this disease now appears to respond to chrysotherapy, that means it is rheumatoid arthritis. We need to know a lot more about rheumatoid arthritis and about the action of gold before any such conclusion would be warranted. Pleuropneumonia arthritis of mice responds very strikingly to gold therapy, yet present evidence does not point to this disease being the same as rheumatoid arthritis.

Dr. Edward W. Boland (closing): Although the results from gold therapy were striking in each of our three cases, the number of cases reported is too small to warrant sweeping conclusions. Further, the remissions obtained were not absolute in any case, although a marked reduction in the frequency and severity of attacks resulted. During the periods of quiescence or relative quiescence, maintenance doses of gold were continued. Whether the attacks will recur with their former frequency and severity when treatment is discontinued entirely cannot be answered.

Whether this form of acute recurring arthritis is a separate clinical entity or an atypical form of rheumatoid arthritis cannot be settled at this time. For several reasons we lean toward the idea that it is an atypical form of rheumatoid arthritis. However, the favourable results from chrysotherapy could be interpreted as meaning that another form of arthritis may respond to gold. In addition to rheumatoid arthritis, pleuropneumonia-like arthritis of mice and some cases of psoriatic arthritis are known to be benefited by chrysotherapy.

Regardless of whether this form of "hit-and-miss" arthritis is a separate entity or not, we must not lose sight of the fact that it was first described by Hench and

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1 J. Amer. med. Ass., 1940, 115, 2207.
Mobilization of the Stiff Elbow in Chronic Arthritis

J. G. Kuhns

Boston

The elbow joint is involved in about 35 per cent. of patients suffering from rheumatoid arthritis. Stiffness commonly follows deformity in flexion and pronation. Limitation of motion usually results from four causes: (1) contracture of the articular capsule and flexor muscles; (2) fibrous or bony ankylosis of the joint; (3) excessive thickening of the synovial membrane about the olecranon; (4) loose bodies in the joint. (Methods of prevention, correction, and after-care were then described.)

Discussion

Dr. J. Albert Key (St. Louis, Mo.): Has Dr. Kuhns had any experience with arthroplasty of the elbow while the disease is still active?

I doubt very seriously if Dr. Kuhns's contention is true that weight-bearing is the cause of destruction of the elbow. When you have disease of the lower extremities, you often have it in the upper, and I think the destruction is due to the disease and not to the fact that the patient uses his hands when he gets out of a chair.

I am not sure that complete denervation of the joint is a good thing in rheumatoid arthritis.

Dr. Duncan Graham (Toronto, Canada): For economic reasons we denervated one elbow joint in a steel riveter. He was relatively free from pain for about six months, after which all his symptoms returned. The denervation was done through three incisions.

Dr. J. G. Kuhns (closing): I have not done any denervations at the elbow joint.

I can cite cases for and against weight-bearing on the elbow joints. Benekoff shows fairly conclusively that with greater thickening in the cartilage it not only withstands longer use but it has a certain elastic function as well. But whatever we did in Still's disease was of little value. Most of them went on to severe damage, and many to ankylosis.

All our cases were of rheumatoid arthritis.

I found no serious limitation of motion or stiffening in any patient with osteo-arthritis. Some of the patients showed secondary spur formation, but they were all cases of active rheumatoid arthritis.

We have been afraid to do operation in the active cases. We have been pushed into operation on a few hips and a few knees, and we have always been sorry. Either the joint itself has not done well, or there was an exacerbation of the arthritis.

Endocrine Factors in Nucleoprotein Metabolism and in Gout

W. Q. Wolfson, R. Levine, H. S. Gutterman, H. D. Hunt, C. Cohn, and E. F. Rosenberg

Chicago

In six patients with gout the 17-ketosteroid excretion averaged less than half the minimum normal values. Possible causes are a disturbance in the metabolism of 17-ketosteroids or a "chronic alarm reaction" in which a low 17-ketosteroid output is accompanied by a high output of 11-oxysteroids. The latter was indirectly studied by (1) urate excretion relative to urea excretion, (2) the frequency and magnitude of creatinuria, (3) serum protein partition, (4) serum cholesterol, (5) serum electrolyte patterns, (6) renal functions, (7) hematological findings, (8) associated diseases and physical findings. Data available at present do not permit a definitive statement as to the presence or absence of increased 11-oxysteroid in gout.

Discussion

Dr. Theodore B. Bayles (Boston): From the evidence in this paper one can conclude that, despite demonstrated change in 17-ketosteroids, the 11-oxysteroids are apparently unchanged in gout. This is an extremely interesting finding.

The Genetics of Gout and Hyperuricaemia

C. J. Smyth, C. W. Cotterman, and R. H. Freyberg

Eloise, Michigan

Hyperuricaemia without arthritis is a common finding among relatives of gouty patients. Eighty-seven relatives belonging to 19 gouty male patients were studied. Uric acid determinations were made on serum by the indirect Folin method. Results show that hyperuricaemia in relatives of gouty patients is apparently due to a single autosomal dominant gene, but only a portion of the heterozygotes for this factor develop gouty arthritis. Sex and age are significant factors affecting the level of serum urate. The data are consistent with the view that gout may develop in a heterozygous individual of either sex who possesses an elevated blood urate level for sufficient time, this being much less probable in a heterozygous female owing to a lower normal value in women and to a smaller average effect of the abnormal gene in this sex.

Discussion

Dr. W. Q. Wolfson (Chicago): Our data confirm those of Dr. Smyth. The difference between normal
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males and females in our series is about 15 per cent.; between unaffected males and females relatively the same amount; between affected males and females relatively the same amount. The average urate levels are lower in female patients with gout than in males with gout. As Dr. Smyth pointed out, there must be two factors involved which are responsible for the increased incidence of gout in males; one factor is a hereditary one for hyperuricaemia, the other one regulates the difference between males and females.

Dr. Robert M. Stecher (Cleveland): Dr. Solomon and I, in collaboration with a geneticist, Dr. Hersh, have made a study of genetics of hyperuricaemia based on forty families. Our observations and conclusions closely approximated those of Dr. Smyth and his collaborators.

We also found a difference in the serum uric acid levels between men and women. We arbitrarily accepted 6-5 mg. per 100 c.cm. as the upper limit of normal. A statistical analysis of nearly 1,000 determinations proved 6-5 mg. to be the upper limit of normal for men and 6-0 mg. for women. Changing the upper level of normal for women in this way did not affect the status of any woman in the series from being considered normal as to hyperuricaemia.

Dr. C. J. Smyth (closing): We made no effort to study the incidence of diabetes in this group of patients. We have had an opportunity to review the paper of Drs. Stecher, Hersh, and Solomon. In spite of the fact that the geneticists who assisted us used entirely different mathematical methods from those used by Dr. Stecher’s group, the results are strikingly similar.

I think it perhaps is too early to decide what the exact difference is between the serum urate levels in males and in females.

With respect to Dr. Wolfson’s data, I think it is particularly significant, because young men apparently do not manifest hyperuricaemia, even though they belong to gouty families, until they reach the age of puberty, and now comes data which indicates that there is some definite endocrine change.

Dr. Stecher’s data, although he did not refer to it, indicates that in women at the menopause there seems to be an upswing in the level of hyperuricaemia. I think it is probably important to find out how old women are before they begin to develop hyperuricaemia. I have seen no data on that point.

These explanations which we have presented do not, of course, exclude the existence of other factors which may be important in the production of gouty symptoms and which are wholly unrelated to changes in the serum urate concentration of the blood.

Psoriatic Arthritis

William H. Kammerer and Russell L. Cecil

New York

Between 1935 and 1948 a total of 930 patients with rheumatoid arthritis have been studied in private practice. Of this number fifty-three patients also had psoriasis, an incidence of 5·7 per cent. Data as to age, sex, duration of psoriasis and arthritis, severity of the two conditions, and laboratory findings were analysed. The relationship of the two diseases was examined as regards time of onset and exacerbations. Particular attention was devoted to those cases demonstrating arthritis of the terminal interphalangeal joints with psoriasis of the nails and nail beds. Forty of the fifty-three patients were treated with gold salts. The results of treatment were compared with the results of chrysotheraphy in cases of rheumatoid arthritis without psoriasis.

