

5-1-1934

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Chronic Arthritis With Special Reference
To Infectious Arthritis

Senior Thesis

University of Nebraska
College of Medicine
1934

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Chronic Arthritis

History-

The term arthritis is derived from the Greek word "Arthron" meaning joint and signifies inflammation. Arthritis is one of the oldest diseased states of which there is any historical record, and evidence of its existence in the animal kingdom goes back to the Mesozoic period, long before the advent of man. The preservation of such evidence, after the lapse of some ten or fifteen million years, is due to the fact that the lesions of arthritis and the rheumatoid syndrome frequently involve or produce osseous structures which persist long enough to permit of being transformed into fossil form. The arthritis and rheumatoid syndrome is by no means confined in its expression to the bony system however, and it is certain; therefore, that the soft yielding structure must also have been involved (1).

Diseased processes at large apparently evolved more or less parallel with life itself, but there are only a few evidences of a pathological state older than the characteristic of arthritis.

These pathological manifestations perhaps hardly represent disease entities and consist in the following:

dental caries, pyorrhea alveolaris, fracture, ostio-myelitis, callus and parasitism. They appear in the age of amphibians during the latter part of paleozoic time, at which period bacteria and fungi were also abundant.

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. There are specimens showing involvement of the caudal vertebrae of Diplodocus, a giant dinosaur, and multiple arthritis in Platecarpus, a large swimming reptile.

Through the ages long subsequent to this, and after the arrival of mammalia, other animals were victims of arthritis and the cave bear of Europe and sabretoothed tiger of California seem to have been especially subject to it. It is, therefore, not surprising to find that the early evidences of man show that he too had suffered at remote periods from arthritis. The remains of men of the stone age are by no means as numerous as those of many other varieties of animal life, preceeding and contemporaneous with man, so that the probability of finding specimens showing arthritis is not great unless the disease were well nigh universal. Notwithstand-

ing this fact a considerable number of specimens have been found demonstrating that primitive man probably suffered from arthritis which as we do today(2).

Examination of mummies unearthed among the ruins of pre-historic people revealed the presence of arthritic disease much as we see it now. It was probably as prevalent among pre-historic dwellers of Nubia and the upper Nile as it is among the population of New York or Chicago today. Indeed, the physicians who participated in an archeological survey of the Egyptian Government in 1907 wrote in an interesting article, "The majority of the lesions discovered in the skeletons of old Egyptians, coming from a period extending over more than three thousand years, were typical of chronic arthritis. The spinal column was most often the seat of the disease, the alterations varying from slight overlapping to complete ankylosis (3).

To understand the origin of the many names now used for the various diseases included under "chronic arthritis", some acquaintance with the development of our knowledge of disease of the joints, both acute and chronic is indispensable. The diseases are not new. Bones, thousands of years old, have been found in Egypt

which show unmistakable signs of deforming pathological processes in the joints.. The ancient authors as far back as 41 A.D. had some conception of gout; they seem to have been familiar with chronic joint diseases other than gout. The term rheumatism meant liability to "rheum" and dates back to times when physicians believed that harmful phlegm flowed down from the brain and injured other organs of the body, a part of the humeral pathology which had adherents until the latter part of the seventeenth century; "rheumatism" seems to have been used, at first, as a name for some of the complications of gout. At the end of the sixteenth century, G.D. Baillow reversed the ancient usage of the word arthritis, applying it to the gouty affections, and the word rheumatism to the acute diseases of the joints. As early as 1683 Sydenham distinguished "chronic rheumatism" from "gout", asserting that they are essentially different diseases.

In the year 1800, in a Paris Thesis, Landre Beauvais separated from true gout a condition to which he gave the name, "primary asthenic gout", stating that it affects chiefly females, has a chronic course, and leads to enlargement and deformity of the joints, without tophi.

The same disease was recognized by William Heberden, the elder, 1710-1801, and carefully described by him; at the same time he described as *digitorum nodi*, the nodes, which bear his name, on the distal joints of the fingers. In the first half of the nineteenth century, the French writers referred to the chronic non-suppurative joint disease as "gouty rheumatism", and as "dry arthritis". Soon after this three names began to be employed which were destined to play an important role in terminology: they were primary progressive chronic articular rheumatism (Charcot 1853), rheumatoid arthritis (Garrod 1859), and arthritis deformans (Virchow 1869).

In America, Goldthwaite (1904) whose conception of the arthropathies have strongly influenced American workers, discarded the term "arthritis deformans", and in addition to "chronic infectious arthritis", used the term "hypertrophic osteoarthritis" and atrophic arthritis (4).

There is evidence to indicate that it is a disease from which man has suffered from time immemorial. It was the disease "par excellence" of the ancient Egyptians and the emphasis which the Greeks and Romans put on hydrotherapy indicates that it was a common disability. Today it represents a great economic problem and is one

of the great scourages of society. It ranks next in importance to heart disease and tuberculosis as a chronic disabling disease. Lack of knowledge and lack of satisfactory application of the knowledge we possess of the disease makes it less preventable than tuberculosis. Chronic arthritis is now recognized as probably the greatest cause of human morbidity.(5).

Classification

The classification of chronic arthritis is a problem that has interested students of medicine for many years. Twenty years ago Barker published a comprehensive review of the subject in which he said, "Despite the real progress which has been made it must be confessed that the arthropathies are still veiled in deplorable obscurity; and, as we shall see, the dimness, while due chiefly to our ability as yet to look at the processes from an etiological viewpoint, is to some extent dependent upon an intervening dust-cloud of terminology" (6).

Dr. Barker's remark still holds true today. The etiology of many cases of chronic arthritis is still unknown, and the terminology for the various types is still in a state of confusion.

