5-1-1933

Chronic non-tuberculous arthritis

Eldon C. Swanson

University of Nebraska Medical Center

Follow this and additional works at: http://digitalcommons.unmc.edu/mdtheses

Recommended Citation

CHRONIC NON-TUBERCULOUS ARTHRITIS.

ELDON C. SWANSON.
INTRODUCTION.

Arthritis is defined as a diseased state characterized by disability and usually by structural changes in one or more joints, the word being derived from the Greek arthron, meaning joint, and the ending itis, meaning of the nature of and now signifying inflammation.

The disease is admittedly a difficult one with which to deal. Its classification is still under consideration, its etiology obscure, its stubbornness in yielding to treatment, notorious. These factors have long constituted an efficient barrier to the interest of many practitioners who choose to devote their time and energy to the more spectacular and perhaps better understood fields of their art in which results are more easily achieved.

It is doubtful whether any disease or group of diseases has such a multifarious and contradictory nomenclature as the forms of non tuberculous arthritis under consideration. It is the purpose of this work to review the literature in regard to the subject of chronic non tuberculous arthritis limiting myself to that group which is generally classified as apparently non specific in origin. This will not include arthritis as the result of Acute Rheumatic Fever, Gout, Traumatic, Gonorrhea, Syphilis, Typhoid Fever, Pneumonia and Sacillary Dysentery.
THE HISTORY OF CHRONIC ARTHRITIS.

Chronic arthritis is not a new disease. Its historical frontiers date back to the Mesozoic period, centuries prior to the earliest recovered human fossils. Because it etches its ineradicable imprint on bone, a tissue easily fossilized and which defies the ravages of time, arthritis has been traced to the early age of Reptiles, 150,000,000 years ago. Since that time the paleontologic evidence of the disease has become increasingly abundant. It is not possible in this work to present a complete history of the disease, but to portray arthritis adequately as it exists today, it is important to consider briefly the highlights of its history in order to realize how deep rooted it is in the biologic history of man.

Arthritis was a cause of suffering and disability to the reptiles of the cretaceous period as is clearly shown by the fossil bearing beds of Kansas and Wyoming. Other animals were victims of arthritis and the cavebear of Europe and sabre toothed tiger of California seem to have been especially subject to it. A considerable number of specimens of men of the old stone age demonstrate that primitive man suffered from arthritis.

Arthritis was a well known and even common ailment in ancient Egypt. Flinders Petrie found undisputed evidence of the disease in skeletons unearthed in the tombs of Gurod, which
date back to 1300 B.C. While Hippocrates was elucidating his aphorisms on gout 300 years before the Christian era, Erasistratus was employing modern hydrologic methods of treatment for arthritis. Two centuries later Pliny and Seneca were calling the ancient Romans to account for their riotous living and attributed the prevalence of arthritis to excesses of diet. Aix Les Baines was almost as popular a cure for arthritis at the dawn of the first century A.D. as it is today. Celsus and Galen advocated bleeding, purgations and local applications to the joints of their second century patients.
CLASSIFICATION OF CHRONIC ARTHRITIS.

Taking into consideration that the medical profession has known of arthritis from the earliest times, its universal prevalence and the large number of cases found everywhere it is interesting to note that there is still much controversy as to the true nature of the disease. The nomenclature and classification of arthritis have added materially to the difficulty of studying this condition.

By the earlier writers, the condition was usually considered manifestations of "rheumatic gout." Hagarth named the condition "nodosity of the joints." Adams, a Dublin surgeon (1857) gave the general name of "chronic rheumatic arthritis to the forms of chronic arthritis, dividing them into a polyarticular and a "monarticular type." Charcot (1881) described the conditions as chronic articular rheumatism and also differentiated two types. The first more rapid in its course affecting younger persons and with but little tendency to the formation of new bone and the second type more gradual in its onset and course, affecting older persons and associated with periarticular growth. Garod (1890) also recognised two types and christened the first rheumatoid arthritis of which he recognised acute and chronic forms, and to the second type he gave the name "osteo arthritis."

With increase in the knowledge of etiological factors it
is probable that the terms will eventually be standardized and many will fall into disuse. This will cause less confusion in the prognosis and treatment.

Nichols and Richardson in 1905 reported on the clinical manifestations of 75 cases of arthritis. They divided these cases into two clinical groups which they labeled Group I and Group II. Nichols and Richardson after spending eight years in histologic studies of sixty-five cases, found that the cases again fell into two main groups which they called proliferative and degenerative and that the clinical Group I corresponded to the proliferative and Group II to the degenerative type. The authors stressed the point that the cases of the two groups were not necessary of different etiology and from their point of view there was considerable overlapping.

In 1928, the British Ministry of Health adopted a classification which in essence agrees with that of Nichols and Richardson, using however the term rheumatoid arthritis for the atrophic type, and osteoarthritis for the hypertrophic type.

It is an exceedingly difficult problem to devise a satisfactory nomenclature for the various forms of arthritis which shall be accurate, non cumbersome, and yet embody the essential and outstanding features of the disease.

The American Committee for the Control of Rheumatism accepted Nichols and Richardsons classification which may be said to be based on pathology. Thus the terms proliferative and degenerative are used synomously with Atrophic and Hyper-
trophic and with the **English term** rheumatoid arthritis and Osteoarthritis.

Proliferative = Atrophic = Rheumatoid
Degenerative = Hypertrophic = Osteoarthritis.

A review of recent literature will indicate that the committee's classification is not being used by all the workers in the field. Most classifications are based on one aspect of the disease only, either the pathological picture, or the roentgenological characteristics or presumed etiology. Thus Cecil and his coworkers have based a classification on whether the disease is sub-acute or chronic and whether it is infectious or non-infectious in character. Other such etiological classifications are those of Kauffman, Swift and Fite.

Some authorities as Holbrook suggest a clinical classification based on history, physical examination, laboratory, x-ray and response to treatment.

Fisher suggests a compound classification on the clinical, etiological, pathologic, anatomical and roentgenologic aspects.

Shapiro declares the facts to be considered in the classification of arthritis may be tabled as follows.

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Etiologic</th>
<th>Pathologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>Specific infection</td>
<td>Proliferative</td>
</tr>
<tr>
<td>Subacute</td>
<td>Gonorrhea</td>
<td>Degenerative</td>
</tr>
<tr>
<td>Chronic</td>
<td>Staphlococcus</td>
<td></td>
</tr>
<tr>
<td>Recurrent</td>
<td>Streptococcus</td>
<td></td>
</tr>
<tr>
<td>Monarthritis</td>
<td>Trauma</td>
<td></td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>Metabolic (Gout)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arthropathic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Charcot</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Syringomyelia</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anatomic</th>
<th>Roentgenologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periarticular</td>
<td>Atrophic</td>
</tr>
<tr>
<td>Synovial</td>
<td>Hypertrophic</td>
</tr>
<tr>
<td>Chondroosseous</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td></td>
</tr>
</tbody>
</table>
THE ECONOMIC ASPECT OF CHRONIC ARTHRITIS.

Arthritis knows no geographical boundaries. All nations and races are susceptible. Thus in England, before the World War, the Cambridge Committee for the study of Special Diseases selected arthritis as the medical and economic problem most needing investigation. A large program to this end was under way when the war broke out.

Since the war another movement of great significance has been launched in Europe for the study, treatment and prevention of arthritis. This originated with the International Committee on Rheumatism with headquarters in Amsterdam. The profession in twenty four countries, notably the United States, England, Sweden, Holland, Germany and France have organized activity in the study of this disease.

In Sweden putting aside cardio-vascular and senile conditions articular rheumatism comes first on the list of disabling maladies in that country causing "permanent pensionable invalidity." It accounts for 9.1 per cent of cases as against 5.8 per cent for tuberculosis. In England including the articular and non articular cases as lumbago, one sixth of the total industrial disability is caused by arthritis.

A recent study by the Massachusetts State Department of Health estimated that out of a total population of 4,400,000 there exist 10,000 cases of Cancer, 25,000 cases of Tuberculosis, 85,000 cases of Heart disease and 150,000 of so called "rheumatism" or arthritis.
The American Committee said in 1930, "The disease chronic arthritis prevalent in all temperate zones, represents one of the most important if not the most important of existing social and industrial handicaps."

In this country in 1925 the Hospital for Ruptured and Crippled of New York City organized an Arthritis Clinic, the first to be devoted solely to the study and treatment of arthritis. A group of specialists in the various branches of medicine and surgery were assembled in a single unit aided by the laboratory to determine the relationship of their specialties to the problem of arthritis. An American Committee to co-operate in the international attack upon the problem of arthritis was formed in Philadelphia on March 17, 1928 by Dr. Louis B. Wilson of the Mayo Clinic Foundation.

Thus research has proven that a relatively large percentage of the population is suffering from the disease and its cure or mitigation is therefore a matter of vital social and economic significance.
ETIOLOGY

The etiology of chronic arthritis has been one of the mysteries of medicine. However considerable light has been thrown on this aspect of the disease during the last few years by the work and study of many investigators. Various theories of etiology have been advanced such as heredity, exposure to cold and wet, the neuropathic theory, disturbed carbohydrate metabolism and inadequate circulation in the joints, the intestinal putrefaction theory and finally infection and the focal infection theory which now has many supporters.

Much difference of opinion exists concerning what chronic joint diseases should be included in the term chronic arthritis. There are the changes mostly proliferative which from the anatomic appearance might well be considered infectious in nature. The relation of an infectious process to the joints showing retrogressive changes in the bone and cartilage is not so evident. Nichols and Richardson, however noted a decided overlapping in these two processes. The question arises whether the various anatomic proliferative and degenerative changes noted in nonspecific joint disease may not be different manifestations of a common injury. It is therefore difficult to separate the discussion of the etiology or the treatment of one type from the other.

One of the most important phases in the work on the etiology of chronic arthritis was the introduction by Willings
and his workers of the theory of focal infection in 1912. These men called attention to the specific relationship of dental, tonsillar and other infections to the arthritic complex.

According to this theory not only the general symptoms but also the local pathological changes in the affected joints are due to the action of micro-organisms or their toxins, derived usually from some focus of chronic infection elsewhere in the body.

Although the doctrine of focal infection is generally credited to Billings, Benjamin Rush in 1819 recognized the existence of a dental infection in a case of arthritis which recovered upon its removal. It is said that Hippocrates also refers to a more or less well defined relationship of the same kind.

Billings found these foci most frequently in the tonsils or at the roots of devitalized teeth. At times the foci were also found in the sinuses, middle ear, gall bladder and genitourinary tract.

Billings work has been corroborated by numerous observers. Cecil and Archer, found in a series of 200 cases that the tonsils were obviously diseased in 122 cases. In 37 cases both the tonsils and root canals were infected. In 21 cases the root canals alone were infected. In 9 cases the root canals were associated with some other focus than the tonsil. Other less important foci were sinuses, gall bladder, prostate and colon. Infections of the cervix and adnexia seemed to play a comparatively small role in the etiology of arthritis.
Cecil and Archer found the average age of onset in those with dental infection was thirty whereas the average age of onset in those with dental infection was forty two. They suggest that tonsils would be suspected first in young people with infectious arthritis while the teeth should be under suspicion in patients of more advanced years.

In a study of 545 cases of arthritis in civil life Pemberton found that the teeth constituted the site of most of the focal infection in arthritis. Infection of the teeth constituted 54 per cent while infections of the nose and throat and accessory sinuses existed in 31 per cent.

Pemberton emphasizes that caries alone do not seem to be a factor of very great moment unless of extreme degree, under which circumstances it is very apt to be accompanied by further pathology. The lesion which gives the most serious consequence is infection around the root of the tooth the so called apical abscess. The importance of X-ray examination of the teeth in doubtful cases has been emphasized as this may reveal signs of apical infection although to ordinary examination the teeth appear sound and there is absence of pyorrhea.

Another important site of infection within the mouth is the gums which may be the seat of a mild gingivitis or extensive pyorrhea. This may involve so much of the gum tissue as to produce large pockets around the roots of the teeth, tantamount in their nature and influence to apical infections. Barret and Smith believed that the Entameba Buccalis was the causative organism of pyorrhea. Vicents bacillus may also produce an infection of the gingival tissues which may act
as a focus of infection. In his series of army cases Pemberton reported gingivitis present in 25 per cent of the cases.

The appearance of tonsils productive of systemic harm is not constant or characteristic. They may be large or cryptic, scarred and inflamed or they may be inconspicuous to the ordinary examiner. Some laryngologists state that the hypertrophied tonsil is less apt to be a source of danger than is the buried or inconspicuous type because of better drainage. Even badly infected tonsils may apparently give rise to no symptoms of which the patient is aware. The peritonsillar tissues especially the anterior pillars may show evidence of tonsillar infection by a chronic hyperemia.

The sinuses constitute an important source of focal infection. They are less accessible than teeth or tonsils and drainage and lavage of purulent contents cannot be so easily achieved.

The third most common site of infection in the production of arthritis is the genito urinary tract. In a study of 700 cases Pemberton found it present in 14 per cent of the cases. It is more common in men than in women which he explains as being the result of a better drainage of the tract in women than in men.

In man the chief focus is the prostate. This may be entirely non venereal in nature though in some cases it has its incipiency in venereal disease. On examination the prostate may feel boggy, tender, enlarged or nodular. By expressing its secretion in rectal palpation one may show a varying number of pus cells. The organisms responsible for this type of in-
fection may be varieties of streptococcus and the staphylococcus or the colon bacillus.

Infection may also be resident in the seminal vesicles bladder or elsewhere. This requires accurate and thorough analysis and should be conducted by one thoroughly conversant with this field.

A frequent finding in women arthritis is a cervicitis or endocervicitis resulting from parturition. Venereal disease may leave as a complication an infected condition of the vaginal mucosa with leucorrhea or infection of the glands of Bartholin.

In connection with the genito urinary tract it is important to analyze the urine for evidence of pyelitis or infection of the kidney proper.

The climacteric is the general period of greatest incidence in women at least as regards hypertrophic arthritis and Cecil has even classified this type of arthritis as "arthritis of the menopause."

The intestine may be a focus of infection especially in the lower portion. Favorite sites may be diverticulitis, the appendix and in ulcerations of the walls.

The Mutch theory of intestinal infection assumes that infective pathogenic organisms are absorbed from some portion of the intestinal tract into the circulation and carried to the affected joint or joints. In his opinion a long chained streptococcus not normally found in the bowel is the pathogenic organism. The organism has a pronounced glycophile tendency and may explain the benefit that may follow a decrease of the carbohydrate intake as sponsored by Pemberton and others.
A site of great frequency of involvement is the gall bladder or biliary tract which may harbor stones or be the seat of a cholecystitis. This should be diagnosed by the history, Graham roentgen ray dye method, biliary drainage or its modifications.

It is the contention of Hosenow and his associates supported by the work of Haden and Cecil that an "elective affinity exists by virtue of which an organism obtained from a focus of infection or an affected joint in a patient suffering from arthritis will upon reinjection into an experimental animal, tend to produce an analogous lesion in a comparable joint in that animal." This view has been made to extend on the basis of experimental evidence to many conditions as rheumatic fever, gastric ulcer, myositis, endocarditis and epidemic parotiditis.

When rabbits are injected intravenously with sublethal doses of streptococci from a focus of infection in an arthritic patient, a large proportion of them develop signs of arthritis in one or more joints. It is usually unnecessary to make more than one injection in order to produce joint symptoms.

Various explanations have been advanced to explain this tendency to selective localization. Haden believes that the degree of clumping, the state of blood supply of the part, the food supply, and the so-called "resistance" of the tissue are important in determining the site. The most important factor seems to be some peculiar property probably chemical in nature, inherent in the organism.
The localizing capacity of bacteria apparently varies at different times and is doubtless dependent upon local conditions at the focus of infection. Rosenow has stressed the fact that "the focus is of importance not only as affording the entrance way for bacteria but also as a place where varying affinities for certain tissues may be acquired." He also advanced the theory that an alteration in the blood supply of a part afforded opportunity for the activities of the given bacteria to develop their characteristic effects.

In view of the few evidences of the action of bacteria in arthritis in a frankly destructive sense, such as seen in septic joints and tuberculous arthritis, it is hard to explain their action as being the result of conduction from the focus where they originate to direct action in the joint structures. Even if it be granted that all cases of arthritis are characterized by bacteria in the joint tissues it seems more probable to explain their action as a deviation of the normal physiological processes acting in the bone. Thus the bony tissue may become rarified, atrophic and impoverished in lime salts in one type or overgrown, thickened and showing evidence of new bone formation in the other.

One explanation may rest on an allergic bases. Zinsser defines allergy as a state of the body in which it is sensitized to bacteriological antigen probably from disintegration in an inflammatory focus, of the organism concerned. The reactions concerned in this resistance however may be harmful and may result in pathological changes or disease.
Zinsser believes that acute rheumatic fever for example represents an allergic state for the following reasons:

(1) In the phenomenon of anaphylaxis, joint symptoms occur bearing more or less resemblance to articular rheumatism.

(2) In acute articular rheumatism culture of the joint fluids usually shows them to be sterile. (3) The joint lesions produced by injection of bacteria into animals are also usually sterile. (4) The sensitiveness of joints in experimental animals seems to some extent to run parallel to the general sensitiveness. It is thus conceivable that when the body has long harbored a definite infection it may become allergic to bacterial substances given off from the growing bacteria. These products however may have little or no effect upon normal animals.

This mechanism may explain the reaction of synovial proliferation in atrophic arthritis as being an allergic reaction from sensitization to bacterial substances given off from disintegration in an inflammatory focus.

Another theory of the etiology of chronic arthritis is that the disease may be due to a specific infection, rather than to the discharge of bacteria or their toxins from chronic infected foci.

There is abundant clinical evidence that atrophic arthritis is infective in character. It appears with the most acute onset in children and is frequently referred to as Stills disease. Fever, leukocytosis, inflammation of the joints, enlarged spleen and lymphatic glands are abundant evidence of
its infective character. However the disease in adults is usually more insidious in its onset. The course of the disease is usually one of remissions and exacerbations with a tendency for the evidence of infection to disappear.

A considerable amount of research work has been done on the bacteriology of chronic arthritis to prove its infectious nature. Popoff in 1887 was able experimentally to produce arthritic lesions with streptococci. This was followed and confirmed by Leyden, Singer, Chvostek, Thirlois, Turboulet and Coydin and Apert from 1894 to 1899. In 1899 Wassermann caused an infective arthritis in rabbits by the injection of streptococci.