Discussion

Dr. Russell L. Cecil (New York): After watching these patients for a good many years, I have come to believe there is an aetiological relationship between psoriasis and rheumatoid arthritis when they occur together. It is not unusual to see skin rashes of various kinds in rheumatism and arthritis. Furthermore, the histopathology of the two conditions is not dissimilar. I see no point in dividing these patients with psoriatic arthritis into different aetiologic groups. Psoriatic arthritis should be looked upon as one more clinical variant of rheumatoid arthritis.

Dr. Philip S. Hench (Rochester, Minnesota): Dr. Kammerer has used the terms “arthropathy” and “arthritus” rather interchangeably, as, of course, all of us sometimes do. In studying cases of chronic arthritis with psoriasis, I believe that we would do well to consider the possibility, if not the probability, that psoriatic arthritis is a different condition from psoriatic arthropathy, or as I prefer to call it, from “psoriatic osteoarthropathy”.

During the last fifteen or twenty years Dr. Slocumb and I have collected about 300 or more cases of what we, by our criteria, are willing to call “psoriatic arthritis”. In about 8 per cent. of these cases a lesion which we believe is a distinctive one, and which represents an osteoarthropathy, not simply “arthritis”, has been demonstrated radiologically in addition to the arthritis. Our idea that psoriatic osteoarthropathy may be distinct from psoriatic arthritis appears to be supported by the outstanding case which Bauer and others reported in 1941. I have practically never seen such pathologic or radiographic changes in any variety of rheumatoid arthritis.

Dr. Kammerer, in what percentage of cases of psoriatic arthritis did you see an “osteo-arthropathic lesion”?

I note that Dr. Cecil has not found any difference between the histopathology of the articular lesions of psoriatic arthritis (not psoriatic osteoarthropathy) and that of rheumatoid arthritis. We have gained a different impression from the few articular biopsies we have made. In a few cases of acute psoriatic arthritis we have noted a pathologic lesion unlike that seen in ordinary rheumatoid arthritis or in subacute rheumatoid arthritis. In a few cases of acute psoriatic arthritis we have noted an acute polymorphonuclear and somewhat haemorrhagic reaction.

Let us all be more diligent in our attempts to develop the clinical entity of psoriatic arthritis and to differentiate
it from chronic arthritis (usually rheumatoid) with coincidental psoriasis. We have gone about as far as we can with studies of the clinical manifestations; henceforth we should perform a biopsy on more articular specimens.

Dr. Kammerer, in what percentage of your cases did you perform biopsy, and on what are you and Dr. Cecil basing your conclusion that the articular pathalogy of psoriatic arthritis is the same as that of rheumatoid arthritis?

Dr. Howard C. Coggeshall (Dallas, Texas): Most of these cases that have been reported, psoriasis with rheumatoid arthritis, have come from northern cities. I think there is a definite geographical difference in the percentage, because the association of psoriasis and rheumatoid arthritis is infrequent in the south. None of the 2,000 cases of rheumatoid arthritis that I have seen during the last few years have had psoriasis. It would be interesting if we had further data with reference to the geographic distribution. It seems to me there are two types of psoriatic arthritis: first, the rare condition described by Hench, and second, the common type of psoriasis associated with typical rheumatoid arthritis.

Dr. William H. Kammerer (closing): Our choice of terms was dictated by the attempt to avoid repetition as we consider the terms "psoriatic arthritis" and "psoriatic arthropathy" to be synonymous.

I know of only two cases we have seen exhibiting changes which were identical with those on the radiograph I presented. We have several biopsies of skin sections from the dermatological department. We have no biopsies of terminal phalangeal joints. We relied on Dr. Bauer's monograph for that.

It is admitted that psoriasis does not occur in southern climates as frequently as in northern, nor in negroes as frequently as in whites. The significance of this is unknown. Dermatologists point out that neurodermatitis is much more frequent in patients from northern climates than in those from the south, and say that sunlight benefits neurodermatitis.

The psoriatic nail change occurs rather frequently, without arthritic involvement of the terminal phalangeal joints. There were thirty-six patients who had psoriasis of the nails; of these twenty-five had arthritis of the terminal phalangeal joint. Thus eleven had psoriasis of the nails without having arthritis of the terminal phalangeal joints.

Clinical Study of Visceral Lesions and Endocrine Disturbances in Eight Cases with Diffuse Scleroderma

Javier Robles Gil

Mexico City

Eight cases with diffuse scleroderma were studied, including the gastro-intestinal tract and the cardiovascular system. All the cases had arthritis or arthralgia. The adrenals were studied in six and found to be insufficient as determined by a low 17-ketosteroid, low blood protein, cholesterol, and glucose, high potassium, a flat glucose tolerance test, and low Kepler test. Good therapeutic results were obtained by huge doses of vitamin D.

Juvenile Rheumatoid Arthritis

L. Maxwell Lockie and Bernard M. Norcross

Buffalo

Clinical findings of twenty-eight cases are discussed as to aetologic factors, the course, duration, severity of the disease process, and the differential diagnosis. The treatment included general care, proper use of orthopaedic appliances, controlled use of physical therapy, radiotherapy, transfusions, removal of foci of infection, and gold. The interference of skeletal growth and development was found in four cases. The pessimistic concept firmly held in the past needs revision, for the results showed 12 complete recovery (no residual), 6 minimal joint residual, 3 moderate joint residual, 2 severe joint residual, 2 deaths, and 3 still active cases.

Discussion

Dr. Nathan R. Abrams (Cincinnati): Although some of these cases appear inactive, the arthritis is dormant in a number of them. Two cases of former juvenile rheumatoid arthritis were stirred up considerably by pregnancy after several years of inactivity.

Dr. Charles L. Steinberg (Rochester, N.Y.): Did Dr. Norcross do any streptolysin titres on these patients?

Recently we have found titres of over 600 units in several cases of juvenile rheumatoid arthritis. We have had the same experience as Dr. Norcross in having difficulty in differentiating juvenile rheumatoid arthritis from rheumatic fever. Many of these children develop loud systolic murmurs, and on occasion we even stretch our ears to believe we are hearing a presystolic murmur and rumble.

Dr. Hugo A. Freund (Detroit): Without having a description of the individual cases that Dr. Norcross presented, I would wonder if the paper, "Arthritis in Childhood," might not really be divided into those classes of cases which seem to simulate Felty's syndrome, those cases which are of mono-articular origin and may have started with infection or be the residual of rheumatic fever, and the true rheumatoid arthritis that begins in childhood and progresses into adult life. To my mind those cases that improve are usually cases that have had an initial mono-articular arthritis or in which several joints later become involved.

My own experience with a number of cases of so-called Still's diseases, or the true juvenile form of rheumatoid arthritis, is that they are progressive, become chronic, and continue through life. I have never seen one get well. The usual course is downward, with tremendous deformity, secondary invasions of the heart and various other tissues of the body, and ultimate death.

Dr. Bernard M. Norcross (closing): As far as we know, no cases of amyloidosis occurred in this group.
The two fatal cases showed no evidence of amyloidosis at autopsy.

Differentiation of this disease from rheumatic fever is difficult. Four patients were observed for six months to as long as five and a half years before we were certain of the diagnosis. All four patients presented transient, migratory joint complaints, cardiac involvement and fever. There was some response to salicylates, and four different cardiologists made the diagnosis of rheumatic fever at some time during this observation period. However, as time elapsed the cardiac findings disappeared. There were no longer any murmurs or abnormalities on the electrocardiograph. The joint changes became definite. These children lost weight and developed lymphadenopathy, splenomegaly, and the other signs that help us to arrive at the diagnosis.

Some of these children were in bed up to eight months, others for only a month or six weeks. Treatment was continued until the disease became inactive.

No rheumatic nodules were seen in this group. The type of arthritis present at autopsy was similar to rheumatoid arthritis in the adult.

We did not determine the antistreptolysin titres in our patients. We did determine the antifibrinolysin titre and the figures did not seem significant. Coss and Boots reported that the average figure for antistreptolysin titres in their group was significantly higher than the figure accepted as normal.

We are in favour of discarding the term “Still’s disease” and substituting instead the term “juvenile rheumatoid arthritis”. We feel that some of them begin as a monarticular process but later develop the typical joint manifestations of rheumatoid arthritis.

Surgical Reconstruction of Arthritic Feet

J. ALBERT KEY
St. Louis, Mo.

Many severe chronic arthritides have deformity of the feet, especially the forefeet, so that the wearing of shoes is painful and activity is restricted. Multiple minor operative procedures may be performed, including correction of bunions, hallux valgus, and hammer-toes, resection of metatarsal heads, removal of exostoses, shortening or partial amputation of toes, and excision of large bursae. Both feet may be operated upon simultaneously, and radical reconstruction of the forefoot may be done at a single sitting. The results are unusually gratifying.

Discussion

DR. WALTER BAUER (Boston): The orthopaedic surgeon, after careful evaluation of a badly crippled arthritic foot, can combine a number of surgical procedures of the type Dr. Key described and thereby render a service to these patients.

DR. J. F. HAMILTON (Memphis, Tennessee): If the patient is happy over the operation, I think it can be considered successful in most cases. Partial phalangeotomy, in properly selected cases, will give you happy patients.

DR. J. ALBERT KEY (closing): One of the most grateful patients I had of this type was a man 75 years old. Now he is quite a dude, walks all over the place, with a red bow tie.

I have found that in most arthritic patients, the circulation of the feet is all right. I have not seen rheumatoid arthritis combined with the diseases of the blood vessels of the foot.

Plantar neurectomies I have not performed except for Morton’s toe. I took out a plantar nerve once for a woman with a painful foot, and I think she has more pain than she did before I operated on her.

Cellular Aggregates in Skeletal Muscle of Patients with Rheumatic Diseases other than Rheumatoid Arthritis

JOSEPH J. BUNIM, LEON SOKOLOFF, SIGMUND L. WILENS, and CURRIER MCEWEN
New York

Muscle biopsies were done on more than twenty-five patients with typical rheumatoid arthritis. Cellular nodules said to be characteristic of this disease were found in a large majority of cases.

To determine the specificity of this lesion biopsies were also done on patients with rheumatic fever, inactive rheumatic heart disease, Still’s disease, ankylosing spondylitis, nodular fibrositis, gout, osteo-arthritis, gonococcal arthritis, tuberculous arthritis, Pott’s disease, Boeck’s sarcoïd, lupus erythematosus, and dermatomyositis. Nodules of lymphocytes and mononuclear cells were found in the skeletal muscle tissue in many diseases of the control group. The histologic appearance and anatomic location of these were strikingly similar to, and in some cases indistinguishable from, those seen in rheumatoid arthritis.

Discussion

DR. G. A. BENNETT (Chicago): We have also observed lesions such as were described here, in conjunction with a good many conditions that were not rheumatoid arthritis and not associated with rheumatic fever. Although our observations are limited, it is my impression that they lend support to what has been said.

The subcutaneous nodule represents the most highly distinctive pathological change of any seen in rheumatoid arthritis. The small collections of lymphoid cells and other inflammatory cells [as illustrated on the screen] seem to be far less specific. Were these lesions near the affected hip joint, and was Dr. Bunim able to detect any other inflammatory disease in that patient? As far as I know, these lesions have no consistent relationship to the pathology of degenerative joint disease.

DR. HUGO A. FREUND (Detroit): For a long time many
clinicians felt that rheumatoid arthritis was a systemic disease. The paresthesias, the interosseous atrophy, the hyperpyrexia, and the numerous peripheral changes of rheumatoid arthritis, were not explained alone by the joint pathology. Personally I believed that perhaps we would find something in the central nervous system. So we decided to do complete autopsies in a number of cases of rheumatoid arthritis. In the examination of the brain and the spinal cord, nothing was found. I thought we had not gone far enough and decided to look at the peripheral nerves. It was in the peripheral nerves that the first changes were found, namely, a perineuritic nodule composed of three zones, an outer (looser), a middle (more compact), and sometimes a central necrotic zone. These were perineural or epineural nodules, so different from anything that had been previously described that we thought they must have a definite role in producing symptoms and being an anatomical-pathologic connexion between the symptoms and signs of the disease.

It was just a few years later, in the course of trying to find whether some of the smaller nerve fibres also contained similar nodules, that we were able, in an amputated leg of rheumatoid arthritis, to demonstrate muscle nodules of similar type.

I think all pathologists who have examined the muscles in rheumatoid arthritis, from biopsies and from post-mortem muscle tissue, have sometimes found these nodules. They have appeared in 98 per cent. of our biopsies. The work has been repeated in the U.S.A. and in England and the findings confirmed.

It has been my observation that more stress has been placed on the importance of these muscular nodules than on the perineuritic nodules. Not enough autopsies have been reported. I believe that the disease is a combination of all the pathological changes described by Dr. Bennett a number of years ago, plus these perineuritic and muscular nodules. The English group have come out rather flat-footedly in their statement that they have not found these specific nodules in some of the conditions that have been described here by Dr. Bunim. Whether these nodules actually will be found when a larger series of cases have been gone through remains to be seen. Our controls have been rigid.

At the meeting of the American Association of Pathologists in Chicago Dr. Clawson of Minneapolis presented a large number of cases in which he, too, believed that these muscular nodules (not the perineuritic nodules—they were not discussed) were found in other conditions. He did not describe his cases as clearly as Dr. Bunim has today; yet he, too, made the statement that lymphocytic aggregations are found in a number of biopsied muscles of other conditions. This point needs clarification.

We have found the presence of muscular nodules in cases of disseminated lupus but one must bear in mind that most cases of disseminated lupus begin with some type of rheumatic involvement. We have had the opportunity of examining six cases of disseminated lupus at autopsy in the last three years. We have not found perineuritic nodules, but we did find a muscular nodule similar to rheumatoid nodules but much richer in collagen. The rheumatoid nodule is more compact.

I always believed that the characteristic thing in rheumatic fever was the Aschoff body. The Aschoff body recently has been thoroughly described in the American Journal of Medicine by Dr. von Glahn. It differs in every detail from this so-called rheumatic nodule. In ten cases of true rheumatic fever examined at autopsy by Dr. Zueler at the Children's Hospital in Detroit, none showed any nodules of the lymphocytic type, but they did show Aschoff bodies. So far as Still's disease is concerned, we have found them definitely in two cases. Byankylosing spondylitis, I suppose Dr. Bunim means Marie-Strümpell disease. We have never found nodules in true Marie-Strümpell disease. We have never found them in gout. In fibrositis we have found nodules in a few, and in others not (however the clinical diagnosis was in doubt). In uncomplicated osteo-arthritis we have never found them, nor have we found any in a few cases of gonorrheal arthritis. In tuberculous arthritis we have found lymphocytic accumulations in conditions that have been described as the so-called Poncet type of rheumatism.

A number of years ago a case of diffuse, protracted neuritis came to my attention. I was suspicious that the patient had early rheumatoid arthritis. Biopsies were done in another clinic and the diagnosis was of periarteritis nodosa. I did not see the patient again until a few months ago, when he came under our observation with typical ulnar deviation and contractures of his hand. He presented, as a typical case of rheumatoid arthritis. We again did a biopsy, and found the same muscle and subcutaneous lesions that had been found elsewhere. The case proved to be one of dermatomyositis.

So this type of lesion may occur in other diseases besides rheumatoid arthritis. I believe it does occur in disseminated lupus. We have seen it in dermatomyositis and in the region of trichina cysts. We are inclined to believe it is specific for rheumatoid arthritis, though it may be seen in other conditions. The question arises, why these nodules? What is their source? It may be a slow reaction to a hypersensitivity, an anti-body-antigen reaction which, over a period of time, may produce the picture of periarteritis nodosa, or a lesion like that seen in lupus erythematosus disseminatus. Are they due to a virus? There was a recent article in the Lancet on the possibility of rheumatic fever being due to a virus.

May there be an enzyme; or is a metabolic condition provoking the formation of lymphocytic nodules and accumulations of cells in nerves as well as muscles?

Dr. Joseph J. Bunim (closing): We have not yet seen a case of primary fibrositis, either of the Minnesota or Massachusetts variety.

Very few authors have stated how many serial sections were done in their control material, and I think that may account for many discrepancies. So I would make a plea that all those who plan to do this type of work should state exactly the methods and procedure followed in the control groups as well as in the rheumatoid or experimental group.

I am glad to hear that Dr. Bennett found this nodule in conditions other than rheumatoid arthritis. One of our patients had a monarticular osteo-arthritis secondary to trauma of the right hip. Biopsy was taken of the left calf. This patient was ambulatory. He had no in-
fectious process in the left limb. We had one patient with osteo-arthritis of both hips. No other condition co-existed. He, too, had a positive biopsy. Eight other cases of osteo-arthritis were negative. In this connexion the results of muscle biopsies reported by De Forest and his associates are of interest. They compared seventeen rheumatoid cases with thirty-seven controls, including four patients with osteo-arthritis. In one of these four the biopsy was positive and De Forest went back to the patient and obtained a history in the distant past of fever associated with arthritis lasting several weeks.