In 1917 Moon and Edwards obtained positive blood cultures from arthritic patients in 26 per cent of 123 cases. The organism isolated was the *Streptococcus Viridans*.

In 1902 Poynton and Paine obtained positive cultures from the synovial membranes of arthritic patients of a diplococcus *rheumaticus*.

Davis in 1911 cultured the various foci of infection which he found associated with chronic arthritis. In a majority of cases the hemolytic streptococcus was the predominant organism. With these organisms he was able to produce arthritis experimentally in rabbits. Blood cultures, and joint fluid cultures were negative but Davis felt from his investigation that the hemolytic streptococcus was probably the etiological agent.

Rosenow cultured the regional lymph glands in 54 patients. In 32 he recovered non hemolytic streptococci.
Billings, Coleman and Hibbs made cultures of regional lymph nodes in 28 patients. Of these 19 showed nonhemolytic streptococci, 1 showed a hemolytic streptococcus and 1 a mixture of the two forms. They made joint cultures in 19 patients, 5 of whom showed non hemolytic streptococci and 1 a mixture of hemolytic and nonhemolytic streptococci.

Forkner, Shands and Posten, secured positive joint cultures in 22 per cent of their cases. Positive cultures from the neighboring lymph nodes were obtained in 47 per cent. The microorganisms in both joint and glands was a nonhemolytic streptococcus.

Cecil, Nichols and Stainsby with care in the selection of cases, obtained positive streptococcus cultures from the blood in 62.5 per cent of patients. Of these streptococci 83.3 per cent were considered attenuated hemolytic streptococci and the remainder being veridans or indifferent strains.

Klugh recently cultured the joint fluids of 74 cases of chronic arthritis and obtained positive cultures in 53 cases which he classified as streptococcus veridans.

Richards in 1920 made blood cultures from 104 patients with chronic arthritis and recovered streptococcus viridans in 16.

Dawson, Olmstead and Roots made agglutination tests with various strains of streptococci using serum from patients with rheumatoid arthritis. They found that the serum agglutinated all strains of hemolytic streptococci in a very high titer. The agglutination was just as marked with streptococci from erysipelas, scarlet fever or rheumatic sore throat as with the
specific strain of streptococcus hemolyticus isolated by Cecil from rheumatoid arthritis.

They also made joint cultures in 80 cases of chronic arthritic patients and found positive blood cultures for streptococcus veridans in 2 cases.

Hadjopoulos and Burbank while experimenting on the agglutinating power and the treatment of chronic arthritic patients, found positive blood cultures for streptococcus veridans in 10 cases of 104 studied. They also found positive cultures of this organism in joint fluid.

Gray and Gowan, in 1931 reported the blood cultures of 71 arthritic patients as being positive for streptococcus veridans in 41 cases or a percentage of 58. In this same series the culture of joint fluids was positive for streptococcus veridans in 5 cases of 8 studied.

In 1931, Wetherby and Clauson obtained blood cultures in 57 cases of unselected types of chronic arthritis and from 50 normal persons as a control. In 7 of the cases staphylococci were found in the blood cultures. Streptococci in pure culture were found in the blood cultures of 23 of the remaining cases. One of the 24 strains of streptococci was a typical hemolytic streptococcus while the remaining 24 were of the veridans type. They did not represent a special strain type.

Animal experiments showed that animals could be made hypersensitive to streptococci but could be desensitized by the intravenous injection of streptococccic vaccine which also protected them from the development of experimental lesions as
produced by streptococci in non vaccinated animals. 

Other investigators as Crowe have found staphlococci and diphtheroids rather than streptococci.

A review of the literature indicated that the average percent of positive streptococci cultures obtained have been blood, 35 per cent, joint fluid 35 per cent, joint tissues 44 per cent, lymph nodes 61 per cent and subcutaneous nodules 72 per cent. A total of approximately 1,297 cultures have been reported with 520 or 40 per cent positive for the streptococcus. Most of the cultures have been positive for streptococcus veridins.

The streptococci from both acute rheumatic fever and chronic arthritis have tended to fall into a well defined group which grew poorly when first isolated and produced a faint green discoloration in the blood agar plate when incubated at 37 degrees C. for 24 hours. These organisms do not seem to represent a specific strain.

Barrow cites six cases of arthritis whose stools and urine showed the presence of a variety of parasites of which the Chilomastix mesnili comes first, amoebae second, trichomonads third, giardia or lamilia fourth and craigia and waskia last. Hereported very good results from treatment for the protozoa.

Pemberton says the alleged results of treatment have not as yet had such corroboration at the hands of others as to lead one to unqualifiedly to accept amebiasis as a main or underlying cause of hypertrophic arthritis.

Ely and his associates found the Amoeba histolytica around
the roots of teeth and believed that they gained access to the system through alveolar infection and caused hypertrophic arthritis by passing to the marrow spaces contiguous to joint structures. In a series of 73 cases he found the amoeba in the stools of 3 cases. A portion of a femur removed by operation in a case of arthritis deformans and stained and examined at the university of California revealed a pure infection of amoebae about the lesions in the bone. They had the characteristics of Endameba Dysenteriae found in amaebic ulcers in intestinal amaebiasis.

Hench of the Mayo Clinic believes that arthritis is primarily of infectious origin. He emphasizes the systemic character of the disease.

Osgood states that rheumatoid arthritis is a disease in which no specific organism can be found responsible for its causation. He concludes that there are probably many different types of organisms and many other factors that play etiological parts in its onset and course.

The predominence of streptococci in cultures speaks strongly for this being the most frequent etiological agent in rheumatoid arthritis at least. However it speaks against a specific streptococcus as the etiological agent. Whether rheumatoid arthritis is due to a specific streptococcus or whether different microorganisms are capable of producing these changes is still an open question.

Working on the assumption that chronic arthritis was a streptoccic infection, Hastings in 1913 resorted to the
complement fixation test as a method of determining which type of streptococcus was causing the infection. By using the old Wasserman technic, Hastings obtained positive complement fixation reactions with serum of arthritic patients and strains of streptococci isolated from foci of infection. In this way he believed he could determine the exact biological type of streptococcus with which the patient was infected.

More recently Burbank and Hadjopoulos have repeated this complement fixation work with a slightly modified technic. They found that patients with periarticular or deforming arthritis reacted positively to some form of hemolytic streptococcus, whereas patients with osteo-arthritis reacted positively to streptococci of veridans group.

Nichols and Stainsby found that serum of patients with chronic arthritis agglutinated streptococci in higher dilution than normal persons.

Clawson and Wetherby, tested the serums of 81 normal individuals and found that most of the serums showed agglutination in dilutions of 1:400 to a strain of streptococcus isolated from a patient with chronic arthritis. Sixty patients with chronic arthritis showed agglutinations in the dilutions of 1:1180.

In another experiment they tested the serums of 74 patients with chronic arthritis of both types. The organism used was a strain of streptococcus viridans isolated from the blood of a patient with acute rheumatic fever. A week saline suspension of the organism was mixed with increasing dilution of patients serum in Wassermann tubes. The tubes were then incubated in a water bath and allowed to stand in a cool place for from 18 to
20 hours when the degree of agglutination was then determined.

They found that cross agglutination occurred in high dilution with many strains of streptococci of both acute rheumatic and chronic arthritic origin. Most of the patients showed an agglutination titer of 1:200 to this strain used in this experiment.

From these experiments and clinical experience they concluded that the height of the streptococcic agglutination titer seemed to be reliable indication of the protection possessed by the patient against the streptococcus. Also that clinical improvement was most frequent when the titer was 1:6400 or more.

Skin tests have been used by a number of persons in rheumatic fever, chorea, scarlet fever, measles, nephritis and chronic arthritis. Birkhaug tested rheumatic, arthritic, and normal persons with bacterial suspensions of autolysates and filtrates of several streptococci of rheumatic origin. He found a higher percentage of positive tests in patients with rheumatic fever and chronic arthritis than in his series of controls.

Clawson and Wetherby used a bacterial suspension of streptococci injecting 0.1 cc intradermally (2,000,000 organisms). They obtained similar results in a study of 127 cases of chronic arthritis and 107 normal persons. They concluded that a positive skin test indicates in most cases that the person is hypersensitive or allergic to the strain of streptococcus used in the test. They also concluded that the high percentage of positive skin and agglutination titers suggests
a possible etiological relationship of the streptococcus to chronic arthritis.

Focal infection is not entirely a satisfactory explanation since the most advanced dental sepsis can be repeatedly demonstrated in the absence of chronic arthritis. The same is true of local foci. In order to explain this some added factor has been suggested to be responsible for the development of arthritis such as a special constitution, loss of endocrine balance, an altered hydrogen ion concentration in the tissues, or an allergic change.

One of the interesting facts which recent studies have brought out is the marked influence of heredity in the production of chronic arthritis. This does not mean that the disease is inherited per se but it goes mean that the background upon which the disease is implanted is definitely inherited in about fifty per cent of cases.

A clinical and statistical study of 1,100 cases of chronic arthritis by Pierce and Pemberton showed that hereditary influences either direct or collateral, were observed in 58 per cent of the cases.

The build which seems most conspicuously associated with the familial tendency toward arthritis is that of the rather slender long bodied possibly visceroptotic type especially as regards the atropic variety of arthritis.

In many cases a severe shock, either mental or physical may be followed by an attack of chronic arthritis. A death in the family, a difficult labor, a surgical operation or business calamity may be predisposing factors. Fatigue either
mental or physical or overwork and strain are others.

It has been shown experimentally in rabbits that when a joint is injured, as in trauma, and streptococci are then injected into the bloodstream, the bacteria have a strong predilection for the injured tissue.

Pemberton in his statistical study of arthritis in soldiers found that sudden or repeated exposure to dampness, rain and cold was one of the commonest predisposing causes of atrophic arthritis. This has been a common observation among the laity for years, hence the popularity for "red flannel underwear" as prophylaxis.

The important part played by altered metabolism in gout is well known. It is also well known that some of the joint manifestations in gout are similar in nature to those in atrophic and hypertrophic arthritis.

Cawadias has found that there is an excess of total sulphur eliminated in patients with arthritis, there being a relative increase of the neutral or imperfectly oxidized sulphur. This relative increase of the neutral sulphur he regards as being due to a general deficiency in the oxidation processes of arthritic patients. He considers that such metabolic trouble must be considered as a result of the infection or intoxication which causes the disease and that a certain predisposition towards hypo-oxidation and towards sulphur demineralization exists before hand hereditarily and constitutionally and that it helps the development of the disease.
It is Pemberton's contention that the derangement of function which constitutes the background of arthritis has to do with the disturbance of the finer blood supply to various parts of the body.

Pemberton, Hendrix and Crouter studied the respiratory functions of the blood in arthritis. It was found that during the conduction of a test revealing a lowered sugar tolerance, there takes place in most cases a rise in the percentage saturation of that blood with oxygen. Thus the ratio of the oxygen content to the oxygen capacity increases, which means that more oxygen is left unutilized. They also found that on subjecting a patient to a therapeutic electric bake the percentage oxygen saturation of the peripheral blood tends to rise. This rise in the oxygen saturation is presumably due to the acceleration of the circulation that occurs. These several factors suggest that in the arthritic patient there is a change in the circulatory condition or rate such that the tissues do not extract from the blood as it passes through them the usual amount of available oxygen.

Pemberton, Cecil, Archer and others have observed that in many arthritics a lowered caloric intake was followed by beneficial results. This evidence suggested that an increased circulatory rate might explain the lowered sugar tolerance by an unduly rapid absorption of glucose. Pemberton in collaboration with Cajori and Crouter, tested this by feeding urea and potassium iodide coincidentally with the glucose, in the conduction of a test for low sugar tolerance. They found no sug-
gestion that an increased rate of absorption accounts for the variety of low sugar tolerance but that the low sugar tolerance was the result of a failure of the blood to adequately reach a certain area or tissue of the body.

They then determined by an other experiment to reduce the blood flow in parts of the body in such a way as to simulate the arthritic condition and then to conduct a test of sugar tolerance in the usual manner. This was done by elevating an arm throughout the experiment for an hour and a half thus interfering with gravitation in relation to limb circulation. The results indicated that denial to the muscular tissues of their usual degree of contact with the circulating blood interferes with the withdrawal of glucose so that when sugar is fed a lowered tolerance results. This suggests that circulatory changes contribute to the pathology of arthritis and focal infection with which a lowered sugar tolerance is closely associated.

Pemberton and Pierce compared the red cell count to the first issuing drop of blood or supposedly capillary blood with that of the fourth or subsequently issuing drops of blood from a finger stab. They found that in a normal person the red cell count of the first drop was frequently higher than the count of the freely flowing blood. However in arthritis the condition was the opposite and these patients had a lower count in the first drop than in the free flowing blood. This indicates that there is a disturbance of the peripheral blood flow in arthritis in the nature of vasoconstriction so that fewer cells issue forth following a stab.
By direct observation of the blood flow in the capillaries under the microscope it was found that the arthritics showed less blood in the field, closure or narrowing of many capillaries, irregularity and slowing down of blood flow and often a difference in the amount of blood in the venous as compared with the arterial limb of a capillary.

By studies of the surface temperature of arthritic patients it was found that as a whole they have a temperature lower than normal persons because of decreased blood flow. Exposure of these patients to environmental cold shows that whereas the initial temperature is lower, the subsequent fall of temperature is less. Upon the return of the subject to room temperature the rise of the lowered peripheral temperature is slower and less than with normals. This approaches a rigidity of the finer vascular system of the periphery and may account for added discomfort these patients experience from changes in environment and also for their lowered metabolic rate.

Pemberton believes that the general constriction of the capillary bed of an arthritic patient is best explained as being the result of intermediation of the nervous system by virtue of inherent weakness in it, an imbalance of it, or influence of intoxicating factors operating centrally or peripherally on it. The influence of the nervous system in producing arthritis has been observed in Charcot's joint of Tabes and in Syringomyelia.

In a series of experiments Pemberton found that 20 per cent of the cases of chronic patients suffering from chronic arthritis showed a basal metabolism slightly below normal. This lowered
sugar tolerance varied in proportion to the severity of the arthritis. It was found to grow less or disappear as convalescence proceeded whatever the method of therapy but it returned to normal most abruptly after the removal of foci of infection. Pemberton concluded that "a lowered sugar tolerance is not specific for arthritis and should be interpreted only as reflecting part of the underlying pathology of this disease which apparently consists in an interference with the respiratory functions of the circulating blood. These do not, however, express themselves conspicuously in terms of the end-metabolism as shown by basal metabolism studies."

Normal data has been obtained regarding the blood fats, and cholesterol, the blood calcium, blood urea and non-protein nitrogen in chronic arthritis.

Arbuthnot Lane and his coworkers believe that arthritis may be due to the absorption into the circulation and their deposit in joints of putrefactive products from the bowel in cases of intestinal stasis. Pemberton however as the result of his analysis, does not consider that protein putrefaction in the bowel plays an important part in causation.

Pemberton has called attention to the malfunction of the colon as being a frequent and important cause of chronic arthritis. In these cases the colon is characterized by a tendency toward greater caliber, greater length, a more convoluted appearance and sometime reduplication as shown by the X-ray. There may be ptosis of the organ as a whole. The spaces between the haustra may be obviously increased, giving
the contour of the bowel a smooth appearance. It may be congenital and may constitute part of the anatomical and constitutional background, for the existing arthritis or it may be acquired as the result of pregnancy, malposture, and general asthenia. The cases are chiefly women at or beyond mid-life though any cases may present this picture.

Rowland produced dilatation of the colon in rats by the restriction of vitamin B in their diet, which was also high in carbohydrates with a deficiency in proteins. He further believed that such deficient diets played a part in the arthritis of domestic pigs and that he could prevent the onset of their arthritis by feeding them vitamin B freely. He suggests that the presence of the streptococcus in the intestinal tract is a possible factor in the etiology of the disease.

Fletcher has shown that concurrently with decrease in carbohydrate intake and a sufficient intake of vitamins and protein that the large bowel often returns to normal. He believes that such nutritional disturbances favor the development of arthritis and other infections.

Hench has also demonstrated a relatively frequent appearance of hyperglycemia in 60 per cent of cases of arthritic patients studied.

The beneficial results of ganglionectomy described by Rowntree and Adson, suggest that ischemia may be an important factor in preventing recovery. Rowntree believes that ischemia may be also an important etiological factor.

The presence of both atrophic and hypertrophic arthritis in the same individuals has been a stumbling block for every
one who has attempted to classify chronic arthritis. The pathology of the joints in hypertrophic arthritis, at least of the extremities that have been studied and the clinical signs and symptoms suggest a non infective etiology. Many theories have been advanced as to the etiologic agencies that might explain degeneration of cartilage which is the outstanding pathologic finding.

Fisher claims that "osteoarthritis is not a disease sui generis, but a physiological response to some form of irritation either mechanical or chemical." He arrived at this conclusion after a careful study of the normal and pathological physiology of the knee joint. He experimented on rabbits, by shaving off a thin layer of cartilage from the center to the periphery of the articular cartilage. Six weeks later the animals were killed. The central portion of this cartilage showed no tendency to regenerate, in fact it was necrotic. The peripheral portion however, showed marked regeneration. He concluded that trauma which will cause degeneration of the central cartilage is followed by proliferation of the marginal cartilage. This difference in reaction he ascribes to the better vascularity of the peripheral portion. It is his opinion that damage or loss of the central cartilage gives rise to a sequence of events physiologic and compensatory in character which we recognize as osteo-arthritis.

One of the most important predisposing factors in the etiology of hypertrophic arthritis is old age. As the years advance it seems that the wearing quality of the joint is
diminished, depending perhaps upon some disturbance in the
dlocal circulation.

Pemberton tied a purse string suture around the patella
of a dog which interfered with the blood supply. Later
characteristic hypertrophic changes developed in the patella.

The spine appears to be the point of selection for hyper-
trophic arthritis in patients past forty years of age. Allard in
2,000 roentgen rays of the spine taken at the Mayo Clinic
found hypertrophic arthritis of the lumbar spine present in
67 per cent of men past fifty years of age and in forty per
cent of the women. It is claimed that the Egyptian hierogly-
phic symbol for old age is the figure of a man crippled with
chronic arthritis.