In one patient with classical Marie-Strümpell spondyilitis no peripheral joints were involved other than the hips. He had complete ankylosis, with fusion of the sacro-iliac joints and calcification of the lateral ligaments of the spine. The only unusual feature about this man is his age—67.

One patient with muscle nodule had tuberculosis of the knee joint. From the synovial fluid we were able to recover acid-fast bacilli. In reference to Boeck's sarcoïd, our series includes one such patient who showed a muscle nodule, but we did not consider the nodule typical.

It is a question of terms whether we call this muscle nodule specific or not. If a muscle nodule which is histologically indistinguishable from that found in rheumatoid arthritis is also found in a number of unrelated diseases, then we can hardly consider it a specific lesion, though in most cases of rheumatoid arthritis it may be of diagnostic value.

Knee Contractions in Rheumatoid Arthritis

DONALD F. HILL, W. PAUL HOLBROOK, C. S. STEPHENS, L. J. KENT, AND EDNA MCCARTHY

Tucson, Arizona

The most disabling deformity, and a very common one, in rheumatoid arthritis is flexion contraction of the knee. With rare exception, this can be corrected easily in the early stages and movement of the joint can be maintained. Methods include rest, exercises, and casts. In more severe and prolonged cases additional steps must be taken, including manipulation and after-care up to walking. Sixty-five cases are presented with data on age, sex, and duration of arthritis, and of contraction. Good to excellent results have been obtained in over 90 per cent. of cases.

Discussion

DR. JOHN G. KUHNS (Boston): We commonly manipulate rather slowly and in several stages because we have had a number of subluxations of the tibia on the femur. I wonder if Dr. Hill has had any such experience. In about a fourth of the patients we manipulate, we are unable to get any further extension of the knee. I would like, also, to ask him how many failures he has had in his group.

DR. DAVID H. KLING (Los Angeles): There are fulminating types of rheumatoid arthritis where contraction and ankylosis occur very rapidly under the best management. This is the dry form of rheumatoid arthritis which was excellently presented in 1890 by Archibald E. Garrod in his book, "A Treatise on Rheumatism and Rheumatoid Arthritis".

I would not condemn all braces in favour of crutches. Patients who have arthritis of the upper extremity handle crutches with difficulty.

DR. J. ALBERT KEY (St. Louis, Mo.): I do not think you should be too free in condemning the doctors because patients develop contractures. Most of us treat our patients at home, and most of us treat poor people. They could not stay in an institution month after month and year after year and exercise their legs. They have to get out and make a living.

It is easy to correct deformities over a period of a few weeks in patients who are not having much pain. But take nervous individuals who are having a lot of pain and who are at home, and whom you see occasionally. If you persist in trying to correct deformities, they get another doctor and sometimes I do not blame them. You have to take these things into consideration when you say deformities in arthritis are preventable. The same thing is true in poliomyelitis. Also there are some deformities that you cannot prevent.

DR. CURRIER MCEWEN (New York): Much can be done to prevent contractures and to correct many of them after they have occurred. But much can be done, too, for many of the patients whose disease has progressed beyond that stage and who are practically helpless through ankyloses in bad positions. We tend to be too pessimistic about these patients too.

The opportunity I have had during the past two years to watch the work of Dr. Howard Rusk and his associates in our Department of Rehabilitation at New York University has given me an entirely new view. I think of a woman who had been bedridden for seven years. Not much could be done for her through orthopaedic correction, but she has become a happier person and a useful citizen, earning her own living, simply by being given a new outlook and by learning how to make the most of what physical capacity she has left. In other words, our job as physicians carries through prevention and treatment and correction of deformities to another neglected field—namely, teaching the patient to get along with what he has left if his disease progresses to a disabling conclusion.

DR. DONALD F. HILL (closing): With lifting the head of the tibia during the time of manipulation, plus rotation, you can often release adhesions that will correct a certain amount or some degree of subluxation.

Sixty-three patients out of sixty-five were improved. Two we considered failures because they ended with straight ankylosed knees and could not walk. Before, they were bedridden; now they are bedridden with straight knees.

Our experience is that a patient can walk more normally with crutches, get up, in and out of a car, sit down at a desk, and carry on much more normal life, if he can bend his knees, than if he is trying to juggle a couple of braces. I do not believe the patients have been handicapped by crutches. We have not seen instances of arthritis made.
worse in the shoulders or upper extremities by the use of crutches. I think that this is because we do not allow the patient to put weight on crutches.

Dr. Key alleged that all our patients are rich. One of them lives in a small house on the desert, that is, about a 12 by 14 ft. wooden frame shack. She was able to finance two weeks in hospital, and we took care of her at home afterwards. Another patient went from the hospital on the fifth day after we took her out of the casts to a tent where she was living, and she was given her physical therapy and after-care in a tent in the desert until she regained normal walking.

Serum Complement in Rheumatic Fever

EDWARD E. FISCHEL and RUTH H. PAULI

Quantitative serial studies were made of total serum complement (C') in normal subjects and in various pathological conditions using a spectrophotometric technique for determination of the 50 per cent. haemolytic unit with optimal amounts of magnesium and calcium according to Heidelberger and others. Thirty-three normal subjects had a total C' of 37±3-9 units per ml.

Thirty-seven cases of acute rheumatic fever were studied serially. In six instances sera were obtained before a recurrent attack. In thirty-three cases the C' was consistently high during activity. Two cases showed curves of low titre gradually becoming normal with subsidence of activity. Isolated determinations on two other patients were also low, and one of the patients died of acute rheumatic fever. Acute infections and rheumatoid arthritis also presented high complement levels. Of known allergic reactions, one case of serum sickness presented typically low C' titres while six cases of drug allergy similar clinically to serum sickness gave levels higher than normal.

The elevated complement levels in rheumatic fever do not support the hypothesis that the disease is an antigen-antibody reaction, but neither do the results negate this hypothesis.

The observation of serum complement, either increased or diminished, is another indication of persistent or subclinical rheumatic activity and may be of help when other findings are normal.

Studies on Intra-articular Temperature

JOSEPH L. HOLLANDER and STEVEN M. HORVATH

From the Arthritis Section and the Department of Physical Medicine, Hospital of the University of Pennsylvania

A comparative study was made of the deep temperatures under the patella and on the surface of the knee joint of normal individuals and patients with various forms of arthritis. Copper constantan thermocouples were threaded through an aspiration needle inserted into the joint space of the knee. The electromotive force developed was measured with a potentiometer. The fluctuations in temperatures of knee joints proper were at variance with that of the overlying skin. Weight-bearing exercise increased joint temperature. In patients with rheumatoid involvement of the knees, the internal joint temperature was higher than normal. If the patients had been at rest for several hours the joint temperatures of those with degenerative changes could not be distinguished from those of normal controls.

Various physical agents were employed to modify the surface and deep temperatures of the joint. Whenever heat was applied externally, the joint temperature dropped several degrees, and conversely when cold was applied externally the temperature inside the joint rose. The effects of diathermy and other deep-heating modalities were studied and showed a significant depth to surface differential.

Discussion

Dr. Charley J. Smyth (Eloise, Michigan): I spent the greater part of a day in Dr. Hollander's laboratory and was impressed with the relative simplicity of this machine. It is compact and can be wheeled to the bedside on a small table. The patients tolerated the procedure well and it was practically painless. It seems to me to offer considerably more than the needle-type thermocouples, which were, in our experience, somewhat inaccurate. I think the use of this instrument offers a new means of obtaining considerable important data regarding joint physiology, about which we have limited information at the present time.

The striking thing in their data is the fact that when you increase joint skin temperature you actually lower the temperature in the interior of the joint. Conversely, if you put cold on the outside of the joint, according to their measurements, you actually increase the interior temperature of the joint; this reverses some of our former thinking in this respect. It offers to those who are trying to evaluate clinical results of therapeutic measures one additional objective measurement of joint change.

Dr. J. Albert Key (St. Louis, Mo.): The older of us remember how Pemberton especially supported the theory that in degenerative arthritis the circulation was reduced. We all know that in proliferative arthritis it is increased. The joint temperature must parallel the circulation, must be varied by the amount of blood going through the joint. It would be interesting to put an arthroscope in the joint and see what capillaries do when hot and cold packs are applied, whether they dilate or contract. It seems incomprehensible to me that the temperature should be above normal in hypertrophic arthritis (or degenerative joint disease, as some now like to call it). This confirms some work of Huggins in which he showed that, as one descends from the trunk down to the toes, the red marrow disappears and becomes white as the temperature is lowered. The present work shows that there is such a
difference between the temperature in the knee joint and
the body temperature.