Exposure is also a predisposing factor in hypertrophic
arthritis though probably to a less extent than in atrophic
arthritis. Elderly people who lead hard and exposed lives
appear to be more prone to hypertrophic arthritis than those
whose circumstances have been more fortunate.

Trauma is apparently a more outstanding etiological factor
in the hypertrophic than in the atrophic type of chronic ar-
thritis. It may be acute or chronic but is most often a result
of chronic trauma.

Key has discussed the relation of traumatic or mechanical
factors in the production of experimental hypertrophic arthritis.
He produced hypertrophic arthritis in rabbits by resecting a
small piece of cartilage from the patella and at the same time
causing unequal pressure or strain by giving the rabbit a
"knock knee." He concluded that any disturbance of the posture that leads to faulty weight bearing or strain may be a factor in the development of hypertrophic arthritis. Thus physical defects such as curvature of the spine, subluxation of the sacro iliac joint, flat feet and old fractures involving the articular surface of the joint, all predispose to degenerative changes in the joints affected.

For many years Goldthwaite has also emphasized posture as a factor in the etiology of hypertrophic arthritis.

Overweight in obesity may cause the weight bearing joints to suffer chiefly from the strain and trauma of the joints rather than the diet.

Occupation has an important bearing on the etiology of degenerative arthritis. A study of workers has shown that a man employed at a machine where he must frequently reach upward and pull a lever may develop hypertrophic arthritis in his elbow or shoulder. If he must frequently press a pedal with his foot he may acquire hypertrophic arthritis of that extremity.

Some of the authorities believe infection plays a less important role in hypertrophic arthritis than in the atrophic type. Cecil was unable to obtain positive blood cultures in 18 patients with this type of arthritis. Keys made joint cultures from 6 patients with hypertrophic arthritis. He reported positive cultures in 3 cases and negative in the others. The predominating organisms were a staphlococcus and a minute bacillus. These were found at times in pure culture
and at other times mixed.

The recent experiments of Clauson and Wetherby indicated however that the streptococcus was an important factor in the etiology of both types of chronic arthritis.

Hypertrophic arthritis is very common in horses over four years old. Hare examined 146 horses about to be slaughtered and found evidence of hypertrophic arthritis in 31. In 9 animals cultures were positive but he obtained such a variety of microorganisms that he came to the conclusion that the growths were contaminated.

In Miller's opinion one type of arthritis may favor the development of the others. Thus a patient may develop chronic atrophic arthritis in his foot which may result in deformity or muscle atrophy. These factors may in turn cause a chronic strain or trauma on other joints at the knee, hip or spine favoring the development of hypertrophic arthritis. Also the patient may develop atrophic arthritis in his youth while the same disease may cause hypertrophic changes in later years.

The American Committee for the Control of Rheumatism recently declared: "The committee conceives of the disease as a generalized disease with joint manifestations. Certain prodroms may be recognized. It is the opinion of the Committee that at the present time no single infectious agent or completely defined dietary deficiency or metabolic disorder has been conclusively shown to be the sole cause of these disorders. The committee inclines to the belief that any one of these factors or certain combinations of these factors, under appropriate circumstances, may basically underlie the onset of the disease."
PATHOLOGY

The American Committee for the Control of Rheumatism, have accepted the pathological classification first introduced in 1905 by Nichols and Richardson. Their first classification was based on clinical manifestations but after spending eight years in the histologic studies of 60 cases, they found that the cases again fell into the two main groups which they called Proliferative and Degenerative.

Nichols and Richardson concluded that a certain pathologic alteration of a joint may be the result of a variety of irritants or agents and that a given irritant or agent may produce a variety of pathological changes.

Thus a proliferative arthritis if it continued sufficiently long, might develop changes characteristic of the degenerative type, particularly osseous hypertrophy. J. Agood and J. Strangeways who spent many years studying chronic arthritis have also pointed out this possibility.

Histologically, the main distinguishing features of the proliferative group are of a definitely inflammatory nature, with collections of inflammatory small round cells in the synovial membrane, villi, and elsewhere, and a pannus on the articular surface. These features do not occur in true Degenerative arthritis, which is a combination of degeneration with what may be termed sub-inflammatory changes.
The terms proliferative and degenerative have been confusing however because they carry an implication opposite to the true appearance of the types they represent. Consequently the Committee have substituted the terms Atrophic for Proliferative and Hypertrophic for Degenerative.
ATROPHIC OR PROLIFERATIVE ARTHRITIS.

In the earliest stage there is a round cell proliferation of the synovial membrane beginning at the junction of the synovium with the articular cartilage. This synovial pannus is composed of a highly vascular tissue resembling granulation tissue. This granulation tissue is later replaced by connective tissue and finally by fibrous tissue. This pannus slowly creeps over the surface of the cartilage towards the centre of the joint. This infiltration is not always confined to the articular surfaces but may extend into the periarticular tissues, thus accounting for the spindle shaped deformity.

As the pannus spreads over the joint cartilage, the underlying articular cartilage undergoes an alteration in the staining properties of the cartilage matrix indicating an altered vitality. The deeper layer of pannus can then be seen actively invading and replacing this altered cartilage. In this way the normal smooth and cartilaginous surface becomes replaced by a layer of connective tissue which not infrequently contains nodular areas of newly formed cartilage.

While the above inflammatory reactions are occurring in the articular cartilage important changes are to be seen in the cancellous spaces immediately subjacent to the deeper layers of the cartilage. There is a proliferation of the endosteum and of the connective tissue of the narrow spaces immediately below
the zone of provisional calcification. There is a proliferation of the connective tissue cells of the marrow associated with the formation of new blood vessels and accompanied in many cases by aggregations of lymphoid and plasma cells. There is an increase in the number of the osteoclasts and in many cases the latter actively attack the original osseous trabeculae so that the cancellous spaces are enlarged by resorption. Later however, osteoblasts can be seen laying down new bone upon the surface of the original trabeculae which may actually become thicker and denser.

This vascular granulation tissue with an advance guard of osteoclasts gradually extends toward the joint cavity and actively attacks the articular cartilage from its deep aspect. When this process is active the joint cartilage may then be destroyed and removed from two directions; from the over lying outgrowths of synovial pannus and from the under mining upward growth of the new granulation tissue springing from the marrow. The matrix is dissolved, the cartilage cells disappear, and are replaced by a new formation of connective tissue, cartilage or bone. Eventually the invading tide of vascular connective tissue meets and merges with that derived from the synovial pannus, and islands of necrotic or degenerate articular cartilage may often be seen surrounded by this newly formed connective tissue. The result of these changes is that the cartilage of altered vitality is eventually replaced by a layer of connective tissue. However as the articular cartilage usually degenerates in patches, and as these patches are replaced by this fibrous tissue the
articular surface may assume an irregular appearance. The fibrous covering of the articular surface therefore is made up of two superimposed layers, one arising from the hyperplasia of synovium, the other from the sub-articular bone.

Sometimes the degenerate articular cartilage becomes worn away before it can be replaced by connective tissue and the underlying bone is thus exposed and may become eburnated. This however, is of the nature of a secondary osteoarthritis change.

When the changes described above occur on opposed articular surfaces and when the joint is put at rest, the two layers of connective tissue remain in apposition, adhere and unite so that fibrous ankylosis results. Cartilaginous or bony transformation of the connective tissue bond may occur, resulting in cartilaginous or bony ankylosis. In rare cases where movement has been maintained the layer of pannus may ossify and constitute an articular surface beneath which the remains of the original cartilage may be seen. The end result of such a process may be the complete fusion of one bone with another and the establishment of a continuous marrow cavity between the two.

Four general processes may thus be going on at the same time: (1) The formation of a pannus by the proliferation of the synovial membrane. (2) Proliferation according to Nichols and Richardson of the perichondrium of the articular cartilage. (3) Proliferation of the connective tissue of the marrow spaces of the epiphysis, accompanied by the formation of numerous
blood vessels and vascular granulations tissue. (4) Proliferation of the endosteum of the marrow spaces with the formation of new trabeculae. These may extend upward with the granulation tissues of the marrow into the cartilage and become true bone.

Fisher believes the changes represent an effort on Nature's part to replace the degenerate articular cartilage by a new articulating surface of dense fibrous tissue. Thus if we maintain regular movements of the joint we are assisting her in her reparative efforts, and the articular cartilage may be replaced by a layer of smooth and glistening fibrous tissue which may undergo partial cartilaginous transformation. Treatment by rest, plaster and splintage, militates against this process and hastens the cohesion of the opposed connective tissue layers and resulting ankyloses.

Even in the earlier stages there is increased permeability of the epiphysis to the X-rays particularly in the region of the articular cartilage. This is explained as being the result of the active resorption of the osseous trabeculae and also to the absorption of calcium salts. It has been found experimentally that if the joints of animals are immobilized this same increased permeability rapidly ensues. This would indicate a secondary bone atrophy, which at least in part is due to disuse and is most marked in those cases with ankylosis.

The character of the joint changes speak strongly for an infective origin. This view receives further support by the finding of microorganisms in a limited number of patients.
in the blood, joint fluid and adjacent lymph glands. Fisher claims that there is no essential difference in the gross or microscopical pathology of the joint in rheumatic and in gonorrheal arthritis.

T. P. Strangways, of England further subdivides atrophic arthritis into specific types. (1) A Capsular Type. The changes (thickening and fibrosis) are practically confined to the capsule of the affected joint. (2) A Dry Type. The characteristic feature is the absorption of the synovial fluid, the atrophied, fibrous and tightly contracted capsule gripping the bones firmly and causing the articular surfaces to lie in close contact.

(3) The Adhesive Type. This begins with inflammatory changes in synovial membrane and capsule, going on to the replacement of cartilage by inflammatory connective tissue, which becomes fibrous and ends in bony ankylosis.

(4) The Atrophic Form. This is marked by great rarefaction of bone and much fatty change in bones, muscles and other tissues. The capsule, synovial membrane and articular cartilage atrophy and as the early inflammatory changes subside, bony ankylosis often occurs.

(5) The Villous Type. Swelling is chiefly due to numerous pedunculated villi, though increased fluid may be present. Mellon seed bodies are found.

(6) The Infective Type. Here the arthritis is usually due to some definite microorganism. Examples: gonococcus,
the pneumococcus and possibly streptococci and staphylococci. These cases, may resemble the adhesive type.
HYPERTROPHIC ARTHRITIS

This type has been classified as degenerative by Nichols and Richardson because the changes in the joint cartilage have been degenerative rather than inflammatory. However, as emphasized before the committee prefers the term hypertrophic because there is over-growth or hypertrophy of cartilage and bone of the joint as a whole.

In the earliest stages the changes in this type of arthritis are first manifested in the central or poorly nourished portions of the articular cartilage. Fisher believes this is because the central parts are exposed to a greater degree of pressure and friction in addition to having the poorest blood supply.

Normal cartilage on being broken across shows well marked vertical striae. These striae presumably represent the more collagenous portion of the matrix between the vertical columns of cartilage cells, the latter being contained in the more mucinous portion of the matrix.

Fibrous tissue develops in these striae resulting in a series of extremely delicate ridges over the surface of the articular cartilage. There is also often a change of color from the normal semi-translucent white to a more opaque yellowish tinge.
This is followed by a splitting of the cartilaginous matrix which usually takes place at right angles to the surface. As the superficial portion of the matrix is normally arranged in horizontal lamellae, the fibrils first formed by the splitting of the matrix are long and lie horizontally. Later and in some cases forming the first recognizable sign of abnormal change, there is a vertical splitting of the articular matrix. This vertical fibrillation of the cartilage in hypertrophic arthritis is doubtless due to the persistence of these columns of more collaginous matrix.

Although this fibrillation is the most characteristic appearance presented by the cartilage, in some cases the changes take the form of localized pits, depressions or erosions around which the cartilage may show very little change. This softening and eroding of cartilage is termed degeneration and is the characteristic feature of this type of arthritis. This process results in the exposure of the underlying bone at the bottom of these pits, and as the process goes on, the bones of the articulation may eventually come in contact or even articulate.

In addition, corresponding to the areas of eroded cartilage and bone, there takes place on the opposing articulating surface a more or less compensatory over-growth of cartilage or bone, which tends to keep the joint surfaces as a whole in contact. The line of articulation becomes very irregular however. These elevations with smooth surfaces are
due to the invasion of the deeper layers of the cartilage by vascular ingrowths of osteoblasts actively forming new bone, or from ossification occurring in the centre of the articular cartilage which has previously undergone local hyperplasia. One of these epi-articular ecchondroses may become detached and form a loose body in the joint.

The degeneration of cartilage may continue until all cartilage within the joint is destroyed. At this stage the joint may be constituted by the apposition of the bones themselves, one to another. The rate of progress is usually slow and for a long time confined to certain parts of the joint only, so that motion may be long preserved. Thus true ankylosis never occurs in this form of arthritis, although there may arise a so-called ankylosis or deformity due to impingement of one part against another.

As the changes progress, the cartilage gradually disappears from mechanical friction, revealing the subjacent bone. Even before the bone is actually exposed it has already begun to undergo sclerotic changes, the sub-articular lamella or trabeculae of bone becoming greatly thickened and the marrow spaces nearly obliterated. This change in the sub-articular bone is evidently an attempt on the part of the osteoblasts to compensate for the loss of the articular cartilage by forming a thicker layer of bone, when the articular cartilage has been destroyed. Under the friction of use this bone acquires a high degree of polish and is then termed eburnated. The head of the femur may thus grow to resemble a billiard ball or
porcelain in its smoothness and polish. Eburnation is pathognomonic of hypertrophic arthritis and never occurs in the atrophic type.

In the very earliest stages of osteo-arthritis the lateral portion of the cartilage shows no changes visible to the naked-eye, although the superficial grooves previously mentioned as occurring in the central parts may be present, and in rare cases actual fibrillation. When however the fibrillation of the central parts has become well marked, the lateral portions of the articular cartilage project more than usual forming the condition known as lipping. These lateral projections of cartilage are termed chondrophytes by Fishcr. Eventually the adjacent bone sends osteoblasts into the chondrophytes and they become ossified and are termed a chondro-osteophyte. The cartilage covering these projections may in turn degenerate and the subadjacent bones may become eburnated. This process increases the size of the head of the bone and in the case of the phalanges of the hands gives rise to the lumps on the ends of the fingers known as Heberdens nodes. This deposit of new bone is generally within the joint capsule and therefore increases the area of articular surface. Beyond the articulating surface of the chondro-osteophytes the new formations are recurved, so that the movements of the joint usually remain unimpaired. However when an osteophyte reaches a certain size it is very liable to be detached, often by quite a slight injury, and form a loose body in the joint. This is the result of the extremely open and rarified texture of the bone.
Beneath the layer of condensed bone, the shaft of the bone undergoes a diminution in the number of bony trabeculae, the cancellous spaces having an unusually open and fatty texture. This may be the result of the resorption of bone from disuse or because of the greater age of the patients in whom this type of arthritis is apt to occur. Occasionally cartilaginous nodules of variable size may be seen lying beneath the sclerotic zone and from degenerative changes in these masses of cartilage well marked cysts quite visible to the naked eye may be formed. These cavities may be filled with mucoid material and are most common especially in the end of the femur.

Owing to the atrophic processes in the bone immediately underneath the articular layer, considerable alteration in shape of the articular surfaces may occur, as the absorption is most marked where pressure is greatest. Limbs may thus become shortened and various deformities may occur which may closely simulate dislocations or fractures. In some cases the atrophic bone itself may actually undergo fracture.

The synovial membrane very rarely shows any obvious changes to the naked eye until the first sign of lipping of the articular margin appears. At the periphery where the membrane folds, the synovial membrane becomes thickened and papillary masses, either pedunculated or broadly attached may arise. This proliferation consists of granulation or dense connective tissue and may become converted into cartilage or even bone. These formations may be laminated or nonlaminated, pedunculated or free. The
synovial villi simply form chondromata. These proliferations or chondromata may undergo mucinoid degeneration with the formation of cystic cavities, and may become free in the joint cavity and constitutes loose bodies known as joint mice. Their presence may account for the recurrent synovitis so frequently observed in patients with osteoarthritis.

The villous proliferations differ from those observed in rheumatoid arthritis, not only in their later appearance but also in the form of the villi. They are much shorter, do not extend over the entire joint surface and do not show the same tendency to degeneration. The crunching sound elicited in the knees in osteoarthritis is due to the rubbing together of these villous masses.

In the late stages of the disease, the hypertrophied synovial villi undergo secondary changes and the membrane becomes comparatively smooth and atrophic. Strangeways explains this as being due to arterio-sclerotic changes in the vessels of the joint.

Intra-articular fibro-cartilaginous menisci, such as the semilunar cartilages of the knee-joint, degenerate and may eventually disappear altogether. The same changes occur in intra-articular ligaments such as the ligamentum teres or the crucial ligaments, and it is this disappearance of ligaments that form a source of deformity and of joint instability or of dislocation. In cases associated with much erosion and shortening of the articular ends, the joint capsule migrates and accommodates itself to the altered conditions in a remark-
able manner.

Tendons that pass through osteo-arthritic joints often undergo disintegration, while those which are attached to the articular capsules of such joints may present similar changes or their attachments may become profoundly modified. The tendon of the biceps is an example. In disease of the shoulder joint the intra-articular portion of the tendon may completely disappear and the intra-articular portion may acquire a new osseous attachment to the margins of the bicipital groove of the humerus. Rupture of the partially disintegrated tendon on one or both sides may occur suddenly and simulate traumatic rupture.

Owing to changes in the shape and direction of the articulating surfaces and alterations produced by osteophytic developments many tendons in the vicinity of joints have their courses and relations to these joints modified and may thus tend to bring about or increase the deformity. When tendons pass in close proximity to an osteo-arthritic joint associated with marked lipping such tendons may become temporarily entangled by an osteophyte, and locking may thus occur.

A new formation of bone may take place in tendons in relation to an osteoarthritic joint. This occurs most frequently in Charcot's disease but is often seen in non tabetic cases.

Rarer complications of osteoarthritis are supuration or formation of inflammation in the joint with formation of purulent matter as in a case reported by Fisher.

Fisher also reports a case of tuberculous synovitis which followed an osteo-arthritis in the knee joint.
Knaggs adds a third type to chronic arthritis by considering spondylitis deformans, because "clinically the actual condition in producing the rigid and usually bent spine may be far from clear," although it is acknowledged to be a manifestation of either the first or second of the other types. Pemberton does not believe however that there is any justification for creating such a third new type.

The muscles constitute part of the background of the rheumatoid disability. Osler and other authorities classify this form of disability as Myositis. The pathological picture in this type of disability consists chiefly in changes in the fibrous tissues. There is a dilatation of the smaller blood-vessels between the muscle bundles, with minute hemorrhagic extravasation. The interstitial tissue then becomes invaded by cellular infiltration and leukocytes range themselves between the individual muscle bundles and fibrils. The nuclei of the connective tissue soon undergoes proliferation and this newly-formed tissue infiltrates the muscles. As the process progresses, an interlacing character is acquired by the fibers of connective tissue which may then become so closely arrayed as to exert compression and separation of the muscle bundles and smaller muscular fibrils. This pressure induces degeneration of the muscular tissue, and late in the disease the latter becomes largely displaced and replaced by the newly-formed fibrous tissue. Thus there is a loss of muscle bulk, and this atrophy constitutes one of the later features of arthritis, especially of the proliferative type.
Thus in summary, degenerative or hypertrophic arthritis is characterized by fibrillation and degeneration of the joint cartilage, especially in its central portion together with an overgrowth of bone at the edges of the joint. Muscle atrophy when present is less rarely marked and consequently the deformities observed in atrophic arthritis are less common. Ankylosis due to adhesions does not occur but there may be locking of the joint due to exostoses. As the name implies this is primarily a senile degenerative process with little evidence of inflammation.
THE CLINICAL PICTURE OF CHRONIC ARTHRITIS.

It has already been pointed out that from the pathological point of view, the two great groups of chronic arthritis present definite distinguishing features. Both types however are definitely systemic in nature and the bony tissues are often caught up only incidentally to the march of the disease as a whole. Many persons who suffer great invalidism from the arthritic syndrome may yet show very little evidence of joint pathology. It is interesting to note therefore that the two types of the disease differ not only in the pathological picture presented but present a different clinical picture as well.
ATROPHIC ARTHRITIS.

Although this group is frequently encountered in both sexes it occurs more frequently in women than in men and although it may commence at almost any age from childhood to old age, it is much more frequently encountered between the ages of 20 and 40 years.

In a series of 100 cases recorded by Garrod, females were affected in 77 per cent and males in only 23 per cent. 63 of the total number of cases occurred between the ages of 20 and 40 years. Miller reports that the incidence is at least twice as frequent in women.

There is frequently a history of characteristic arthritis in one or more of the immediate members of the family.

The patients affected are more often than not undernourished, of the asthenic and ptotic build, "active in mind and body but easily fatigued", are moderately anaemic and frequently have had most of the infections as they came along, or have been chronically in poor health. However atrophic arthritis may arise in the midst of apparently robust health and may be practically, the first evidence of disease to which the patient has ever been subjected.

As discussed in Etiology the onset of typical cases of atrophic arthritis is often preceded by a period of unusual mental or bodily strain or severe exposure, and in many cases is preceded by an illness, particularly influenza. In monarticular cases, a history of some preceding injury to the affected joint
can often be obtained but not so frequently as in the hypertrophic type.

The onset of the disease may vary from an acute type, somewhat resembling rheumatic fever, to the more common subacute or insidious type with vague or migratory pains, intangible aches here and there or a general malaise.

In the acute form a number of joints are usually involved and the patient has a high fever. This type of onset occurs more frequently in the form in which peri-articular changes predominate.

Chronic arthritis is usually a polyarticular disease which may involve any joint in the body. When the onset is sudden, among the first complaints may be a development of pain, stiffness and swelling in several joints, accompanied by irregular fever varying from 99° to 101° Fahrenheit.

The joints usually first affected are the smaller joints of the hands and feet. In the hands the proximal interphalangeal and the metacarpo-phalangeal joints, and in the feet, the metatarso-phalangeal joints are the most commonly affected.

In the fingers there arises a somewhat symmetrical enlargement of the phalangeal joints usually at the midfinger joint. This swelling may consist in merely a slight thickening of the superficial tissues over the articulation or it may at once take a somewhat fusiform shape tapering both distally and centrally. This characteristic spindle shape is due to the fact that the capsular and synovial structures are particularly involved, with as a rule only a slight or moderate amount of synovial
effusion. There is an absence of bony enlargement and lipping except in late and chronic cases with the development of the hypertrophic types of changes.

On examination the affected joint may yield a "doughy sensation to the touch."

Pain is often a marked feature and is increased by movement, the patient usually taking the position in which he has the greatest ease. This pain and associated tenderness may be due to inflammatory changes in the joint, pressure upon enlarged synovial fringes, stretching of scar tissue or adhesions, mutual apposition of articular surfaces covered with sensitive connective tissue, or to reflex muscular spasm, the latter particularly applying to pain on movement in the more acute cases. In addition nerve pains are very commonly encountered and are either referred along the branches of the nerves supplying the affected joint or involve other nerves having no direct connection with the joint. A combination of arthritis and neuritis is thus very frequently encountered.

Lateral pressure over the joint margins will often elicit tenderness. Often this tenderness on pressure is present long before any other symptoms have become apparent.

In the earlier stages there may be a limitation of movement due to reflex muscular spasm which is increased by attempts at movement. This may lead to disuse of the joint and adjoining muscles. Gradually the more powerful flexors overcome the weakened extensors so that flexion often combined with other deformity occurs from the unopposed action of various muscle
groups. Characteristic deformities thus arise from atrophy of certain muscle groups and spasm of others. In the later stages however the deformity becomes fixed by the definite shortening of the capsule, ligaments and tendons, particularly on the side of flexion or in whatsoever direction the muscular spasm has been most marked.

Fisher has advanced the theory that Nature has favored the flexed position of a damaged or diseased joint because it is an actual advantage in the majority of four footed animals and is the position in which the limb least interferes with progression.

There is often a rapid muscular wasting which is not entirely the result of disuse of the joint or extremity. Fisher explains this as the result of a reflex wasting from impulses from the irritated articular nerves which interfere with the trophic action of the anterior cornual cells. This may also be the result of the development of fibrositis in the muscle tissues as explained in the discussion of Pathology. Muscle atrophy is most marked in the interosseous muscles of the dorsum of the hand.

The joint itself may undergo irreparable deformity from the destruction of the cartilage and atrophy of the bone characteristic of this type of chronic arthritis.

The subacute form involves many joints in succession. Alternating periods of quiescence and activity may occur, with each fresh subacute outbreak involving new joints so that the patient unless properly treated may become more and more crippled and helpless.

In the acute forms fever is a frequent feature of the
onset of the disease. It may rise to 102 or 103 F. but is frequently lower, often persisting for weeks at a maximum of about 100 F. In the chronic type it usually takes the form of a moderate nocturnal rise with morning remissions. In many cases fever is absent throughout. In other cases periods of fever with increased activity in the joints may alternate with afebrile periods.

A characteristic of most cases of atrophic arthritis is the rapid pulse. This is also rapid in proportion to the fever, the most frequent range being from 90 to 110 and often present even in afebrile cases. A return of the pulse rate to normal is considered by Fisher to indicate a subsidence of the active stages and carries a good prognosis.

Despite the close resemblance to acute rheumatic fever, cardiac involvement is the exception rather than the rule. Bannatyne found signs of cardiac involvement in 17.9 per cent of a total of 293 cases.

In the subacute of chronic type there may be a period of weeks, months or even years of mild discomfort as headache, mild fleeting pains in muscle groups or intangible aches in the joints before the typical joint symptoms are manifested.

These patients may also have a prodromal stage in which they have a sensation of intense fatigue. They may complain of tiredness even after a good night's rest although they may give no other indications of disease.

They may show the evidences of an unstable vasomotor system in which they may complain of sensations of tingling in the
extremities, their hands and feet may feel cold and clammy and they are notably affected by alteration in barometric pressure and humidity changes, they feel the damp and cold days uncomfortably and welcome the heat of summer. This trophic disturbance may lead to a seating glossiness of the skin especially of the soft parts surrounding the joints. The skin may sometimes show irregular areas of yellow pigmentation especially on the face and arms.

The nails may develop a change in the texture and appearance. They become striated longitudinally so that they tend to break easily.

The fingers may show a thickening at the peripheral edge. This may be complicated with a soft tissue infection which may be a source of chronic tenderness. Pemberton explains the basis of such infection as also being a result of decreased peripheral circulation.

In patients confined to bed or a wheel chair there may be edema of the dependent extremities. This peripheral stasis may be the result of an altered permeability of the smaller vessels or due to the failure of adequate muscle contraction to help the peripheral circulation.

Some cases may show glandular enlargement especially in those glands related to the affected joints. The spleen may be also enlarged especially in the younger patients.

Subcutaneous nodules occur in some cases and are sometimes very tender. They most frequently occur on the ulnar surface of the forearm and the dorsum of the fingers. They may be
identical with the rheumatic nodules encountered in children suffering from rheumatic fever in its more chronic form. Coates and Combs concluded that the constitution of rheumatic nodules in atrophic arthritis, Stills disease, and endocarditis lenta was histologically identical with those of true rheumatic fever. Garod observed that they are more tender and more permanent and occur at a later period of life than true rheumatic nodules.

The blood often shows an anemia, which may be very slight or may assume such large proportions as to constitute more of a complication than a symptom. This may be the result in some cases of infection with the streptococcus especially the hemolytic variety. It is especially more common in women than in men. There is rarely much increase in the leucocytes and the differential count seldom shows any peculiarity. The urine does not show any change of moment.

On physical examination these patients usually reveal evidence not only of foci of infection as in the teeth and tonsils but may show as Osgood states it "foci of ill health as may be revealed by evidences of endocrine, metabolic and gastrointestinal or central nervous system disfunctioning."

The reflexes are usually increased in acute cases and a return to normal is of good significance. They are sometimes absent.

Unless early recognized and appropriately treated, the end result of such a picture lead to an increasing down hill course characterized more and more by anorexia, deforming contracture, and hence disuse increased with terminal circulatory and trophic disturbances, ultimate confinement to the wheel chair or bed,
complete uselessness, utter despair and release often times only after many years of suffering by the tender agency of some intercurrent disease.

Cases in children resemble closely the disease in adults but in many cases may show striking differences. In the variety described by Still, the general enlargement of the joints is associated with enlargement of the lymph glands and the spleen. The onset is usually before the second dentition, and girls are more frequently affected than boys. At first there is slight stiffness in one or two joints; others gradually become involved. The onset may be acute with fever or even with chills. The enlargement of the joints is due rather to periarticular thickening than to bony change. The limitation of movement may be extreme, and there may be much muscular wasting. The enlargement of the lymph glands is striking, increases with fever, and may be general; even the epitrochlear glands may be as large as hazel nuts. The spleen can usually be felt. Sweating is often profuse and there may be anemia, but heart complications are rare. The children look puny and generally show arrest of development.
HYPERTROPHIC ARTHRITIS

In contrast the victim of hypertrophic arthritis is usually an individual who is hale and hearty. This type rarely makes its appearance before the age of 40, and invariably in an insidious manner, unaccompanied by the migratory aches and pains characterized by the atrophic type. These patients are well nourished, often obese and seldom anemic. With rather great regularity, one can obtain the history of a similar form of arthritis in antecedent members of the family.

Patients suffering from this type of arthritis will often give a history of an injury to the joint involved or may be engaged in an occupation in which the joint surfaces have been under a chronic strain or unfavored alignment. They seldom give a history suggestive of chronic infection and examination often fails to reveal any foci.

Chronic hypertrophic arthritis occurs so frequently after the menopause that Cecil has set aside a separate classification for this type of arthritis.

The onset of this type in many cases is so gradual and associated with such slight symptoms that patients may delay seeking advice until the changes have progressed to a marked degree.

The earliest symptoms are usually found in the terminal finger joints, the hip joint or the spine, but any joint in the body may be affected. The first evidence may be a trifling tenderness in the terminal phalangeal articulations upon
accidentally hitting the hand against some object. The first objective sign is apt to be a slight enlargement of the bone on one side of the joint in the form of a circumscribed round projection. This may from the onset involve both sides of the joint or later affect the joint itself. This nodular formation may increase in size and other fingers may become involved in a similar way. These nodules were first described by Heberdon in 1803 and they have been known for years as Heberdon's Nodes. At one time it was thought that they indicated there would be no further joint involvement, but this is no longer believed by such authorities as Pemberton and Fisher.

This type differs from the atrophic in that the enlargement in the shape of the joints is due principally to changes in the articular extremities themselves and changes in the capsule and periarticular structures are less marked.

Pain in this type is often less marked than in atrophic arthritis. In some cases definite hypertrophic changes may apparently give rise to no pain or other disability whatsoever. However in other cases, where the clinical and radiographic signs are slight, the patient may complain of severe pain. It is therefore impossible to estimate the probable severity of pain and other disability from the degree of hypertrophic changes present.

When weight bearing joints are involved as the knee the pain is often greater when aggravated by the trauma of use.

As mentioned under pathology the hypertrophic type of arthritis never leads to true bony ankylosis except in the spine.

Contact of bone with bone in opposed articulating surfaces
leads to loss of bone by friction, to eburnation, and to more or less compensating overgrowth but never to merger of one bone with another and the formation of a common medullary cavity.

Such limitation of movement as may exist is due to osteophytes and general alteration of alignment of the articular surfaces, to capsular and ligamentous contractions, and to muscular spasm with secondary shortening of periarticular tendons. In some cases as in the shoulder, hip and wrist, the shortening and alteration of alignment maybe so great that dislocation or even fracture maybe simulated.

Heberdons Nodes are permanent, but in the larger joints it is rare for the condition to advance to absolute, crippling, although there maybe considerable interference with function. Spondylitis rarely advances to complete immobility of the whole spine.

Because pain and disability are less marked than in atrophic arthritis movement of the involved joint and active use of the associated muscles are rarely completely inhibited. Muscular wasting is consequently not such a prominent feature as in rheumatic arthritis.

A common symptom in hypertrophic arthritis of the hip joint is a stiffness which is more marked in the early hours of the morning after the night's rest, and lessens or even completely disappears after exercise. In the early stages, such stiffness is the result of muscle spasm but in the course of time is supplemented by stiffness and limitation of movement due to organic changes.
The systemic reaction is usually less than that of atrophic arthritis. There is usually no fever, no leucocytosis and enlarged lymph glands are less frequent in this type.

Some authorities classify the vertebral form of chronic arthritis under a separate group termed spondylitis. This includes those cases which are characterized by a painful stiffness of the spine accompanied in many instances by a kyphotic deformity.

This may occur alone or with involvement of the peripheral joints.

Kneagle and Pemberton believe that these cases are simply expressions in the spine and associated structures of the two main types of chronic arthritis.

There are two varieties of general involvement which are sometimes regarded as special diseases. In the Von Bechterew type the spine alone is involved, and there are pronounced nerve root symptoms as pain, anesthesia, atrophy of the muscles, and ascending degeneration of the cord. Von Bechterew thinks it begins as a meningitis, leads to compression of the nerve roots, loss of function of the spinal muscles, atrophy of the intervertebral disks, and gradually ankylosis of the spine.

In the Strumpell-Marie type the hip and shoulder joints may be involved and the nervous symptoms are less prominent. Thus the root pains are less conspicuous or absent and the picture as a whole is that of progressive arthritis involving the spine and shoulder and pelvic girdles.

Besides the involvement of the muscles (fibrositis) and
nerves (neuritis) there may be an involvement of the uveal tract to the eye. The patient may show an injection of the inner or outer half of the ocular conjunctiva with few subjective symptoms.

The involvement of the articulations of the ossicles of the middle ear may lead to deafness. Tinnitus maybe present when the eighth nerve is involved.

Arthritic patients may show extreme nervousness, apprehension and irritability or they may appear depressed and melancholic.

Often a diagnosis of neurasthenia may be made before the joint symptoms of arthritis may be recognized.

Pemberton declares "skin diseases form frequent concomitants of arthritis the chief of which is probably psoriasis. Herpetiform eruptions are not uncommon and urticarial out-breaks are sometimes the cause of much discomfort. They rarely proceed to the point of angioneurotic edema.

The following table of differential characteristics of the two types of Chronic Arthritis is taken from Cecil with variations."
<table>
<thead>
<tr>
<th></th>
<th>Atrophic.</th>
<th>Hypertrophic.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Age at Onset.</td>
<td>Any age. Usually between 20 and 50.</td>
<td>Rarely before 40, most frequently in 5th and 6th decades.</td>
</tr>
<tr>
<td>Past History.</td>
<td>Frequent history of focal infection.</td>
<td>Less easily demonstrated.</td>
</tr>
<tr>
<td>Mode of Onset.</td>
<td>Rarely acute usually sub-acute, or insidious often accompanied by migratory pains.</td>
<td>Usually insidious and not accompanied by migratory pains.</td>
</tr>
<tr>
<td>Patients General</td>
<td>Usually undernourished, anemic, or chronically ill.</td>
<td>Well nourished, frequently obese, seldom anemic.</td>
</tr>
<tr>
<td>Evidence of infection.</td>
<td>Frequently slight fever leucocytosis.</td>
<td>Seldom fever, or leucocytosis.</td>
</tr>
<tr>
<td>Special joints.</td>
<td>Fusiform fingers.</td>
<td>Heberdens Nodes.</td>
</tr>
<tr>
<td>Appearance of joints.</td>
<td>Early-periarticular Swelling, late ankylosis, extreme deformity.</td>
<td>Early-Slight articul ar enlargement, late-Ankylosis never complete and usually no deformity.</td>
</tr>
<tr>
<td>Sediment Rate.</td>
<td>Usually greatly increased value.</td>
<td>Normal or slightly increased.</td>
</tr>
</tbody>
</table>
RADIOGRAPHIC APPEARANCE OF CHRONIC ARTHRITIS.

ATROPHIC ARTHRITIS.

In the early stages there is no obvious osseous change, but the spindle shaped enlargement of the soft parts may be demonstrated and in some cases evidence of fluid. In some types the hypertrophic synovial membrane can be observed.

Later, rarefaction of the cancellous tissue adjacent to the affected joints may be seen, which becomes even more prominent in late stages.

With commencing destruction of the articular cartilage the articular interval becomes appreciably lessened, and often one part of the joint is affected more than the other.

The final stage shows an absorption of the articular bone but there is an absence of the lipping as found in hypertrophic arthritis.