**Dr. David E. Markson (Chicago):** Artificial fever in
the treatment of rheumatoid arthritis was first introduced
by our group at Northwestern University. We believe
that it has merit in selected cases. Its effect on the peripher
circulation and probably in the joints themselves
has been proved in the first instance and theorized in the
second. Dr. Ivy, working with dogs in studying the bends
at the Bethesda Hospital, has proven conclusively that
man has poor circulation in the joints as compared with
dogs. When he decreased the blood pressure in a dog
to 67 mm. Hg he was able to produce the bends in a
pressure chamber with the same ease that it can be pro-
duced in man and at the same levels.

Drs. Neymann and Osborne were able to show clearly
that, using inductothermy as the agent to raise body
temperature, the normal heat gradients are not disturbed
by this method. That is, the temperature of the brain,
the liver, the abdominal cavity, the muscle tissue, etc., were
maintained at a higher range of temperature, from one
to three degrees, above the skin temperature. The joints,
however, were not studied and I would like to ask Drs.
Hollander and Horvath why the knee joint should not
correspond with our findings in other cavities. The difference
in our findings may possibly be explained on the
difference in the reactions of local heat and that of
the reaction of general fever. I would like to con-
gratulate the authors on their excellent work.

**Dr. Joseph L. Hollander (closing):** The normal joint
returns to basal temperature within fifteen to twenty
minutes after treatment. In rheumatoid arthritis, it may
take over an hour. In degenerative joint disease it may take
several hours.

In degenerative joint disease the rate of cooling is
greatly slowed. While we have not measured accurate
friction effect upon these joints in detail, the slowed rate
of cooling (as shown by the rate of cooling after dia-
thermy) may be why our half-hour basal temperatures
were elevated. The patients with osteo-arthritis were all
ambulatory, and we had only kept them at rest for half an
hour. We kept one such patient quiet for two hours,
and the temperature was still steadily dropping toward a
normal value, or what we call normal. We feel that in
a longer time the temperature would go down to normal.
In other words, these joints probably do heat up more
than normal and cool more slowly, indicating a lowered
circulation.

We are planning plethysmographic measurements of
the joints to determine actual blood flow. These tem-
perature measurements indicate blood flow changes, but
we want to check with plethysmographic studies what the
blood flow actually may be.

**Relief of Pain in Osteo-arthritis of the Hip by
Partial Denervation of the Hip Joint**

**B. E. Obletz**

**Buffalo, N.Y.**

Conservative treatment of patients with osteo-
arthritis of the hip often fails to relieve pain. Many
people can be given satisfactory relief of pain by
means of partial denervation of the hip joint which
consists of neuroectomy of the obturator nerve and
neurectomy of the nerve to the quadratus femoris
muscle. While complete relief of pain may not be
achieved, gratifying relief is obtained in two-thirds
of a small group of patients. The operation is
applicable to patients of any age and general con-
dition, and the patient may be out of bed on the day
following surgery.

**Discussion**

**Dr. Edwin W. Ryerson (Chicago):** These obturator
neurectomies have been done for a good many years
in cases of spastic paralysis, and spastic paraplegia; as
far as I know, no joint trouble has resulted. But is it
not possible that following such operations something
may happen, such as happens in tabes dorsalis, the pro-
duction of a Charcot joint?

**Dr. J. Albert Key (St. Louis, Mo.):** I do not think
that we are going to get any neurotrophic joints because
we do not take all the nerve supply but, as you say, we
might. I have not seen any neurotrophic joints yet but
patients do get weakness, especially after the intrapelvic
neurectomy. They cannot cross their legs. They cannot
walk as far. When they do not get relief of pain, then
they are not very happy. I still do the operation oc-
casionally. However, I am doing more extrapelvic than
intrapelvic now, because there you can be more selective
and still leave some adductor power.

**Dr. B. E. Obletz (closing):** Dr. Key was kind enough
to answer Dr. Ryerson. We have not had any experience
with the Charcot hip or anything like that, because we
do not do a complete denervation. There are always
sensory fibres present. We have not had serious weak-
ness in the hip joints after the procedure, even though we
have used the intrapelvic route for most of the cases.

Some of the arthroplasties done in suitable patients
show good motion following the procedure but there is
some pain. Dr. Kuhns informed me that he has done
the obturator neuroectomy for the relief of pain following
successful arthroplasties. Most of our patients were in
the age group and in the condition in which we would
not consider an arthroplasty. We are only satisfied to
see if we can get some measure of relief from pain.

**The Diagnosis of Gonococcal Arthritis**

**Max Michael, Jr.**

**Chamblee, Georgia**

The test employs a soluble antigen prepared from
a single strain of organisms. Multiple tests were
made with various types of arthritis over periods of
two to twenty-four months. The test is specific for
gonococcal infections: false positives were not
obtained. Sixteen patients with culturally proven
gonococcal arthritis and 55 patients in whom clinical
features were compatible with the diagnosis had
antibody titres which were positive. The antibody titres may be delayed for two months and may persist for a year. The quantitative gonococcal complement fixation test is a valuable diagnostic aid.

Discussion

DR. PHILIP S. HENCH (Rochester, Minnesota): We need badly some laboratory method to help us differentiate gonorrheal arthritis from "postgonorrheal rheumatoid arthritis". Dr. Michael has not told us in how many of his cases cultures of synovial fluid were positive for gonococci. Therefore I do not know how many of his cases were cases of proved gonorrheal arthritis. I suspect that many of them were not, and I think some of them were cases of "post-gonorrheal rheumatoid arthritis".

DR. JOSEPH J. BUNIM (New York): This test gains in importance now that so many of the patients arrive at the hospital with a history of treated gonococcal urethritis followed by arthritis. The urethritis had already been treated by this physician or the Board of Health before the patient came to the ward, so that there is no urethral smear to study and the patient has polyarthritis. The bacteriologic examination of the synovial fluid so often is negative, and many times fluid is unobtainable. Therefore diagnostic proof must depend either on biopsy of the synovial membrane, which is very difficult to obtain, or else upon a gonococcal complement fixation test. Thus, because of the advent of chemotherapy and the use of penicillin in particular, this test gains in diagnostic importance.

We are very much interested in this group of patients with a history of gonococcal urethritis followed by arthritis, where the synovial fluid is sterile. We wondered whether the pathogenesis here may not be different from the pathogenesis in those with demonstrable gonococci in the synovial fluid.

We have also observed a difference in response to therapy. Those patients with positive synovial fluid respond, as a rule, better to penicillin than those with a negative synovial fluid. I wondered if that was his experience as well.

What is the longest period of observation of the patients in his series who had sterile synovial fluid, and did they develop anything like rheumatoid arthritis?

DR. EDWARD W. BOLAND (Los Angeles): In our experience during the war the majority of soldiers who developed arthritis following gonorrhea did not have true gonorrheal arthritis but had chronic rheumatoid arthritis which was either precipitated or aggravated by a genital gonorrhea. The differentiation between gonorrheal arthritis and postgonorrheal rheumatoid arthritis is not always easy but is of extreme importance because the treatment and prognosis of the two conditions are quite different.

We learned to look upon gonorrheal arthritis as a self-limiting disease which usually involved a few joints (often the larger ones) and which did not tend toward progressive involvement of more and more new joints. Usually gonorrheal arthritis runs its active course within six months in untreated cases and does not go on for years with progressive crippling of more and more new joints. Further, gonorrheal arthritis should respond to adequate treatment with penicillin, sulphonamides, and/or prolonged artificial hyperpyrexia. Actually, true or typical gonorrheal arthritis was uncommon, and synovial fluid cultures for the gonococcus were rarely positive. The complement fixation test was not considered by us as giving reliable evidence for or against the diagnosis of gonorrheal arthritis.

An acute genital gonorrhea may precipitate the onset of rheumatoid arthritis, may reactivate a quiet rheumatoid arthritis, or may aggravate an already present mild rheumatoid arthritis. Thus, an acute gonorrhea may act as a "trigger", to set off or to aggravate the disease, just as many other types of infections may. Among soldiers the most common articular pattern associated with genital gonorrhea was that of a chronic persistent arthritis with negative joint cultures, with progressive involvement of new joints, and with failure to respond to penicillin, sulphonamides, and, or artificial hyperpyrexia. I wonder if some of Dr. Michael's cases with negative joint cultures might not have been cases of postgonorrheal rheumatoid arthritis rather than true gonorrheal arthritis.