Occasionally osseous loose bodies are shown and small cysts may be found immediately adjacent to the articular surface.
HYPERTROPHIC ARTHRITIS.

The first change demonstrable by X-ray is the early periarticular lipping. Slight atrophy of the cancellous tissue adjacent to the articular surface shown by abnormal translucency is often present, but less than found in the atrophic type.

The late changes are characteristic. Narrowing of the joint interval is followed by erosion of the articular bone and alteration of the articulating surfaces.

The characteristic feature is the periarticular lipping. There may be cyst like spaces in the underlying cancellous tissue and also loose bodies, composed of cartilage, bone or of both usually derived from detached periarticular chondro-osteophytes.

In some cases, the X-ray shows formation of new bone upon the adjacent shaft due to ossifying periostitis.
PRINCIPLES OF TREATMENT

"Arthritis is a wide syndrome depending upon deviations of physiology expressing themselves in many or all tissues of the body, these depend in turn upon a large number of prodromal and precipitating influences. To expect to influence this varied syndrome by any one measure of therapy be it operative physiotherapeutics, drug or vaccine must appear unphilosophical and clinically inadequate."

In discussing a logical form of treatment for chronic arthritis we must consider first and foremost that it is a constitutional disease, with its most pronounced symptomatology in the joints and surrounding tissues. We can then classify our mode of treatment under two heads, general and specific.

Goering declares, "No routine method of treatment can be applied to all sufferers of this disease." Each patient should be considered as a separate problem. In every case it is highly important to take a very careful history of the individual. An initial hour spent in careful study of the case in question will oftentimes enable one to formulate a routine of treatment which may speedily and successfully combat the condition. Such a record includes not only the actual mode of onset of the symptoms and subsequent progression but also a detailed analysis of any and all factors in the patients environment which are and have been productive of fatigue and emotional upset.

A complete physical examination should follow, accurate
note should be made as to the body mechanics, and of all joints with any abnormality thereof; together with a record of the possible range of motion. Evidence of vaso motor instability is sought as a sign of disturbance in the sympathetic nervous system, for example abnormally pale, or cyanotic or sweating hands and feet, pronounced blood pressure changes with slight exertion or unusual coldness of extremities.

X-ray should be ordered of the more seriously involved joints to aid in confirming the diagnosis of the type of arthritis. Suggestive activity in possible foci of infection observed in the initial examination should then be investigated in detail.

A complete examination should include such details as menstrual history, a pelvic examination, urinalysis, blood count, and a basal metabolism study may be indicated.

Survey of the information thus gained will indicate the lines along which treatment is directed and may indicate the value of further examination.

In reviewing the subject of chronic arthritis one is impressed particularly by the great significance of early recognition of the prodromal signs of the disease. It is at this period in the patient's life that the greatest possible good can be done with the least expenditure of time and effort. As stated before at this stage, joint signs may not be the chief complaint. Early recognition of these cases followed by prompt appropriate treatment will immeasurably aid in reducing the present unnecessary and excessive social and economic loss from chronic arthritis.
From the important studies made as to the etiology of chronic arthritis it is clear that removal of existing foci of infection is an important step in the removing of one of the fundamental causes of the disease in many cases.

Foci of infection which may be inactive at any particular time may, under circumstances of reduced resistance in the patient produce disease. Therefore most authorities agree that the removal of all sources of infection is the proper therapeutic approach as such foci always constitute a potential menace.

Cecil emphasizes that in order to obtain the best results from the elimination of foci of infection, such elimination must be carried out early in the course of the disease. In a study of 200 cases of chronic arthritis Cecil and Archer found that the prognosis depended upon the promptness with which foci of infection were discovered and removed. 82 per cent of the cases treated early were either cured or definitely improved. In a group of 40 cases where no improvement was noticed, the disease had lasted 5 years before the treatment was instituted.

This may be explained as the result of the originally localized focus of infection becoming more widespread. Thus in early forms of buccal, nasal or pharyngeal infection the patient may be constantly swallowing septic organisms which may give a diffuse secondary infection of the intestinal tract. The organisms may also gain access to the circulation and be carried to the joint which may then itself act as a focus from which other joints may be infected.
The infective focus may disturb the body metabolism or bring about endocrine disturbances so that although the primary focus may be satisfactorily treated, the change in physiology may still persist.

Another important reason for speedy action in removal of foci of infection is the fact that when definite changes of degeneration or hyperplasia have once taken place in the joint, the removal of infective foci cannot restore the joint to its normal condition.

When on examination the tonsils show evidence of disease, particularly if on pressure pus is made to exude from their crypts, they should be removed. As stated before the appearance of tonsils productive of systemic harm is not constant or characteristic. Margolis states, "It is far safer for the patient with arthritis to lose tonsils removed on suspicion and later found innocent, than to ignore the small tonsils that are so frequently the source of concealed infection."

If the patient has a very active case of arthritis it is a good policy to postpone the removal of the tonsils until the patient has had a series of injections of vaccine in order to ward off the possibility of an acute exacerbation following the tonsillectomy.

Infection in the teeth found either by dental examination or by x-ray should be eliminated. It is often very difficult to determine correctly if teeth harbor infection so the examination should be a careful one and done by an expert dental surgeon.
When an infected tooth is removed an attempt should be made if circumstances permit, to obtain a culture to determine the infective organism and to prepare a vaccine for possible subsequent use.

In many cases it is unwise to remove more than one or two infected teeth at a time because of the danger of a severe reaction with aggravation of the arthritis.

The extraction of normal teeth is never justified as teeth are important structures and have an important function in adequate digestion.

Another important site of infection within the mouth is the gums which may be the seat of a mild gingivitis or extensive pyorrhea. If present this should be eliminated by vigorous treatment against the causative organism.

This may consist of medical treatment or by a radical operation consisting of laying back a section of gum flap and excising the necrotic tissue.

The nasal accessory sinuses are frequently the source of chronic infection. The usual diagnostic methods of X-ray and transillumination are indicated. The principle of treatment of all such cases should be adequate drainage and a radical operation by a skilled operator may be indicated. In some patients this may be too severe without a preliminary attempt to build up his resistance to infection. Pemberton declares with the exception of the maxillary sinus the other antrums often fail to drain adequately even after operation which has led him to adopt a more conservative attitude. He suggests the building up of the patients resistance.
so that the mechanism of nature may overcome the infection.

In many cases the genito-urinary tract may serve as a site of focal infection. In a study of 700 cases Pemberton found it present in 14 per cent of the cases, and more often present in men than in women.

In man the chief focus is the prostate. This may be entirely non venereal in nature though in some cases it has its incipiency in venereal disease. The usual methods of diagnosis by rectal examination and examination of secretion expressed after rectal palpation may reveal the causative organism. As a rule infection of the prostate is slow in recovery. Massage of the gland is one way to establish drainage. Pemberton recommends the use of an autogenous vaccine if possible, or depending upon the etiology of the infection, stock vaccines may be used.

Dr. Pelouze has called attention to the frequency with which prostatic infections are associated with other foci of infection and stresses the importance of removal of these sources before improvement in the prostate can be expected.

Infection in the seminal vesicles, bladder or elsewhere should be carefully analyzed and treated by one thoroughly conversant in this field. Infection of the kidney proper or pyelitis as shown by the urine may be responsible in some cases.

A frequent finding in women may be a cervicitis or endocervicitis resulting from parturition and which may act as a focus of infection. Venereal disease may leave as a complication an infected condition of the vaginal mucosa, or of the
glands of Bartholin. Moench of the Mayo Clinic, reported the improvement of several cases of arthritis following the clearing up of such pelvic foci.

As emphasized before, hypertrophic arthritis is most common in women during the climacteric and Cecil has described this group as "arthritis of the menopause." This suggests the use of Ovarian extract for treatment but Cecil reports little success in its usage.

The gall-bladder, appendix, or diverticuli of the intestinal tract may harbor definite and localized foci of infection. Other sites may be an ulceration of the intestine, or infection of the tubular glands of the colon. Any part of the intestinal tract may be involved and a careful study of the case may be required to make a correct diagnosis. As elsewhere, the best treatment for focal infection is removal if possible. Surgery is usually indicated for pathology of the biliary tract, the appendix and diverticulitis, unless the patient is in too weak condition to stand the strain of such procedures.

The Mutch theory of intestinal infection assumes that infective pathogenic organisms are absorbed from some portion of the intestinal tract into the circulation and carried to the affected joint or joints. In as much as he believes the pathogenic organism is a long chained streptococcus not normally found in the bowel, the treatment suggested is the prevention of stasis which favors bacterial growth and spread of infection. The organism has a pronounced glycophile tendency which may explain the benefit that often follows after a decrease of the
carbohydrate intake.

Arbuthnot Lane believes that arthritis may be due to the absorption into the circulation and their deposit in joints of putrefactive products from the bowel in cases of intestinal stasis. Pemberton does not consider that protein putrefaction in the bowel plays an important part in causation however.

Pemberton has called attention to the malfunction of the colon as being a frequent and important cause of chronic arthritis as discussed in etiology. In these cases the colon is characterized by a tendency toward greater caliber, greater length, a more convoluted appearance and sometimes reduplication as shown by the X-ray.

This abnormal configuration may favor a derangement in physiology such as stasis and absorption of putrefactive products or favor the growth of harmful pathogens.

Care should be taken to avoid as far as possible the use of drugs and to rely as much as possible upon a suitable diet and upon improving the tone of the abdominal muscles. Liquid paraffin is a valuable adjunct in many cases. Following treatment of this nature ample rest should be insisted on. The treatment suggested by Pemberton is adequate evacuation especially by means of colonic irrigation of the lower intestinal tract.

Colonic massage is suggested after a roentgenographic study to determine any possible contra-indications to such manipulation. This consists of beginning at a point in the lower left quadrant of the abdomen and progressing distally toward the rectum, after which another point is selected 2 or 3 inches higher up and the
same process repeated. In this manner points are selected in turn until the final massage begins at the caput coli and progresses the entire length of the colon as far as it can be followed down the sigmoid.

This should be followed by colonic irrigation by one trained in this procedure. The solution recommended is normal saline, or a 5% solution of sodium bicarbonate at slightly above body temperature, 40°C.

In patients who are very constipated it is suggested to give a cathartic such as cascara shortly after the irrigation to provide an evacuation on the subsequent day. The usual frequency of the irrigation is every other day at least at the outset.

Rowland produced dilatation of the colon in rats by the restriction of vitamin B in their diet, which was also high in carbohydrates with a deficiency in proteins. Fletcher has shown that concurrently with the decrease in carbohydrates intake and a sufficient intake of vitamins and proteins the large bowel often returns to normal. Thus the treatment is not one of purgation alone or of "washing out" putrefactive material or bacteria from the colon but the institution of an appropriate dietary as well.

Some cases may show an achlorhydria. This should be treated by the administration of hydrochloric acid with meals.

Ely and his associates found the Entamoeba histolytica around the roots of teeth and believed they gained access to the circulation through alveolar infections and caused hypertrophic arthritis. They suggest as treatment the removal
of the portal of entry by extraction of the teeth. If amoebae are found in the stools he suggests the use of ipecac for their eradication. Barrow cites six cases of arthritis in which he reported good results from treatment by ipecac and its alkaloid emetine in conjunction with enemata. If ipecac is used 3gm (45 grains) is given in enteric pills at night, preceded by 4 gm of bismuth subcarbonate and a hypodermic of morphine sulphate 1/4 grain. The dose is reduced by 5 grains each night, and the treatment continued for five or six nights. Emetine-bismuth-iodide, may be used instead in doses of 3 grains one to 3 times a day by mouth. It is better borne than ipecac but is more apt to produce diarrhea. Emetine hydrochloride may be used subcutaneously in daily dosage of 0.02 to 0.06 gm. (1/3-1 grain. It should not be continued beyond ten successive days.

Pemberton says the alleged results of treatment have not as yet had such corroboration at the hands of others as to lead one to unqualifiedly accept amebiasis as a main or underlying cause of hypertrophic arthritis.
DIET

As long ago as 1909 Llewellyn called attention to the undesirability of total abstention from meat in atrophic arthritis, and pointed out that the vetoing of meat in these cases was due to a confusion with gout.

Pemberton has pointed out that reduction of diet is followed by definite benefit in a certain proportion of cases. Because of the anatomical derangement or physiological dysfunction noted in many cases, the lightening of the intake or burden upon the digestive tract may have valuable results. Cajorl, Crouter and Pemberton have shown that in 60% of arthritics there is a lowered rate of basal metabolism and that the sugar tolerance is lowered in a degree proportionate to the arthritis present. They concluded there is a delayed rate of sugar removal from the blood after ingestion by mouth. This is a function of the blood supply to the muscles which are involved in the first stage of carbohydrate utilization. They suggest the reduction of food intake to cut down the metabolic load upon these structures, especially the carbohydrate intake.

It is difficult to determine beforehand cases in which dietetic measure are appropriate. Decision to this end must be reached partly by the exclusion of other possibly causative factors.

The balance of the health of the individual as a whole must be made the guiding principal with which dietetic res-
triction is used. Thus if the individual is obese or has been a large eater this is easily carried out without detriment to the nutritional needs. In these cases, particularly when the joints of the lower extremity are involved, the reduction of body weight is of particular value in diminishing intra-articular friction and painful tension. Unfortunately many sufferers from chronic arthritis are enfeebled and debilitated and such persons require building up by means of a generous diet. It is also obviously improper and dangerous to institute underfeeding, or merely the theoretical requirements at rest, in the presence of marked focal infection.

In cases of chronic arthritis suitable for dietetic therapy, treatment must be carried to at least the point where the individual is spared the necessity of metabolizing as much food as he had been previously ingesting. The best method of approach is first a study of the actual dietary habits and food intake of the individual over a period of at least one week. The accustomed caloric intake of a given case under the average conditions of his invalidism is thus determined. If the patient be ingesting customarily a fairly large quantity of food, say 3200 calories, this quota can be reduced to 2200 calories without great detriment to his nutritive needs, at the same time sparing him about 1000 calories. If, on the other hand, the food intake has been 2000 calories, or less, the administration of a diet of 2300, calories would fail to achieve its purpose and might tend to aggravate existing conditions. It is also useful if possible to determine the percentage distribution of calories
from protein, fat and carbohydrate because carbohydrate is the chief offender by virtue of its quick combustion and the large role it plays in an average diet. Some questioning as to the taste of the patient should be carried out so that the restricted diet may be made to suit his taste as much as possible.

"In most cases a safe and useful dietary can be drawn up on the basis of 30 calories per kilo of body weight in persons who are of average body contour and not obese." Fats offer the fewest disadvantages to the arthritic from the diabetic standpoint and can be used to increase the caloric value of the diet to the desired level.

In Pemberton's experience, cases of fifteen to twenty years standing with marked deformity have responded promptly, upon the institution of a diet, sometimes in conjunction with other appropriately co-ordinated measures. "Thus cases accustomed to a food intake of 2800 to 3000 calories or more, may do very well from the start and shortly recover entirely following a reduction of their caloric intake to about 2000 calories. It is often possible in these cases to increase this total by two or three hundred calories preferably from fat, a few weeks after convalescence is well established."

In the application of a reduced dietary in the average case of good nutrition it is well to begin with a balanced diet, however limited the nutritional value of it may be. There is no restriction against any particular food outside of a restriction in total calories. Thus so called "acid fruits"
should play a large part in the dietary notwithstanding the prejudice against them which exists in the minds of many of the laity. "There is no evidence of a systemic acidosis in arthritis to which the ingestion of acids could seriously contribute." Any disturbance of the acid-base equilibrium in the joints is more dependent or secondary to a disturbance in the blood supply of the part. Furthermore, fruits are necessary in any restricted ration because of their vitamin and mineral content.

The institution of a great reduction in calories can not be conducted for longer than a week or ten days. The reduction of energy intake must be balanced by comparable reduction of energy outgo which means curtailment of physical and mental activities. If the patient shows signs of asthenia, it may be necessary to place him on a high nutrition diet for a few days. The general nutrition of a subject is the important factor in determining the degree to which treatment can be pushed, and the individual, not the arthritis, must often determine the vigor of treatment. "It is of small benefit to improve the arthritis at the expense of the patient's health as a whole."

When treatment has been successfully underway for perhaps three weeks, small additions can be made to the diet, preferably in the form of fats such as cream and butter. As satisfactory progress continues, an added tolerance for food is acquired. As more food is eaten, more exercise can be allowed and the increase in exercise will increase the demand for food. Such patients should be instructed to follow an established type of
diet and always refrain from over eating.

The subject of making up a diet to confirm to the required amount of calories is beyond the scope of this work. I can best illustrate the use of a diet regime by citing a case reported by Pemberton. 

"T. G. aged 48 had atrophic arthritis of 14 years duration involving all the joints of her limbs. Diseased remnants of tonsils had been removed 8 months before present admission. She was constive and had very long, reduplicated colon with ileocecal regurgitation. She was rested for a week in the ward on ward diet, before treatment was instituted. The ward diet is fairly high in carbohydrates. Objectively the patient became definitely worse during this week and her hands and knees became more swollen and painful. After 48 hours on a relative fast her hands became less swollen and more wrinkled. A further improvement in hands, knees and other joints followed this regimen. On the first and second day she received only the juice of one orange three times a day and ample water. Third day, the juice of one orange, one cup of coffee, one dram of sugar. Fourth day, same as third plus 8 oz. of vegetable soup. Fifth day, same as fourth day plus 3 Uneeda bisquits. Sixth day, a semi-liquid diet. Seventh day, 1221 caloric diet. Ninth day to thirty-eighth day, 1465 calories. Thirty-ninth day, diet of 1800 calories. Thus on bed rest, plus a low carbohydrate, low caloric diet, she became promptly and definitely better. The improvement was beyond dispute and the patient volunteered similar evidence. The two main types of
arthritis atrophic and hypertrophic in nine cases each showed
great improvement of full recovery as a result of the same
measures."

Many authorities have believed that the Streptoccus
hemolyticus contributes toward production of anemia in many
cases of arthritis. Whipple, Minot and Murphy have shown that
meat especially liver substance contributes toward the
regeneration of the blood elements. Therefore to withhold
meat in arthritic cases may contribute toward the production of
a secondary anemia.

"It is of the highest importance that the patient receives
his necessary quota of protein which should be at the very least
0.7 gm per kilo of body weight."