DR. MAX MICHAEL, Jr. (closing): We look on gonococcal infections as being somewhat analogous to β-haemolytic streptococcal infection. If we knew why in a group of individuals who contract β-haemolytic streptococcal sore throat, one individual just has a sore throat, one develops a supplicative mastoiditis, and another develops rheumatic fever, then perhaps we could know why when three individuals contract gonorrhea, one has only urethritis, one has infected joints, and one has this syndrome with non-infected fluids.

One other item we must keep in mind is that the test may be positive as a result of gonorrhea although perhaps rheumatoid is the disease for which the patient is seen. Such a positive test would be a false positive as far as the arthritis was concerned.

The response to chemotherapy was definitely slower in the group with non-infected fluids. Some of these patients have been followed now as long as two and a half years. Once the joint troubles have subsided, which sometimes may take as long as six months to a year, we have seen no recurrences unless the patients develop gonorrhea again. This seems to suggest that the organism perhaps never gets into the joint but that the joint is sensitized to antigenic fractions of the gonococcus.

We have done penicillin sensitivities on occasional cultures from the urethra and joints, and they were all sensitive organisms responding to the range of 0-02 units per ml.

Gold Toxicology in Rheumatoid Arthritis with Particular Emphasis on Bone-Marrow Study

CHAS L. STEINBERG
Rochester, N.Y.

Forty cases of rheumatoid arthritis were studied. The bone marrow was aspirated before treatment
with gold and after each 1,000 mg. was administered. The bone-marrow changes were correlated with depression of the peripheral blood, exfoliative dermatitis, kidney toxicity, and the effect of BAL.

Discussion

DR. OTTO STEINBROCKER (New York): Did the peripheral blood show an eosinophilia commensurate with the findings in the bone marrow? We had occasion to do some studies with massive doses of gold therapy. An outstanding feature of our observations was the high eosinophilia produced in many of these patients. It was as high as 30 or 40 per cent. without any toxic manifestations. When the eosinophilia went beyond 40 per cent. in one case, we did get a toxic reaction. One out of eight patients who had as much as 10 g. of gold within six to eight weeks, developed the highest eosinophilia and exfoliative dermatitis.

DR. MAX MICHAEL, JR. (Chamblee, Georgia): True bone-marrow studies should be done with a button, and histologic sections. The first two or three drops obtained as the needle goes into the sternum is true marrow, but from there on we are withdrawing sinusoidal blood.

DR. GORDON S. BUTTORFF (Louisville, Kentucky): Did the white blood count in these cases show any leucopenia?

We have not seen any eosinophilia like that mentioned by Dr. Steinbrocker, but we have not used any doses comparable to those he mentioned.

With our patients we try not to get toxic reactions, but occasionally we get some pruritus and sometimes a little dermatitis. When we have given BAL the patients have complained of the local reaction. I wondered what amount of ephedrine Dr. Steinberg gave and if it prevented this.

DR. CHARLES W. WAINWRIGHT (Baltimore): Our doses of gold have not been comparable to Dr. Steinberg's but have never exceeded a total of 750 or 1,000 mg. Eosinophilia has been a very constant occurrence. It has reached 25 or 30 per cent. without any toxic response. Our hope that it would serve as an indicator or precursor of toxic reactions, at least in the skin, was unrealized.

DR. DAVID H. KLING (Los Angeles): The danger of thrombocytopenia is serious. Eosinophilia, on the other hand, is not of great clinical importance; it does not necessarily indicate an impending reaction. The absorption of gold preparations in suspension is very irregular. Heavy gold shadows can be seen in radiographs years after the administration of these preparations has been discontinued. In experimental animals, histological studies have shown encapsulated gold deposits at the site of injection. The blood values and excretion of gold in the urine with these preparations are very low, but extended for long periods. It is therefore not surprising that reactions may occur at any time and even after long intervals.

DR. CHARLES L. STEINBERG (closing): We know from studies that have already been published that 28 per cent. of people with exfoliative dermatitis show peripheral eosinophilia. We have some patients which are included in this study and probably will be published later in which the peripheral blood showed no eosinophilia, and yet an eosinophilia was present in the bone marrow. There were 3 to 5 eosinophils per high-powered field. Many of these were young cells, and therefore would not have been picked up by study of the peripheral blood.

The patients who developed exfoliative dermatitis did not develop depression of the other elements of the bone marrow.

It is true that bone-marrow aspiration of this type is diluted with sinusoidal blood. On the other hand a study of these concentrated erythromyeloid layers will show many young cells. This is the important point. The fact that one patient permitted us to repeat bone-marrow aspiration seven times means that this method is more simple than doing a biopsy, though the biopsy is perhaps a much more scientific study.

White blood counts were done weekly on patients with exfoliative dermatitis and those showing changes in the myelocytic series, and in no instance did we find a significant drop in the white blood cells.

I agree with Dr. Kling, who stressed the importance of the peripheral platelet blood count and suggested that this, perhaps, was the most important indication for bone-marrow study. We have series of slides showing that although the peripheral platelet count may drop, the bone-marrow studies indicate no apparent damage.

Electrophoretic Fractionation of the Agglutinin for Group A Haemolytic Streptococcus in Serum

JAMES A. C OSS, JR., AND M. O. LIPMAN
New York

The agglutinating property of serum in combination with various strains of group A haemolytic streptococci were studied in patients with rheumatoid arthritis, miscellaneous diseases, and normal controls. The serum was separated into fractions by electrophoresis.

The serum fraction responsible for the agglutination phenomenon was found to be $\gamma$ globulin and possibly the $\gamma$ plus $\beta$ globulin. Attempts to block the agglutinating power of $\gamma$ globulin by combining it with normal albumin were unsuccessful. Non-agglutinating $\gamma$ globulins could not be made to cause agglutination when combined with albumin fractions from agglutinating sera.

Discussion

DR. RUSSELL L. CECIL (New York): This study of Dr. Coss gives us information as to the character of this reaction chemically but still fails to tell us what we want to know, namely, whether a positive agglutination reaction means a specific antigen-antibody reaction with the haemolytic streptococcus or whether it is non-specific.

It is important to remember that patients do not as a rule develop a positive agglutination reaction during the first months of the disease, the time when we need the test most for differential diagnosis.
Dr. W. D. Robinson (Ann Arbor): In the process of a re-evaluation of some of these immunological reactions we have had difficulty with non-specific reactions in patients with other diseases, and with normal individuals, quite comparable to those obtained in arthritis.

Have the authors been able to correlate the incidence or magnitude of positive agglutination reactions with an increase in γ globulin? More specifically, did the patients with rheumatoid arthritis, in whom agglutination was not demonstrated, have an increase in the γ globulin fraction of their serum?

Dr. Charles Ragan (New York): I have been working on a corollary to this problem, and we have dissociated the agglutinin from the haemolytic streptococcus with strong salt solution. From 43 c.c.m. of serum, in which the agglutinin had been completely removed by adsorption on group A haemolytic streptococci, we have been able to obtain only about 71 γ of γ globulin nitrogen.

We have several patients with rheumatoid arthritis in whom the globulin fraction by the Howe method has been as high as 6-5 per cent. with negative agglutination to group A haemolytic streptococci. Thus, a total γ globulin elevation need have no correlation with this very small fraction which moves electrophoretically with the γ globulin or the γ plus β.

Dr. J. A. Coss, Jr. (closing): We agree that this is a non-specific test, and we are as much at sea as to what the real mechanism of it is as anyone else. It has been of real value in our clinic, however, in differentiating between adult rheumatic fever and rheumatoid arthritis.

We have not tested this fraction of γ globulin against other organisms. Several years ago, in collaboration with Mrs. Lipman, Dr. Dawson showed that it was not just the streptococcus but certain other organisms that would give this agglutination reaction.

I have seen several patients change from negative reaction to positive who have never received any vaccine treatment. We have also seen some patients change the other way, from positive to negative, during the use of gold therapy.