Pemberton has not found any improvement in cases following
the substitution of the fermentative for the putrefactive types
of intestinal flora by the use of feeding of the acidophilus
organism properly fortified by an adequate supply of carbo-
hydrate to form a favorable environment.

Haggart, believes that oxalic acid bearing fruits and
Vegetables should be cut out from the diet despite that most
of them are vitamin containers, because he wishes to avoid the
extraction of calcium and the production of excess calcium
oxalate crystals.

He forbids excess salt, condiments, spices and irritating
food and drink of all sorts, because their action on the mucous
membrane of the gut, allows more permeability and a greater
absorption of streptococci.

He urges that the patient drink 6 to 8 glasses of hot water
between meals each day.

Fletcher has verified Pemberton's observations as to the benefit of a restricted diet, and has obtained the best results in female patients. In a series of 100 cases reduction of the diet alone, resulted in the complete recovery of 8 patients and clinical improvement in 43.

Cecil believes that the diet should be curtailed only when the patient is overweight, when no foci of infection can be found, or when the removal of infection and treatment by other measures has proved ineffective. He does not believe that either the carbohydrates, fats or proteins exercise any specific influence upon the arthritic process.
MEDICAL TREATMENT

In contradistinction to the comparative reliability of action of drugs in many other diseases, as the action of salicylates in acute rheumatism there is no drug that appears to have any specific action in the varieties of chronic arthritis. The etiological factors are so complex that it may be said that no two cases of chronic arthritis are exactly alike. Therefore in any individual case some etiological factor or some particular symptom may predominate in the clinical picture and the physician should prescribe accordingly.

In view of the chronicity of the disease and the restricted diet of many of the patients, cod liver oil may be necessary to supply additional calories and to afford vitamins A and D. Since arthritis is a disease involving bony structures vitamin D may be needed for proper calcium metabolism.

Fletcher has shown that the loss of tonicity and reduplication of the colon in many cases of arthritis may be corrected to a marked degree by the administration of vitamin B. This may be administered in the form of yeast, as one or two cakes a day, or in the yeast extract described by Wakeman and Osborn and known as "Harris yeast". The dose is 6-8 tablets daily. The yeast extract is supposed to obviate the gas which accompanies administration of the yeast itself.

Guaicol carbonate has been used in some cases as an intestinal disinfectant, but is uncertain in its action. It
is given in 0.3Gm (5 grains) capsules.

Some patients may show a low urine ph or a high acidity, Young recommends the administration of calcium salts as calcium lactate to change the urinary reaction, to neutral or slightly alkaline. The dose is 2 to 3 Gm (30-45 grains) twice a day an hour before meals or at bedtime. The same results may be obtained by a milk and custard diet or the use of citrous fruits.

Tonics may be needed because of the loss of weight, anorexia or anemia. Arsenic is used in some cases. It is supposed to improve the appetite and give some relief from pain due to a betterment of the underlying pathology by regeneration of the blood elements. Pemberton suggests the use of Fowlers solution starting with an initial dose of 1 drop three times a day, increasing 1 drop at one dose daily or perhaps every other day. This should only be used under the restriction of the usual contraindications to this drug and should be discontinued when any toxic effects are displayed by the patient.

Strychine may be given in small doses to those patients showing lack of muscle tone. The well known I.Q.S. mixture is a good combination along with postural exercises. It should never be given in large doses and should be interrupted at the first signs of strychnine poisoning.

Potassium iodide or one of its substitutes may be used as an "alterative" during convalescence. It may be used for its affect on the thyroid and so possibly on metabolism at large. Tincture of Iodine in doses of 5 to 10 drops is recommended
by Osler. Young says that as the action of iodin is not definitely known its use must be considered to be empirical.

Experiments have shown that there is apparently a failure of the blood to adequately reach the periphery of the body in many cases of arthritis. With this fact in mind, drugs have been used for their effect on the circulation.

Pemberton recommends the use of Digitalis in small doses as 3–5 ms. t.i.d. as a means of stimulating the heart to improve blood flow. Young however questions this as the heart is not ordinarily involved and the drug does not affect the normal heart unless given in toxic doses.

Pemberton and Pierce have reported a favorable influence on 12 cases out of 32 arthritic patients by the use of nitrites. They used erythroltetranitrate starting with 1/12 gr. and increased it slowly up to 1/4 gr., t.i.d. They do not recommend its routine use as better and more prolonged vaso-dilator effects can be obtained by heat and massage.

Young warns that nitrites may produce methma-globinemia if given over an extensive period of time and the vasodilation is done at the expense of a lowered blood pressure.

One of the most important of the groups of drugs used in the treatment of chronic arthritis are the salicylates. They have no known specific value such as found in acute inflammatory rheumatism but are valuable in meeting emergencies such as discomfort on exertion or during acute exacerbation, because of their analgesic properties. Cushny has suggested that they are capable of opening the deranged physiology. These drugs
in many cases may produce loss of appetite and indigestion. Swift showed that salicylates decrease the properties of the blood for specific antibody formation. Miller showed that the prophylactic administration of salicylates did not protect rabbits against arthritis produced by intravenous injection of hemolytic streptococci. Davis found that rabbits with streptococcic arthritis that were treated with salicylates frequently died sooner than the controls. Young concluded that cinchophen and the salicylates should only be used as analgesics and antipyretics, but no permanent relief should be expected from such drugs.

Aispirin is the least expensive of the salicylates and gives quick action. Phenacetin and acetanilid have a destructive action on the red blood corpuscles so should be used only occasionally when other analgesics become intolerable. One should never use codeine or morphin except under unusual circumstances because of the danger of forming a habit.

Pemberton recommends the use of quinine in doses of 2 gr. three or four times a day as a tonic and mild analgesic substitute in those some cases complaining of fatigue and anorexia.

Since there is no definite information on which to base an opinion as to the role played by endocrines in chronic arthritis it is difficult to evaluate or explain the use of endocrine extracts in this condition. Thyroid in the form of the dried gland has been used in doses of 5 to 15 gr. daily until the pulse rate or nervous condition of the patient
is determined. This type of therapy is most successful in women at the menopause.

Years ago, Nathan suggested the use of thymus extract as treatment but it has practically been abandoned.

If the patient is constipated and does not respond to abdominal exercises or diet, a mild cathartic as the aromatic fluid extract of cascara, or mineral oil may be used to promote evacuation.

In 1926 Young and Youmans introduced the use of ortho-iodoxy benzoic acid in the treatment of chronic arthritis. The composition of the drug closely resembles that of salicylic acid which is ortho-hydroxy benzoic acid. It has been shown to be an antiseptic and also capable of producing non specific antibody formation upon intravenous injection in animals. Young and Youmans reported a series of 43 patients treated with the drug. Fifty-six per cent showed marked improvement, thirty-seven per cent some improvement and seven per cent no improvement at all. The best results were obtained in patients having had the disease for less than 5 years.

Millard Smith reported 12 cases of chronic arthritis in which this treatment was used. Three cases received no relief from the drug but improvement was shown in the remaining nine cases. As the results of his experiments he places this drug as being among the most important drugs available in the treatment of arthritis.

Trauba reported a series of 31 cases treated by this drug. Sixteen percent showed moderate improvement, thirty-seven percent slight improvement and twenty-nine per cent were
unimproved. He found that the drug often caused thrombosis of the veins and this prevented repeated injections.

Cottrell reported 6 cases of chronic arthritis treated with the drug with encouraging results.

After treating a series of cases by this method Pemberton reached the conclusion that the drug is a glorified salicylate in that there may be a large amount of analgesia over a period of time longer than following the usual salicylates but accompanied often by the relapse characteristic of salicylates.

Stein and Taube reported a series of 102 cases with the conclusion that 2 cases of acute rheumatic fever were made worse, 31 claimed temporary relief of pain but nearly all returned later with the same symptoms.

Cecil has used this treatment on a series of cases with discouraging results and any benefit the patient derived was only temporary.

Young believes the drug acts by virtue of its oxidizing properties which bring about a depression of the sympathetics thereby increasing the peripheral capillary and lymph flow. He believes its use should be combined with the removal of foci of infection and general hygiene measures.

Achin found that the drug stimulates phagocytosis of streptococci and staphlococci by human leucocytes and attributed this to stimulation of the opsonins by the liberation of oxygen.

The drug may be given intravenously, orally, or by rectum but the intravenous route gives the best results although it
may be followed by reaction as pain along the course of the
vein, and a smarting of the mouth or face, with perspiration,
cramps, nausea, vomiting and a feeling of intense discomfort.
The vein is partially or completely obliterated in many cases.
The dosage by mouth is approximately 1gm twice or four times
weekly. Intravenously the initial dose is 0.5gm increasing
to 1.5gm depending upon the reaction. Usually about 10gms.
in all are given over a period of 3 weeks, divided as follows,
0.5gm to 1gm weekly for 4 doses, 1 gm 3 times weekly for 4 doses,
1.5 gm at the same interval for 2 doses. The whole course
can be repeated if necessary after the lapse of about two or
three weeks. The sodium or ammonium salt is made up to a 1%
solution at body temperature and sterile. It should not be
boiled or allowed to stand for more than 5 hours after pre-
paration. It is given at body temperatures intravenously by
the gravity method over a period of not less than 7 minutes
to 15 minutes. The dose may be repeated every other day when
well tolerated. The rectal dose of 0.1gm after a cleansing
enema is less effective than the intravenous dosage but produces
a less severe reaction. These injections should come at
intervals of 4 or 5 days and should be about 9 in all.

Young suggests the use of a small needle of about 22 gauge
and elevating the gravity set about 4 feet above the patients
arm. In this way one may avoid too rapid a flow into the vein.
The toxicity of the pure salt depends more on the rate of
injection than upon the amount given. In experimental animals
death is usually of a respiratory nature in toxic doses, but
may be circulatory due to heart failure.

Ulum reports a death in a patient from the use of the drug but a pharmacologist on examining the drug reported it contained some very toxic ingredients aside from the ammonium salt of oxy-iodoxy benzoic acid.

The drugs should only be used in conjunction with other methods of treatment as indicated by the specific condition of the patient. When drug treatment is instituted it should be done with the definite purpose of correcting some phase of the patient's illness and not with the idea of using a specific or a cure-all.
NON SPECIFIC PROTEIN THERAPY

Following the discovery that the body defensive mechanisms may be stimulated by the injection of non-specific proteins, this type of treatment has been used in many conditions.

In 1916, Miller and Lusk suggested the use of non-specific proteins in the treatment of chronic arthrits. They reported 85 cases of chronic arthrits which were treated by the intravenous injection of typhoid vaccine. In the chronic cases about 50 per cent showed improvement. Jobling and Petersen, treated 13 patients with intravenous injection of secondary proteoses, and reported favorable results.

Cecil reported using the intravenous injection of hemolytic streptococcus vaccine on a number of patients with fair results. The vaccine gave a good reaction and the patients felt better for 24 hours but the symptoms returned thereafter and there was no abatement of the disease.

Peterson, gives a long list of non-specific agents ranging from counter-irritants such as blisters, various sera, phylacogens, histamine, egg albumin, milk, colloidal metals, artificial sunlight to Roentgen rays and radium, but the most commonly used non-specific proteins are the typhoid or T.A.B. vaccines, the Bacillus coli vaccine and milk.

The typhoid, T.A.B. and coli vaccines are used intravenously, and milk intramuscularly.

The immediate result of these injections is a definite and often severe reaction which has received many names, but which is generally termed "protein shock".
The intravenous injection as a rule is followed by a more violent systemic reaction than usually takes place after subcutaneous or intramuscular injection.

The reaction also varies with the method employed, the dosage and the general health of the patient.

Generally thirty minutes to some hours after the injection, chilliness, headache, nausea and general malaise develop, and later a rigor, which may be very severe. The temperature may rise rapidly and there is a corresponding rise in pulse rate and a fall in the blood pressure. After 24-36 hours or less the patient commences to sweat, the temperature falls rapidly, the pulse quickly returns to normal and the blood pressure rises again.

In the successful cases, after the period of shock has passed a sense of well-being follows and the arthritic and muscular stiffness and pain, which during the period of shock may be intensified, are greatly diminished.

At the commencement of the reaction there is a peripheral leucopenia in which both the polymorphonuclear and the mononuclear cells are lessened. The leucopenia is later replaced by a definite leucocytosis particularly affecting the polymorphonuclear cells. Both the mononuclear and polymorphonuclear cells counts return to normal.

Pemberton believes that much of the benefit derived may be due to the increased blood flow and heightened metabolism secondary to the hyperpyrexia induced.

By studying blister fluid, Peterson found that the cell
membranes of the capillaries become more permeable and the serum proteose is diminished during the reaction and later increased after the reaction. He concluded that the sensitized cells give up their antibodies and the cellular reaction to toxic poisoning is increased. This increased permeability is related to the ratio of calcium and potassium in the endothelial cells.

Fisher declares the effect may be compared to that of an acute intercurrent infection upon some chronic disease. The improvement may be the result of the increased leucocytosis, the increased lymph flow, the sweating or to an alteration in the ferment and antiferment action of the blood serum.

Miller and Lusk recommended a dosage of 125,000,000 typhoid organisms for the first dose but Pemberton recommends smaller dose of 75,000,000 at the beginning.

Fisher recommends a preliminary injection of 30 million organisms, increasing the dose every fifth day until at the sixth and final injection a dose of 200 million is administered.

Cowie treated 19 cases of arthritis with typhoid vaccine and reported 1 cured, 7 improved and 11 unimproved.

Laurie preferred the use of coli vaccine because of the ease of preparation. His first injection was 25 millions or less, his largest dose 12,000 but he found the smaller doses produced an equally good reaction.

Poynton found the method produced good results in some cases but the improvement was often only temporary.

Cruickshank produced protein shock by giving peptone intramuscularly in amounts varying from 0.3 to 0.6 grams.
Snyder and Ramirez prefer to use the secondary proteoses prepared from milk, using 1/2 to 1 grain as a dose. They obtained good results in 8.5 per cent of their cases whose arthritic symptoms had been present less than two years.

Milk may be used in the form of ordinary milk properly sterilized or preferably in the form of one of the commercial preparations on the market. An objection to ordinary milk is that the nonspecific protein reaction may depend not only upon the protein in the milk, but also upon the organisms invariably present in the milk, even under careful conditions of collection. Therefore standardization is more difficult, since two variables are concerned, especially if ordinary milk is selected. The ideal dose begins with 5 to 10 c.c. intramuscularly.

Another form of treatment is the use of Coley's fluid recommended by Torrey and Klein. This consists of a mixture of streptococcus and Bacillus prodigiosus. The initial dose should be 1/4 minim and increased by an equal amount at intervals of 4 or 5 days or twice that period depending on the reaction obtained, to a maximum of 8 minims. The site of election for most such injections is above the insertion of the deltoid. The greatest benefit from non-specific protein is in the acute and subacute types.

Milk injections are less effectual than Tab or Bacillus coli injections but less severe in the shock they produce. The results are uncertain and although one patient does well, improvement cannot be guaranteed in another case, which is apparently similar in character. In order to obtain a result it
is necessary to produce definite reaction and this requires considerable fortitude on the part of the patient.

Poynton warns that it is a method of treatment in which the patient is made actively ill, and fatal cases have resulted. Patients with severe cardiac disease, greatly debilitated, or with damaged kidneys are unsuitable for protein shock.
VACCINE TREATMENT

In view of the apparently infectious nature of many cases of chronic arthritis especially of the atrophic type, it would seem that vaccine therapy would be of great value.

As discussed in etiology, many investigators have been able to culture organisms from the blood, joint fluid and tissues, the lymph nodes and subcutaneous nodules.

The predominence of streptococci in cultures speaks strongly for this being the most frequent etiological agent. Some authorities believe in a specific streptococcus while others believe that various streptococci are capable of producing the disease.

Birkhaug showed by skin tests that patients having chronic arthritis were hypersensitive to streptococcic protein in a higher percentage than normal persons. Clawson obtained similar results in a study of 127 cases of chronic arthritis and 107 normal persons.

Nichols and Stainsby found that the serum of patients with chronic arthritis agglutinated streptoccci in higher dilution than that of normal persons.

Clawson tested the serums of 81 normal individuals and that of 66 patients suffering from chronic arthritis. The strain of streptococcus used was isolated from a case of chronic arthritis. It was found that sixty percent of the chronic arthritic patients showed agglutination in a dilution
above 1:400 while only 28 percent of the normal persons studied showed agglutinations above 1:400. They concluded that a rise in the titer of streptococcus agglutination indicated that the patient is developing a resistance to streptococcal infections.

Kolmer has pointed out that the anatomical structure of the joints and synovial membrane favors bacterial embolism and he believes that gonococcal arthritis for example is produced in this manner rather than by the elaboration of toxic substances at some removed focus. In any event it would be highly desirable to develop or increase the immunity toward organisms productive of an arthritis wherever they may be located.

Fisher declares, "The use of antigens in the rheumatoid type should never be substituted for the eradication of septic focus but when this object has as far as possible been achieved vaccine treatment is often of great value in increasing the natural powers of resistance and thus enabling the patient to overcome any residual infection."

Stone is of the opinion that the effect of such therapy is to stimulate the production of antibodies, which combine with the infective organism and so alter its physical or chemical nature that it no longer produces systemic reactions.

He does not consider vaccines to be actually bactericidal, and points out as an illustration their inability to destroy the circulating bacteria in subacute "infective" endocarditis.

He declares the type of case most likely to prove
successful is an early rheumatoid arthritic in which there is a definite local focus from which an autogenous vaccine can be obtained. If no local lesion can be discovered he advocates the use of a stock vaccine containing various strains of streptococci. The dosage should be very small at first to avoid if possible any reactions in the affected joints. One million bacteria, given subcutaneously, is the average first dose, after three or four of these the dose should not be doubled but be gradually increased by one-quarter or one half. The interval between the first few doses should be three or four days, after which it should be increased to seven. The course of treatment must be prolonged, and after six months interval may need repetition.

Frank Billings was one of the first to suggest the use of autogenous vaccine from some foci of infection. He suggested doses from ten to five hundred millions. The grave weakness in this form of therapy was the lack of certainty of having prepared a vaccine from the organism which was actually causing the arthritis.

Hastings in 1913 attempted to overcome this difficulty by carrying out fixation tests with the patients serum against the various streptococci isolated from throat, intestines and other possible foci of infection. The vaccine was prepared from one or more strains that gave positive complement fixation reactions, with the patients own serum.
Burbank and Hadjopoulos concluded that most cases of chronic arthritis are due to some form of streptococci and advocated the use of the complement fixation test as a means of determining the type of streptococcus responsible for a particular infection. Cecil however questions this as an individual who at any time has had a streptococcus infection of whatever nature may have streptococcus antibodies in his blood.

Burbank and Christensen reported on the use of vaccine in 1000 cases of chronic arthritis. They isolated streptococci from proven foci in arthritic patients and tested them with the blood of patients by complement fixation. The vaccine is given once a week as an intramuscular injection. Toxic cases are given an initial dose of 5,000 organisms. If there is a reaction the dose is cut down to 1/10 or to 500 organisms. In the less toxic cases 50 to 500,000 organisms. In the original injection.

The vaccine injections are continued at weekly intervals until the patients are practically free from symptoms. The interval is gradually lengthened as much as possible. Some of the more severe cases require some treatment at varying intervals in order to keep symptoms free or even comfortable.

Of the total number tabulated, 1.5 per cent were worse or unimproved, 10.7 per cent slightly improved, 85 per cent moderately improved while 16.7 per cent were symptom free. The very marked improved cases were between the ages of 40 to 60 years.
The dosage was too small to give foreign protein reactions. In cases where the complementary titre was very low vaccine treatment was not given as the patients steadily become worse, even on the small doses.

In every case any reaction was followed by a reduced dose unless it was just a transitory increase in pain followed by a remission.

Because of his theory that the white staphlococcus (Micrococcus deformans) plays an important part in the cause of the disease, Warren Crowe uses a vaccine prepared from this staphlococcus, but alternates it with a streptococcal vaccine. He believes in starting treatment with small doses, as five hundred thousand or less of either vaccine intramuscularly, because of the danger of developing a sensitization of the patient, which may arrest the progress of the treatment and necessitate a return to one-tenth of the last dose given, followed by a slow and cautious increase from that quantity.

In those cases showing an abstinate sensitiveness to vaccine therapy, he overcomes this by the use of peptone intravenously. He considers that only those with large experience of vaccines should treat the acute bedridden cases and start at first with only 10,000 organisms. Crowe claims to have good results in sixty-eight per cent of his cases.

Rosenow and Nickel reported the results of removing the foci of infection and the use of streptococcal vaccines in 109 cases of arthritis. They concluded that improvement
occurred in most cases when foci were removed in which the "causative streptococci were demonstrated and that the use of streptococcal vaccines, whether autogenous or stock improved the results."

Zinsser declares, "an autogenous vaccine, may prove valuable in cases where a scanty number of bacteria are circulating in the blood stream, which provide relatively small amounts of antigen and so a deficient antibody formation. The vaccine in such a case will either rouse the antibodies to further activity or call out a reserve which the smouldering infection has failed to do. He condemns as an unjustifiable procedure the use of stock vaccine without laboratory diagnosis."

Cecil and Archer used a polyvalent stock vaccine with a concentration of 4,000,000 bacteria per cubic centimeter. The initial dose was 0.2cc. subcutaneously every 4 to 7 days until doses of 1cc. was reached. A few of the patients responded favorably for a short time but the vaccine seemed to have no specific action and did not appear to be superior in effect to any other foreign protein.

In 7 cases an autogenous vaccine was prepared from the focus of infection, and gave better results than those cases treated with stock vaccine. However as these patients were also subjected to tonsillectomy or tooth extractions before the vaccine was employed it was difficult to separate the effect of vaccine injections. Cecil suggests the autogenous vaccine treatment should be continued for several months in-
stead of several weeks. The vaccine is administered intramuscularly at intervals of 5-7 days in amounts varying from 10,000,000 to 2,000,000,000 in the case of cocci. The initial dose should be small as 0.1 cc and gradually increased depending upon the severity of the action induced. This reaction is a local one at the site of injection which may be only a slight induration and tenderness at the point of inoculation that wears off in a few days or be characterized by considerable induration, swelling and redness of the skin lasting for five or six days. In some cases a focal reaction results in which the joints are stiff and painful for 24-36 hours after the injection. Cecil believes a certain amount of focal reaction is desirable in this form of treatment. There may be a constitutional reaction characterized by a chill or chilly sensation, fever, malaise, headache and often nausea and vomiting. The patient may have to remain in bed for several days. Some idea of how sensitive the patient is to the vaccine may be obtained by performing an intradermic test before starting the subcutaneous reactions.

Pemberton recommends the use of autogenous vaccines whenever possible, but when not available the stock vaccines may be used. He recommends the administering of the amounts intramuscularly at intervals of five to seven days in amounts varying from 10,000,000 to 2,000,000,000. The initial dose should be small and gradually increased, depending upon the severity of the reaction.

Acute and chronic arthritis has also been treated by
means of so called autoserum therapy, which consists in the withdrawal of synovial fluid from the joint and its reinjection subcutaneously or intramuscularly in amounts varying from 1 to 5 cc. Results achieved by this method however are probably merely non-specific in nature.

Although the subcutaneous and intramuscular injections of streptococcic vaccine have been used extensively for many years in the treatment of arthritis, there are few cases of intravenous streptococcic vaccination in the literature.

Clawson and Fahr, reported the use of intravenous streptococci injected in the treatment of rheumatic fever. Swift and his associates used Streptococcus hemolyticus vaccine intravenously in the treatment of rheumatic fever. Gray and Gawen vaccinated patients having chronic arthritis by combining subcutaneous and intravenous injections. In comparing their results they obtained more rapid and satisfactory results by the intravenous method.

Wetherby and Clawson have applied the use of intravenous streptococcic vaccine therapy after a series of experiments on animals showing clinical manifestations of chronic arthritis.

Swift had contended that animals injected subcutaneously with streptococci were made hypersensitive to that organism while animals injected intravenously were not. Birkhaug had demonstrated by skin tests that patients having acute rheumatic fever are hypersensitive or allergic to streptococcic protein.

Wetherby and Clawson produced hypersensitiveness by injecting animals subcutaneously in one area with a mixture of
agar and streptococci.

They then injected animals intravenously following the method of Swift and believed they had immunized the animals against that particular strain of streptococci used in the experiment.

Each of the group of animals in the three groups normal, hypersensitive, and immune was then injected subcutaneously with a known number of streptococci. All animals were killed five days later and the number and size of the nodules at the sites of the subcutaneous injections determined. The cellular reaction was found to be similar to that found in chronic arthritis. The cellular reaction in the normal animals was 32 per cent, in the hypersensitive animals 88 per cent and in the animals immunized by intravenous injections was only 1.1 per cent. It was also determined that the average streptococcal agglutination titer in the hypersensitive animals was 13200 in the immune animals, 1200000. These experiments indicated that the subcutaneous method of giving a vaccine will not desensitize the hypersensitive animals, for hypersensitiveness is produced and maintained by subcutaneous injections.

In another group of experiments animals were made hypersensitive to Streptococcus veridans by the subcutaneous injection as above and later vaccinated with Streptococcus veridans, intravenously. The degree of cellular reactions or hypersensitiveness was then compared with hypersensitive animals which had not received the vaccine. The non-vaccinated animals showed 88 per cent of tissue response while the
hypersensitive animals which had been vaccinated intra-
venously gave a tissue response of 5.2 per cent. The
average agglutination titer in the non-vaccinated hypersens-
itive animals was 1:3200 and in the vaccinated hypersens-
itive animals 1:50,000. Thus the hypersensitive animals
were desensitized by the intravenous method of vaccination.

To test the protective merits of the subcutaneous and
intravenous methods of vaccination one group of animals was
vaccinated subcutaneously at five weekly intervals with one
billion killed streptococci and another group was vaccinated
intravenously at the same periods with the same doses. The
animals vaccinated subcutaneously had titers ranging from
1;1600 to 1;6400. The animals vaccinated intravenously had
titers from 1;200,000 to 1;400,000. Wetherby and Clawson
showed by these experiments that if the height of the agg-
lutination titer is an indicator of the degree of immunity
produced by vaccination, the intravenous method gives a much
higher degree of protection than the subcutaneous method.

Animals were made hypersensitive to Streptococcus
veridans and vaccinated intravenously with B.Typhosus. The
cellular reaction in the non-vaccinated animals was found to
be 86 per cent and in the animals vaccinated with B. Typhosus
it was 82 per cent as compared with 0.7 per cent in the
hypersensitive animals vaccinated with streptococci. This
indicates the desensitization to streptococci was notbrought
about by a non-specific protein reaction. This is also shown
by the fact that animals vaccinated intravenously with *B. Typhosus* develop a high agglutination titer to *B. Typhosus* but the titer to *Streptococcus veridans* is raised but slightly.

Experiments were then carried on to determine the relation of acquired desensitization and immunity to type and species specificity. Animals made hypersensitive to *Streptococcus veridans* were vaccinated with *Streptococcus hemolyticus*. The response in non-vaccinated animals was 88 per cent and in the animals vaccinated with *Streptococcus hemolyticus* 0.4 per cent indicating the desensitization was not specific, as to type.

By using the method described by Stutcliff and Rhoades for determining the bactericidal power of whole blood it was found that patients with a titer of 1:6400 or more had a much greater bactericidal power for streptococci agglutination than the blood of non-vaccinated patients with an average streptococci agglutination titer of 1:200 or less.

These experiments and results formed the basis for the following conclusions.

"Non-specific chronic arthritis in most cases appear due to a streptococci infection but not a specific strain.

Subcutaneous injections of a streptococci vaccine do not desensitize the hyper-sensitive individual but tend to increase the hypersensitive state.

The subcutaneous method develops only a slight degree of protection."
The intravenous method of giving a streptococcus vaccine desensitizes the hypersensitive patient, does not develop hypersensitization and does cause a high degree of protection to be developed.

Neither the desensitization nor the protection phenomena are type specific but they appear to be species specific. They are not of the nature of non-specific protein reactions.

Following the results of the animal experimentation, Wetherby and Clawson, determined to use the intravenous vaccination therapy in the treatment of 301 cases of chronic arthritis.

The patients were not grouped into distinct classes as atrophic and hypertrophic arthritis. Most patients had multiple joint involvement and all had the complaint of joint pain. The lesions were probably infective in most cases as shown by the presence of subcutaneous nodules.

They declare that the chief causes for division between rheumatic fever and the other arthritides has been the tendency of rheumatic fever to be complicated by endocarditis which rarely occurs in more chronic forms of arthritis. Also in rheumatic fever there is a tendency of the joint involvement to subside without obvious permanent damage. In their series they were unable to place a number of patients definitely in the accepted classifications and they see a gradual graduation in clinical types from rheumatic fever to those termed degenerative arthritis, depending upon the age of the
Children frequently showed clinical manifestations of rheumatic fever while the older adults often developed new bone formations in the joints.

Since the desensitization and immunity from intravenous vaccination are species specific rather than type specific, Clawson and Wetherby used a stock streptococcus vaccine. The organism used was from a case of acute rheumatic fever, and pericarditis. It has been under cultivation for nine years and had been repeatedly used in previous animal experiments. It did not agglutinate spontaneously and was safe for intravenous injections. It cross-agglutinates in a high dilution, (1:50,000 or more) with many other strains of both acute rheumatic and chronic arthritis, origin (beta hemolytic strains as well as Streptococcus viridans.) Each cc. of the vaccine contains 100 million killed streptococci.

The initial dose was 100 million organisms given at weekly intervals in the average case. This was increased by 100 million organisms at each weekly injection and as a rule not more than eight to ten injections were given.

In fifty per cent of the cases, the patients experienced a reaction following an injection. This consisted chiefly of chills of varying degree and duration followed by fever. Nausea, vomiting and diarrhea were sometimes present. The chills and fevers as a rule, lasted from one, to two hours. In most cases the onset of the reaction was from two to ten hours after treatment.
The patient might have a reaction at one injection and not at another injection. There was no correlation between improvement and the quality of the reactions, so both systemic and focal reactions were avoided in so far as possible by careful regulation of dosage and intervals between reactions. Ten grains (0.65Gm) of acetyl salicylic acid were prescribed after treatment to lessen or to avoid a reaction.

In most instances the dose was reduced or held to the same amount, if the reaction following the previous injection had been severe. In some instances the dose was not increased beyond 1,000,000 killed organisms, while in instances as many as 5,000,000 organisms were given to those patients who failed to show clinical improvement or a rise in the height of the agglutination titer.

It does not seem to be advisable to give more than 1,000,000 killed organisms. Some of the unimproved patients received as many as 25 treatments without any change in the clinical course. After 8 injections the interval was usually extended to 3 or 4 week intervals or treatment was suspended for months.

The extension of treatment was guided largely by clinical improvement and the height of the agglutination titer. With the exception of the acetyl salicylic acid no other medication or therapy was advised in order to determine the results as fairly as possible.

The criteria indicative of improvement were, decrease in
pain, definitely increased motility of joints, ability to return to work and statements from the patients that there had been no recent improvement spontaneously comparable to that experienced after vaccine therapy.

In some instances the clinical improvement was very striking while in others it was more gradual and less pronounced. It was impossible to predict improvement in any individual. In general the results were better in earlier and less severe cases, although there was improvement in some cases of many years standing.

There was no definite aggravation of the arthritic process in any case. Patients with permanent crippling lesions may obtain relief from pain and joint effusion when present, but cannot have a replacement of a destroyed synovial membrane or secure absorption of fibrous scar tissue.

To be considered adequate for results, patients must have received at least five injections. Nearly two-thirds of the cases showed improvement after five weekly injections and in nine-tenths of the cases after seven injections. Once manifested, improvement was usually fairly well sustained and increased while under treatment. There were very few cases in which improvement took place if it had not occurred with eight to ten injections.

The blood of all patients was tested for streptococcic agglutinins before treatment was started and at the end of the course of treatment.

The great percentage of untreated patients showed an
agglutinating titer of 1;200 with the strain of streptococcus used in the vaccine. The intravenous vaccine therapy stimulated a definite rise in the agglutinating titer of the serum of most of the patients with clinical improvement showing most frequently when the titer was 1;6400 or more.

About 80 per cent of the patients undergoing treatment reported definite improvement while the remaining 20 per cent showed no improvement and possibly in a few instances became worse though probably not worse than would be expected to be the clinical course without treatment.

The results from vaccine treatment are evaluated from two different angles. 1. There is no evidence that the patients are made hypersensitive to streptococci but tend to become desensitized as indicated by a positive skin test becoming negative and regularly there is an increase in the concentration of the streptococci agglutinins in the patients serum. 2. After intravenous vaccine therapy, about 80 per cent of the patients become clinically improved as indicated by relief from pain, increase in the motility of the joints, ability to go back to work. The mechanism of protection was not determined.

The blood from treated patients with an agglutination titer of 1;6400 or more was found to have a much higher bactericidal power against the streptococci used in the vaccine than did the blood of normal patients, untreated arthritic patients or treated patients with a low agglutinating titer. Once raised the agglutinating titer tends to
remain at a high level but occasionally may drop back unexpectedly. Acute respiratory infections and large doses as too frequent injections may be factors in reducing the agglutinating titer. If eight or ten injections have been given and the titer is 1:6400 or greater and the patient clinically improved it seems best to suspend treatment for several months or until there is a recurrence or aggravation of the joint symptoms. Agglutinating titers should be checked at monthly intervals if possible after suspending treatment. With recurrence of symptoms only a few small injections are usually sufficient to restore the titer to a high level with clinical improvement.

They declare that an autogenous vaccine does not seem to be necessary since both the desensitization and protective phenomena seem to be group specific rather than type or strain specific.

Wetherby and Clawson state that they did not treat pregnant women with chronic arthritis and that they considered it inadvisable to administer the treatment to arthritic patients with glomerulonephritis. In acute phases of arthritis with persistent fever, the dosage was reduced or treatment postponed until the acute febrile period was passed.

The following are cases reported by Wetherby and Clawson:

Mrs. M.A. aged 18, first noticed pain in the toes of the left foot 2 years before this report. Since that time the foot, ankles, knees, hips, fingers, hands, wrists, elbows, and shoulders had been involved. The joints had frequently been
swollen, tender and warm. She had had no fever. The joints had tended to be acutely involved in succession and partially cleared up after a few days to a few weeks. On examination there was limitation of motion present in the left arm at the shoulder. The wrists were definitely swollen and tender to the touch. There was definite limitation of motion at the wrists. The left knee and the foot were moderately swollen.

Roentgenological observations on the left knee and right wrist were, "There is some atrophic arthritis involving the right wrist and the left knee. Slight cartilaginous destruction and some bone destruction are also present. Conclusion—Atrophic arthritis, fairly marked degree of right wrist and left knee. A blood culture gave negative results.

Vaccine therapy—The patient received 12 injections over a period of two and one half months of doses of from 100,000,000 to 3,000,000,000 organisms. The reactions varied from none to moderate chills and fever for a few hours. There was perhaps less joint pain after 2 injections and much less pain was noted after 4 injections. Five days after the 6th injection the patient had pain and was unable to walk for 5 days because of swollen and painful ankles.

The agglutination titer was depressed to 1:000 at that time. Seven hours after the 7th injection the swelling in the feet had subsided and the patient could walk about freely. She was practically free from joint pains while under weekly injections during the following six weeks. Skintests, positive
before treatment were very faint after 5 injections. The agglutination titer was raised from 1:200 to 1:6400 after 5 injections.

Mr. U.J.S., aged 68 yrs., had had pain in the knees and in the back for the past 7 years. (since 1924.) There had also been some pain in the shoulders, elbows, and feet though less marked. Examination showed the patient walked with a slight limp. No gross joint deformities were observed. The roentgen report on the lumbo-sacral region was, "There is a marked degree of chronic hypertrophic arthritis involving the whole lumbar spine. Conclusion-This is chronic hypertrophic arthritis." A blood culture showed Streptococcus viridans.

Vaccine-therapy-The patient received 9 injections of from 100,000,000 to 2,000,000,000 organisms at weekly intervals over a period of 2 months. Reactions either were absent or consisted of slight chills and fever, the patient was always up and about. No improvement occurred whatever, until after 5 injections, after which time the pain was much less marked and remained so. The patient now had no pain at night and sleeps well. Pain is absent except after hard work as a gardener.