Histochemical Studies of Rheumatic Diseases with Special Reference to the Pathogenesis of Fibrinoid

Charles H. Altschuler and D. Murray Angevine

Madison, Wisconsin

The chemical properties of the characteristic material formed in fibrinoid degeneration of the connective tissue were studied in patients with rheumatic fever, rheumatoid arthritis, disseminated lupus erythematosus, bursae, and ganglia. Fibrinoid is either metachromatic to toluidine blue or is in such an anatomical relationship to metachromatic material that the chromatrophic substance must be a component of it. The studies support the concept that the essential feature of fibrinoid formation is the precipitation or coacervation of the acid mucopolysaccharide of the ground substance with an alkaline protein.

Discussion

Dr. Charles Ragan (New York): We have been able to confirm some of these results, in that there is a great deal of metachromatic material in the rheumatoid nodule.

Chondroitin sulphate of tendon appears to react somewhat differently to hyaluronidase than does chondroitin sulphate of cartilage. One cannot be certain one is dealing with hyaluronic acid only, since bull testis hyaluronidase does hydrolyze some chondroitin sulphate readily.

Dr. G. A. Bennett (Chicago): Would the authors comment on what they have observed, with these techniques, in lesions showing fibrinoid changes that are not of the generally accepted type of rheumatic lesions; for example, such lesions as peptic ulcers and placental tissue.

Dr. Charles H. Altschuler (closing): We are aware that hyaluronidase prepared from bull testes has been reported to depolymerize some tissue chondroitin sulphuric acids and hyalurono-sulphuric acid. We feel, however, that this does not negate any of the statements made. The reaction of acid mucopolysaccharides with a protein on the acid side of its isoelectric point is a general characteristic, and we feel that fibrinoid formation is quite general, too. We do not believe that fibrinoid is chemically identical in every instance. Fibrinoid in a blood vessel may be quite different chemically from that in synovial tissue. Not only the acid mucopolysaccharide but the precipitant may vary, and additional substances may co-precipitate. Thus, fibrin may be present in some instances, but it certainly is not invariably present.

We feel that the process of fibrinoid formation in the lesions and sites studied (arteriosclerosis, peptic ulcer, and placenta) is a similar process.

The process in peptic ulcer is particularly interesting. When the basic aniline dye, toluidine blue, is applied to sections of an ulcer the base of the ulcer is frequently divided into roughly three horizontal zones. The surface stains deep blue, indicating a high concentration of acidic nuclear material. This impression is confirmed by the Feulgen reaction. The second layer reacts very little with the basic dye. Since the arginine test seems a little more prominent in this layer, we feel that the zone is more basic in reaction. Deep to this layer we note the metachromatic zone extending for variable distances toward the serosal surface. Fibrinoid generally begins to form in the second layer and extends into the metachromatic zone. We feel that this helps support the thesis presented.

When Grosser described fibrinoid in the placenta, he distinguished it from fibrin but did not believe it was related to fibrinoid occurring elsewhere. He thought, however, that it was formed partly by a combination of degenerating cellular elements and ground substance. Recently it has been shown that the mucoid material in the umbilical cord is in direct continuity with that in the chorionic villi, and hyaluronidase-sensitive material can be shown to be present in the villi. Since the staining reactions are identical with fibrinoid occurring elsewhere,
it is felt that fibrinoid material is formed in a similar fashion.

It is well to emphasize that the increase in mucoid material can be seen frequently on H and E sections. Toluidine blue is used as a tool to identify the nature of material rather than to measure the increase. It is well to remember, too, that basic dyes which show metachromasia disobey Beer’s law. We have no satisfactory method, at the present time, for determining quantitatively the acid mucopolysaccharides of tissue.

**Arthroscopy**

MICHAEL BURMAN  
New York

The principles of arthroscopy and their clinical application to the knee joint were described; also injection of dyes into the knee, especially of 0.05 aqueous eosin to pick up eroded areas of cartilage selectively; natural and induced fluorescence of the knee joint; lavage of the knee; punch biopsy of the knee (valuable in diagnosis of tuberculosis and non-specific chronic synovitis of the knee); and endoscopic fulguration of the knee.

**Pigmented Villonodular Synovitis**

WILLIAM S. CLARK  
Boston

Pigmented villonodular synovitis is a lesion of the synovial membrane characterized grossly by yellow or reddish-brown nodules and microscopically by multinucleated giant cells, compact collections of polyhedral cells, and haemosiderin and/or lipid laden histiocytes. This lesion, frequently referred to as a giant cell tumour, has been interpreted as inflammatory in nature. Recently it has been suggested that it is a sclerosing haemangioma.

The clinical, laboratory, and radiological features of this disease were studied in 10 patients on whom the diagnosis was established by gross and microscopic examination. The synovial fluid was examined in 7 patients. The red cell counts ranged from 28,000 to 2,000,000 per c.mm. The white cell counts ranged between 100 and 4,500 per c.mm. The neutrophils in the fluid ranged between 0 and 40 per cent. The synovial fluid mucin was poor in 5 of the 7. X-ray changes of subchondral decalcification were seen in 3 patients, and subperiosteal bone formation was seen in 1. Treatment has consisted of excision and/or x ray. The results have been good.

**Discussion**

DR. DAVID H. KLING (Los Angeles): A preoperative diagnosis can be made by aspiration of the joint effusions. If there is no history of preceding trauma or haemophilia and repeated aspirations show haemorrhagic fluid with raised icterus index, the diagnosis is almost certain. The only other condition could be haemangiomata of the synovial membrane, which is extremely rare. There is an extensive controversy in the literature as to whether xanthomas of the joints are granulomas or benign tumors. To my knowledge there is no case reported where this condition has become malignant. Xanthomas will recur when they are not completely excised, just as lipomas do. It is often difficult to do a complete excision of the synovial membrane, and for this reason postoperative irradiation is of value.

**Further Observations on the Incidence and Significance of Pleuropneumonia-like Organisms**

L. DIENES, ROBERT L. BERG, AND HOWARD J. WEINBERGER  
Boston

Pleuropneumonia-like organisms have a widespread incidence. In 108 apparently healthy young men, 39 showed positive cultures. To date the organisms have been cultivated from 115 male patients with genito-urinary infections. Acute arthritis was found in 23 patients, nine of whom had Reiter’s syndrome.

The nature of pleuropneumonia-like organisms and their connexion with the usual bacteria are not known. Thus far reversion to bacilli has not been observed in L strains cultivated directly from patients. Variant forms indistinguishable from pleuropneumonia-like organisms have developed in vitro from common organisms under the influence of penicillin. Whatever their nature, bacteria in the pleuropneumonia-like form are sometimes pathogenic.

DR. HOWARD J. WEINBERGER (closing): The method of isolation of these organisms, using liquid medium, is that suggested by Dr. Sabin. It is applicable when one is dealing with pure cultures of these organisms, for instance, from knee-joint fluids or from mouse brains. However, when secondary contamination is likely as in cultures from the genital tract, one or two other organisms when transferred to broth will soon overgrow the pleuropneumonia-like organisms and inhibit their growth. For the primary isolation of these organisms, we believe that solid media is preferable.

We have obtained pleuropneumonia-like organisms from patients who continued to have symptoms and signs of urethritis following treatment for gonorrhea. In 2 per cent. of our patients we have found a combination of gonorrhea and pleuropneumonia-like infection. It has been the experience in these patients that their symptoms do not subside after treatment with penicillin. These organisms usually can be subcultured, after primary isolation. However, in the cases of Reiter’s syndrome we have not been able, with the exception of one instance, to carry the strain for an indefinite period of time.
We have not recovered pleuröpneumonia-like organisms from other joint effusions, with the exception of the two cases of Reiter's syndrome.

**Vitamin B Metabolism in Rheumatoid Arthritis**

**Richard J. Palmer, Mary F. Bassod, R. Elinor Judd, and Theodore B. Bayles**

Boston

Three factors of the B series were investigated to determine the presence or absence of subclinical deficiencies. A group of 12 healthy controls and a group of 39 rheumatoid arthritic patients first had fasting and load tests, and were then placed on supplementary vitamins, following which the fasting and load tests were repeated. Another group of six controls and 14 patients were tested, with an additional set of tests fourteen days after the vitamins had been discontinued. All patients were above the deficient values, and the range of excretions and mean excretions were equal to, or only slightly below, normal controls. While receiving supplementary vitamins the patients grouped themselves at the lower end of the normal range. It can be concluded, that by the urine excretion test, none of the patients showed riboflavin, thiamine, or nicotinamide deficiency as compared to normal controls.