Mr. M.M., aged 22, first noticed pain in the hips and spine 4 years before this report. Eighteen months before soreness developed in the right shoulder. During the past six weeks the knees had been definitely painful. He now had marked difficulty in walking and took short steps. During the past six weeks he had been sleeping poorly because
of pains, he had been unable to work the past month. On examining the patient it was found that he was unable to extend the thighs at the hips because of pain. Tenderness was present over the hips and knees. Limitation of motion of the spine was present. Roentgen observations on the right hip and left knee were, "Some suggestion of arthritis in the right sacro-iliac region; otherwise negative. Ablood culture gave negative results.

Vaccine therapy-The patient received 5 injections over a period of one month. The doses were from 100,000,000 to 2,000,000 organisms. The reactions were chiefly slight chills and fever of from 2 to 3 hours duration. The joints were slightly improved after the third injection and much improved after the fourth. At that time the patient was able to return to work after being out for a month because of joint pains. The pain was practically all gone after the fourth injection.

Mrs. E.J. aged 27, developed a pain in the right shoulder about nine years before this report (1922), which disappeared after a few months. She then began to have pains in her feet and hands with definite swelling, redness and local heat. Since then she had had involvement of both shoulders, elbows, and knees. She continued to have joint pains. Her pain has been somewhat alleviated by a series of general diathermy treatments. Examination showed a fairly marked deformity of both hands, owing to involvement of the phalangeal and metacarpal-phalangeal joints. There was almost complete fixation of the left elbow at a 60 degree angle, and some fixation of the right
elbow and right hip. Swelling was present over some of the joints and there was tenderness on pressure. Roentgen examination of the left elbow was reported as follows, "There is a marked loss of cartilage and considerable destruction especially in the upper ends of the radius and ulna. A small amount of new bone formation has also taken place, but this is minimal. Conclusion-Chronic Atrophic Arthritis." A blood culture yielded Streptococcus veridans.

Vaccine therapy—Twelve injections were given at one week intervals. The dosage was run up from 100,000,000 to 1,000,000,000 organisms in four injections. It was then reduced to 300,000,000 for subsequent treatments. Reactions varied from very slight reactions to chills and fever for four to five hours and increased aching for 24 hours after the injections. The joints remained about the same throughout with the usual fluctuation of pain. The skin tests, positive before treatment became negative. The agglutination titer was raised from 1:800 to 1:25000 after six injections.
CRITERIA OF IMPROVEMENT

Joint pain. (282 Cases).

<table>
<thead>
<tr>
<th>Condition</th>
<th>No. of Cases</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased pain</td>
<td>233</td>
<td>82.6</td>
</tr>
<tr>
<td>Unchanged</td>
<td>49</td>
<td>17.4</td>
</tr>
</tbody>
</table>

Joint Swelling. (192 Cases).

<table>
<thead>
<tr>
<th>Condition</th>
<th>No. of Cases</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased Swelling</td>
<td>160</td>
<td>81.2</td>
</tr>
<tr>
<td>Unchanged</td>
<td>37</td>
<td>18.8</td>
</tr>
</tbody>
</table>

Joint Motion.

<table>
<thead>
<tr>
<th>Condition</th>
<th>No. of Cases</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased motion</td>
<td>206</td>
<td>84.7</td>
</tr>
<tr>
<td>Unchanged</td>
<td>37</td>
<td>15.3</td>
</tr>
</tbody>
</table>

Number of injections for definite improvement.

<table>
<thead>
<tr>
<th>Injections</th>
<th>Number improved</th>
<th>per cent improved</th>
<th>Total per cent improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>5.6</td>
<td>5.6</td>
</tr>
<tr>
<td>2</td>
<td>39</td>
<td>16.7</td>
<td>22.3</td>
</tr>
<tr>
<td>3</td>
<td>46</td>
<td>19.7</td>
<td>42.0</td>
</tr>
<tr>
<td>4</td>
<td>47</td>
<td>20.2</td>
<td>62.2</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>14.5</td>
<td>76.7</td>
</tr>
<tr>
<td>6</td>
<td>18</td>
<td>7.7</td>
<td>34.5</td>
</tr>
<tr>
<td>7</td>
<td>13</td>
<td>5.7</td>
<td>84.5</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>3.4</td>
<td>90.2</td>
</tr>
<tr>
<td>9</td>
<td>11</td>
<td>4.7</td>
<td>97.4</td>
</tr>
<tr>
<td>Over</td>
<td>2</td>
<td>1.3</td>
<td>98.7</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>1.8</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Coordinated along with the other measures which are aimed at the systemic treatment of the disease, the various measures of physio-therapy should be used for both their local and systemic effects.

Heat constitutes one of the most valuable measures in the treatment of chronic arthritis. The first and most obvious effect of the general application of heat is the production of sweating. A considerable quantity of water is lost through the skin and also through the lungs (due to the induced hyperpnea).

Pemberton, Crouter, and Cahori have observed that in addition to the sweat, there occurred increased circulation, and pulmonary ventilation, increased percentage saturation of the venous blood with oxygen resulting from increased blood flow, an increase in the alkalinity of the blood, and an alkaline urine and a change in the reaction of the sweat from its initial point to a reaction less acid or more alkaline. These changes in reaction are brought about by a loss of acid, as uric acid, lactic acid but chiefly carbon dioxide, from the body through the lungs, urine, and sweat.

In the local application of heat, a greater heat intensity may be tolerated. Local applications to joints affected with arthritis act in a somewhat similar manner to massage, by causing hyperemia and thus increasing the
circulation through the affected joints, and relieving musc­
ular spasm. By improving the circulation of the joint by
massage and heat, the nutrition of the joint structures is
improved and resistance to infection is aided.

Where pain is a prominent feature, heat may have an
algesic, antispasmodic action, and may soften scar tissue
and adhesions. As the tissues expand under the influence
of heat they become more malleable and are better acted upon
by massage or movement therapy. If the local use of heat
is continued too long a systemic response may take place,
dependent on a general hyperpyrexia. This must be guarded
against in feeble patients in whom a marked reaction is
contra-indicated.

Dry heat may be administrated in various ways, but the
means and methods of applying physical therapy constitutes
specialities in themselves, so will not be discussed in detail
in this work.

Among the common forms which should be mentioned are the
hot water bag, the electric-light bulb in a suitable apparatus
electrical resistance coils, diathermy and hot air or Turkish
baths in which the air is kept completely dry.

One of the oldest forms of the application of wet heat
is the hot bath. The water used may be pure or it may con­
tain various salts or other substances found in a natural
state in the water at various spas, which Poynton believes
may act as skin stimulants. Fisher declares there is no
scientific evidence to show these have any intrinsic the­
rapeutic action, however.
Another frequently employed form of moist heat is the hot pack, in which the body is wrapped in a sheet or blanket made hot by being dipped in hot water of about 62 °C. and wrung out thoroughly.

Other forms are douches of varying temperatures and steam baths. Experience has shown that the use of general hot baths of temperatures of 102 to 104 °F. or Turkish baths or steam baths, should be reserved for robust patients with sound hearts. They produce the most definite reactions, but are a tax upon the patients strength. It is important to remember that systemic exposure to heat in any form may occasionally have distressing consequences either immediately or after a course of treatment, so care must be used in exposing patients to this danger.

Such substances as mud, peat, fango, and paraffin are added to the water because being bad conductors, they retain their heat and the action may be prolonged.

Massage which is gentle, superficial, slow and rhythmical, is of value in allaying the painful muscular spasm, in cases of chronic arthritis. Fisher declares the modes of action by massage are both reflex and mechanical.

"Mechanically relieves congestion and improves the circulation through the parts by assisting the venous return and by action upon the arterioles through the vaso-motor system. It assists the lymphatic flow, disperses waste products or products of inflammation and stretches structures which are under tension. This may retard the onset of atrophy and fibrosis."

It is very important to use a correct technique in massage
but that will not be discussed here.

Pemberton stresses the influence that muscle tissue, plays in the metabolism of food, particularly carbohydrate, which may be aided by general massage.

General massage constitutes a form of exercise so that general massage in arthritis should be given at the outset only every other day until the response of the individual to it has been determined.
PREVENTION OF DEFORMITY.

Physicians should cooperate with orthopedic surgeons in the prevention of deformity. It is not in the scope of this work to discuss the various orthopedic operations and methods of treatment of deformities that have once developed. However it should be a primary principle of treatment to prevent such deformities from developing if possible.

Deformities that occur in chronic arthritis are primarily due to muscular spasm. Thus they tend to disappear when spasm has been abolished by anaesthesia, by the reflex action of massage, or heat. After a short period, however the deformities may become fixed owing to actual shortening by scar tissue of the structures on the side of greatest contracture, particularly the joint capsule, ligaments, and peri-articular tendons. Fisher has stressed the following principles:

(1) During the acute stages when muscular spasm is prominent every effort must be made to prevent deformity.

(2) Although the aim should normally be the retention of a movable joint, yet owing to the possibility of ankylosis occurring the joint should be placed in the optimum position, if necessary in some suitable form of apparatus. This apparatus should be light, comfortable, and easily removable for local physiotherapy to the affected joint.

(3) When deformity is due to muscular spasm already exists, this must be remedied at the earliest possible moment either by ex-
tension or in some cases by careful movement under anaesthesia, and the joint placed in the optimum position. Every effort must be made in recumbent cases to avoid faulty posture.

The question of deciding at what stage and to what extent movement of the affected joints should be attempted is always a difficult one, particularly in the atrophic type of case where ankylosis is more likely to supervene. It is important not to fatigue the patient to cause undue pain, but it is still more important to ensure that further crippling shall be avoided at all cost.

One leading therapeutic corollary to division of arthritics into two great groups, is the fact that in the atrophic variety some motion by the subject of the part involved is useful to delay or prevent the bony ankylosis which otherwise may arise. Rest to a hypertrophic joint can be indulged in more freely. Rest to the individual as a whole however, is essential in both types in a high proportion of cases and often constitutes the measure on which every other form of therapy must depend.

In a recent article, Fritz declared: "We must admit that the power of restoring joint movement at affections of long standing particularly of the joint and bone and cartilages is limited. However, we frequently find that in spite of extensive lesions, the joint may be quite serviceable and the patient can follow his usual occupation with little trouble. The degree of destruction is by no means so important for mobility as is generally assumed."

It is a generally neglected fact that the lesions or locking
of the joints may in many cases be avoided by suitable early treatment, and that the original cause has often less to do with the subsequent lesions than improper treatment. Perfectly sound joints may become fixed if left quiescent for a long time.

Disability in a joint is determined far more by pain than by the anatomical condition. The pain is due to irritation of the nerves around the joint rather than to those in the joint. Simple inflammatory hyperemia or effusion may diminish mobility and utility of a joint far more than any considerable lesion.

The pain causes the patient to keep the joint absolutely quiet, and he subconsciously resists against the slightest movement. This inhibition may completely dominate the patient and might be called an auto suggested (partial akinetic) fear psychosis. As the joint is kept perfectly immobile, usually flexed for better protection by the muscles, atrophy and contracture of the muscles set in early, the ligaments and tendons atrophy and the whole joint becomes fixed.

When the flexed joint is exercised actively or passively, the patient may be completely dominated by his fear of this pain and his muscles are defensively contracted or relaxed in the highest degree. Moving a joint in this condition naturally occasions pain even when the original cause has disappeared due to the secondary changes set up in the tendons and muscles. The fear psychosis becomes accentuated and more than ever causes the patient to keep the affected joint quiet. A joint may thus in time quite needlessly become fixed simply by missing the right movement for treatment. This applies particularly to cases of
arthritis with effusion, in which the very painful tension inhibits movement from the start. Disastrous mistakes are made by keeping the joints inactive too long, by padding and plaster splints. Therefore the first principal of proper joint therapy is to keep the muscles and tendons of an affected joint in working conditions under all circumstances. This can only be done by early active and passive movements. Physiotherapy must therefore begin much earlier than hitherto, not waiting for the pain to subside completely before energetic passive movements are given. The severity of this treatment, can of course be alleviated by reducing the sensitiveness of the joint by the use of analgesics.

The choice of an analgesic depends on the degree of pain. The short ether inhalation or morphine injection for the first movement to antipyrine etc. taken before the exercises serve to make active movements possible or easier.

This akinetic psychosis has nothing to do with true hysteria. This unconscious inhibition against pain or apprehended pain in the joint is usually quite isolated and independent in an otherwise perfectly normal mentality. Thus explaining to the patient the course and object of the treatment and inducing by suggestion to cooperate actively and energetically forms an important part in therapy.

After this mental preparation the next thing is to restore normal movement as far as possible with the articular surfaces in a normal position.

Gentle massage of the joint muscles and tendons is often
Passive movement should be given a short time but replaced as soon as possible by active exercises, which alone promote motility. These movements should be natural and not jerky. In polyarthritis the patient must first of all again learn to walk. A natural gait is acquired by raising the knees and sitting down the feet fairly quickly. Natural movements must be aimed at in all cases and can be achieved by light housework and exercise. Passive movements tend in time to lessen the zeal and interest in the exercises and thus retards progress.
An interesting phase in the treatment of chronic arthritis is the work of Rowntree and Hench of the Mayo Clinic.

Following the results of sympathetic ganglionectomy and trunk resection in Reynauds disease, Rowntree in collaboration with Hench suggested that lumbar ganglionectomy and trunk resection as employed by Adson, be tried as an experiment in chronic arthritis.

Sympathetic ganglionectomy and trunk resection result in the interruption of vasomotor fibers and improved circulation.

The treatment of certain cases of chronic arthritis by resection of sympathetic ganglia and trunks was instituted by Rowntree and Adson in the hope that this might produce an optimal degree of articular circulation in certain joints at least.

Any superiority in results that come from resection of sympathetic ganglia and trunks may lie in the fact that desired beneficial states are maintained over a protected time, possibly permanently instead of intermittently for only a few minutes or hours at a time as following application of heat, baths and other methods.

The operation is limited to cases of chronic atrophic arthritis, and only in a small percentage of this type.

Indication for operation as given by these authors are:
(1) The arthritis is chiefly periarticular or synovial with little or no bony alterations except atrophy.
(2) Patients should demonstrate alterations in vasomotor tonus as cold clammy, sweating hands and feet, reduction of blood
pressure below 110-115 systolic and subjectively by intermittent numbness and tingling. When arteriosclerosis is present adequate vaso-dilatation may be impossible of attainment.

(3) Vasomotor alterations must be capable of correction or of over correction by means of release from control of the sympathetic apparatus.

(4) The patient should be preferably less than 35 years of age and not more than the age of 45 years.

(5) The arthritis should be progressive and the main disability should be confined to the extremities particularly to the hands and feet.

(6) A reasonable period probably at least 6-12 months of intensive not haphazard treatment by the more established, less radical procedures should be allowed before resection of sympathetic ganglia and trunks should be considered. However rapidity of progression or stress of economic circumstances may necessitate consideration of earlier surgical measures."

The operation affords the greatest amount of relief in the smaller joints of the extremities fingers, hands, wrists, toes, feet, and ankles. When there is involvement of the larger joints, such as the knees, hips, shoulders, and spinal column, little is accomplished either in checking the disease or in ameliorating the symptoms.

In general the results have been disappointing as to the degree of reduction of symptoms, inflammation and articular stiffness obtained. Demy alterations already present are unaffected. In some the marked improvement noted in the early postoperative
course was not maintained.

In a series of 41 patients operated on there has not been a death reported. None of the patients have complained of a sensation of heat from increased circulation. Syndromes may result from the section of the sympathetic nerve supply to various parts of the body as dryness of the skin, Horner's syndrome, and a slight reduction of inhibitory fibers to the bladder and sigmoid but unless they are unilateral they result in little disfigurement and slight discomfort.

Report of a case.

A woman aged 26 years began to have arthritis in the hands especially but had also had arthritis in the feet twelve years before she came into the clinic. She had had two periods of relative quiescence, respectively of two, and two and one half years duration. The arms, elbows and hands, especially were very painful. The arthritis had progressed steadily in spite of treatment which included extraction of several teeth, appendectomy, many prolonged periods of intensive physiotherapy, several courses of administration of typhoid intravenously, a diet high in calories and vitamins and directed against constipation, several weeks of treatment by colonic irrigation, and a diet high in vitamin B and two series of treatments by X-rays. The tonsils had been removed prior to the onset of arthritis. There was marked ulnar deflection of both hands, and contraction deformities of the fingers. The hands especially were cold, clammy and painful and there was flexion deformity of the elbows, without complete ankylosis. The shoulders were mobile but painful. The knees and joints were involved to a less degree than the hands.
Roentgenograms gave evidence of marked destructive and hypertrophic changes, particularly in the fingers, wrists, elbows, and feet, with periarticular changes in the shoulders and knees. Because of the progressive pain, resection of the sympathetic ganglia and trunks was suggested in spite of the definite bony alterations. It was done in the cervical region, with the hope of relieving pain and possibly checking the progress of the disease particularly in the joints, in which thus far changes were in the soft tissues only.

Although the deformity and bone changes present at the time of operation are in the main unaltered at least to date (6 months) postoperatively, the patient has experienced marked analgesic effects from the cervical operation and in addition has less stiffness and more muscular strength in the hands. Because of this she has requested that the lumbar ganglion and trunks be resected also, which will be done.
BIBLIOGRAPHY


33. Ely L., The Second Type of Chronic Arthritis.,
34. Hench P., The Systemic Nature of Chronic Infectious
35. Osgood R., The Orthopedic Aspects of Chronic Arthritis.,
36. Hastings T., Complement Fixation Tests for Streptococcus
and other Bacteria in Infective Deforming Arthritis.,
37. Clawson B., Studies on the Etiology of Acute Rheumatic
38. Clawson B., Experiments Relative to a Possible Basis for
Vaccine Therapy in Acute Rheumatic Fever., J. Infect. Dis.,
39. Clawson B., Experimental Streptococcic Inflammation in
Normal Immune and Hypersensitive Animals., Arch. Path.,
40. Clawson B. and Wetherby M., Subcutaneous Nodules in
41. Clawson B. and Wetherby M., An Experimental Basis for
Intravenous Vaccine Therapy in Chronic Arthritis with Summary
42. Wetherby M. and Clawson B., Intravenous Streptococcic
June 4, 1932.
43. Wetherby M. and Clawson B., A Study of Chronic Arthritis
With Special Reference to Intravenous Vaccine Therapy., Arch.,


78. Rosenow E. and Nichols A., Results of use of Streptococci Having Elective Localizing Power.