**Discussion**

**Dr. Lohman (Holland):** We in Europe feel that if the vitamin B level is low, it plays a very important role. As you know, vitamin B is phosphorous acid and carboxylase, an enzyme which plays a very important role in fermentation and digestion of the carbohydrates. In about 30 per cent. of the cases of chronic rheumatoid arthritis, the carbohydrate was destroyed. The serum citric acid level was higher; the blood sugar in the veins was high, and in the arteries sometimes a little bit higher. I think about 30 per cent. at least, of the cases of primary arthritis are due to a disturbance in carbohydrate metabolism. Vitamin B, carboxylase, nicotinic acid, and phosphorus acid play an important role. We have treated patients with vitamin B, nicotinic acid and phosphorus acid, and we found the laboratory findings, according to the carbohydrate metabolism disturbance, gave beautiful results. If you treat patients with 100 mg. adenosine triphosphate every day for about a week, and continuing every month, intravenously, I am sure you will be just as enthusiastic about the treatment as we are.

**Dr. Theodore B. Bayles (closing):** It is well known that vitamin B and its various fractions are of great importance in carbohydrate metabolism. We also have found that the carbohydrate metabolisms seems to be interfered with in patients with rheumatoid arthritis. From the evidence at hand in rheumatoid arthritis, we were unable to find any abnormality in metabolism of thiamine or riboflavin or nicotinamide.

**Anti-hyaluronidase Studies in Rheumatic Fever and Other Diseases**

**Robert W. Quinn**

New Haven, Connecticut

The anti-hyaluronidase test was found to be a diagnostic measure in rheumatic fever and a possible measure of the activity of the infection. The test was used in patients with rheumatic fever in different phases of activity, patients convalescent from β haemolytic streptococcal infections, non-streptococcal infectious diseases, and rheumatoid arthritis, and in normal individuals. Rheumatic fever patients had a significantly higher mean anti-hyaluronidase titre of sera from any other group of patients or normal individuals. The titre was significantly higher with active rheumatic fever than in any other phase of the disease.

**Discussion**

**Dr. W. D. Robinson (Ann Arbor):** It is necessary to keep clearly in mind the source materials when discussing phenomenon associated with hyaluronidase and hyaluronic acid. Fulton and associates, working in our laboratories, have been unable to demonstrate an increase in hyaluronidase inhibitors in the serum of patients with rheumatic fever or rheumatoid arthritis. However, there is possibly an important difference with respect to the source of enzyme in the techniques used. Dr. Quinn has used an enzyme derived from a particular streptococcus. Dr. Fulton used an enzyme derived from a testicular material. There were also differences in the substrates used in these two studies, Dr. Quinn having used purified hyaluronic acid, Dr. Fulton having used the hyaluronic acid in the capsule of a particular streptococcus.

**Dr. Robert W. Quinn (closing):** The mucin-clot prevention test gives different results from the viscosity reducing method.

Haas (we were able to confirm this result) has been able to show that sera from all the species that he tested, did contain an inhibitory substance against enzymes from many different sources. These same sera, when tested by means of the mucin-clot prevention test, give entirely different results. The mucin-clot prevention test seems to be more specific than the other methods which have been reported.

**Compte-Rendu de la Réunion Annuelle, 1948**

**Résumé**

Le Dr. Marian Ropes a rapporté que le liquide synovial peut être utilisé dans le diagnostic de différents types d'arthrite infectieuse et d'arthrite rhumatismale qu'il permet de distinguer des affections traumatiques des articulations.

L'étude faite par Bauman et ses collaborateurs sur l'emploi du curare dans la spondylite rhumatismale suggère que le spasme des muscles extenseurs de la colonne
vertébrale est un facteur important au début de cette maladie.

William D. Robinson et ses collaborateurs ont présenté un exposé sur l’emploi de la radiothérapie dans la spondy- lité rhumatismale.

Edward W. Boland et Nathan E. Headley ont décrit les bons résultats obtenus dans le traitement du rhuma- tisme palindromique par les sels d’or et ont suggéré que, si leurs résultats sont confirmés par des essais ultérieurs, ils pourront étayer l’opinion selon laquelle le rhumatisme palindromique serait une forme atypique d’arthritis rhumatismale.

J. G. Kuhn a décrit des méthodes pour la mobilisation du coude ankylosé dans l’arthrite chronique.

W. Q. Wolfson et ses collaborateurs ont rapporté que chez six malades atteints de goutte l’excrétion moyenne des 17-cétostéroïdes était au-dessous de la moitié du mini- mum des valeurs normales.

Les données réunies par C. J. Smyth et ses collabora- teurs suggèrent que la goutte peut apparaître chez un individu hétérozygote de l’un ou l’autre sexe chez lequel le taux d’acide urique dans le sang reste élevé pendant une durée suffisante, ceci aurait moins de chances de se produire chez une femme hétérozygote par suite de la valeur normale moins élevée chez la femme et d’une action moins grande du gène anormal de ce sexe.

W. H. Kammerer et R. L. Cecil ont décrit une étude de cinquante-trois malades atteints d’arthrite psoriasique.

J. Robles Gil a rapporté de bons résultats après administration de doses massives de vitamine D dans le sclérodérme diffus.

L. Maxwell Lockie et Bernard M. Norcross ont rap- porté que sur vingt-huit malades atteints d’arthrite rhuma- tismale juvénile, douze étaient complètement guéris, six présentaient des affections articulaires résiduelles minimes, et trois des séquelles articulaires modérées, deux présentaient une incapacité fonctionnelle articulaire grave, deux étaient morts, et chez trois sujets la maladie était encore active.

J. Albert Key a trouvé que la reconstitution chirurgicale du pied arthritique donnait des résultats étonnamment satisfaisants.

J. J. Bunim et ses collaborateurs ont trouvé des nodules cellulaires caractéristiques de l’arthrite rhumatismale dans un grand nombre de biopsies de muscles, non seulement dans l’arthrite rhumatismale mais aussi dans une variété d’autres maladies.

D. F. Hill et ses collaborateurs ont obtenu de bons résultats dans le traitement des contractures du genou dans l’arthrite rhumatismale.

E. E. Fishel et R. H. Pauli ont trouvé que l’augmenta- tion du complément dans le sérum est une indication d’une activité rhumatismale persistante ou inapparente et peut être utile lorsque les autres résultats sont normaux.

J. L. Hollander et S. M. Horvath ont fait une étude comparative des températures profondes sous la rotule et à la surface de l’articulation du genou chez des sujets nor- maux et des malades présentant diverses formes d’arthrite. Chez les malades ayant des affections rhumatismales des genoux la température interne était plus élevée que la normale. L’application externe de chaleur amenait un abaissement de plusieurs degrés de la température interne, et inversement, l’application externe de froid amenait une élévation de la température interne.

B. E. Obletz déclara que les deux tiers d’un petit groupe de malades atteints d’arthrite ostéo-articulaire de la hanche avaient éprouvé un soulagement des douleurs par la dénervation partielle de l’articulation de la hanche.

Max Michael Jr. a trouvé que l’épreuve quantitative de fixation du complément gonococcique constitue une aide précieuse pour le diagnostic de l’arthritis gonococcique.

C. L. Steinberg a présenté un exposé sur la toxicité de l’or dans l’arthrite rhumatismale en insistant particulière- ment sur l’étude de la moelle osseuse.


Les études faites par C. H. Althuler et D. Murray Ange- vine viennent appuyer l’hypothèse selon laquelle le trait essentiel de la formation fibrinoïde est la précipitation ou coagervation du mucopolysaccharide acide de la substance fondamentale par une protéine alcaline.

M. Burman a décrit les principes de l’arthroscopie et leur application clinique à l’articulation du genou; ainsi que l’injection de colorants dans le genou, la fluorescence de l’articulation du genou, et la fulguration endoscopique du genou.

W. S. Clark a rapporté que le traitement de la synovite villonodulaire pigmentée par excision et/ou rayons x, a donné de bons résultats.

L. Dienes et ses collaborateurs ont rapporté que sur cent huit jeunes hommes apparemment bien portants, trente-neuf étaient porteurs de microbes du type pleuro- pneumonique.

R. J. Palmer et ses collaborateurs sont arrivés à la conclusion que les malades atteints d’arthrite rhuma- tismale ne présentaient pas de carence en vitamine B par rapport aux témoins normaux.

R. W. Quinn a trouvé que l’épreuve de l’antihyaluronidase permettait de diagnostiquer le rhumatisme articu- laire aigu et pourrait peut-être permettre de mesurer l’activité de l’infection.