Chronic arthritis is divided into two large divisions. In the literature we may find about six different names for these two classes. The following table will show the most common classifications:

| | | |
|---|-------------------------|-----------------|
| American Committee on Classification | Atrophic | Hypertrophic |
| Nichols & Richardson | Proliferative | Degenerative |
| English | Rheumatoid | Ostie-arthritis |
| Goldthwaithe | Infectious; Atrophic | Hypertrophic |
| Ely | Type I | Type II |

The most commonly recognized classification of chronic arthritis is the one advocated by Cecil (6).

The classification that I will use is the one advocated by him. It is essentially a clinical classification and is quite in harmony with the pathologic classification that has been made of the disease by various workers in morbid anatomy.

Following is a report and classification of 612 cases studied by Cecil and Archer at the Cornell Clinic(6). In this classification of 612 cases they have adopted the terminology of Nicholas and Richardson. The great majority of their cases fell into one or the other of their two groups. It was found that proliferative arthritis

constituted about two-thirds of all the cases admitted to the arthritis clinic, while degenerative arthritis made up most of the remaining third.

Proliferative arthritis includes all of the frankly inflammatory arthropathies. It can be subdivided clinically into:

1. Chronic infectious arthritis, referable to foci of infection.
2. Specific arthritis, caused by specific bacterial infection. The gonococcal, syphilitic and tuberculous cases come in this group, as well as the so-called surgical joints, staphylococcus arthritis, pneumococcus arthritis etc.
3. True arthritis deformans, a chronic progressive polyarthritis of unknown origin.

The cases of degenerative arthritis have also been divided into sub-groups.

1. Arthritis of the menopause.
2. Degenerative monarticular arthritis (Morbus Coxae Senilis).
3. Senile arthritis.

The complete classification of the 612 cases is given in the following table, in which it will be seen

that two types of arthritis make up the great bulk of the material in the Cornell Arthritic Clinic: Chronic infectious arthritis, and arthritis of the menopause.

Proliferative Arthritis

| | |
|---------------------------------------|-----------------|
| 1. Chronic infectious arthritis ----- | 379 cases |
| 2. Specific arthritis ----- | 18 cases |
| 3. True arthritis deformans----- | <u>17</u> cases |
| | Total 414 cases |

Degenerative Arthritis

| | |
|--|-----------------|
| 1. Arthritis of the menopause ----- | 145 cases |
| 2. Degenerative monarticular arthritis - | 30 cases |
| 3. Senile arthritis ----- | <u>17</u> cases |
| | Total 182 cases |

Gout ----- 4 cases

Intermittant hydrops articulum----- 3 cases

Unclassified----- 10 cases

We will now proceed to a more detailed discussion of the various groups of arthritis outlined above.

Proliferative Arthritis

1. Chronic infectious arthritis (focal infectious type).

This was by far the most common type encountered in their clinic. This type of arthritis occurs more frequently in females than in males. It is essentially a disease of young people, the average being thirty-five.

Exposure plays a secondary role. The most common etiologic factor is some primary focus of infection. In their series infected tonsils were the most common focus, occurring either alone or in combination with other foci in sixty-one per cent of the cases. Next in frequency were infections about the teeth. The teeth, alone or in combination with other foci were the seat of infection in thirty-three per cent of the cases. The sinuses, prostate, gall bladder, colon and cervix harbored foci of infection in a few cases. It is interesting to note that the age incidence was much earlier in tonsil cases than in the dental cases, the average age being thirty years in the former, and forty-two years in the latter group.

The patient often dates the onset of symptoms from some disturbance of the physical equilibrium, such as an acute infection, exposure to cold, a surgical operation or a confinement. A majority but not all, of the cases gave history of a preceeding attack of tonsilitis or sore throat.

Chronic infectious arthritis is a polyarticular disease which may involve any joint in the body. It may come on suddenly with fever and other acute symp-

toms, or the onset may be gradual. Locally, the lesions are characterized by inflammatory and proliferative changes in the joints involved. It is almost always migratory in its early stages, but after several attacks the joints become permanently injured. The fingers, knees and shoulders are the joints most frequently affected. This is a painful form of arthritis, particularly in the early stage, when there is considerable periarticular involvement.

Physical examination usually but not always reveals a patient somewhat underweight and anemic. The joints affected usually present a characteristic appearance. There is some swelling of the soft parts, and the overlying skin is warm and sometimes reddened. The swelling is due for the most part to an outpouring of inflammatory exudate into the periarticular structure. Tenderness is usually present, and motion, either active or passive is painful. In the latter stages the swelling may disappear but usually there is enough new growth of fibrous tissue about the joint to cause a persistent periarticular thickening. This is shown most typically in the finger joints, in which the characteristic fusiform enlargement may be present for years. Ankylosis is very common in this type of arthritis, but usually does not occur until the second

or third years of the infection. It is at first fibrous but later may become bony.

The laboratory findings are mostly negative. Cultures from foci of infection yield either *Streptococcus hemolyticus* or *Streptococcus viridans*. In their group *Streptococcus hemolyticus* was more frequently obtained from the tonsils and *Streptococcus viridans* from root abscesses. In fourteen cases blood sugar showed an average of 125.3 mg. per 100 c.c., which is somewhat above the normal limit. In severe cases in which the basal metabolism was determined, the findings were negative.

2. Specific infectious arthritis.

Eighteen cases in their series fell into this group. Etiologically they may be divided as gonococcus arthritis, eleven cases; tuberculous arthritis, five cases; and syphilitic arthritis, two cases.

Gonococcus arthritis.

Ten of these cases were in men and one in a woman. All gave a history of gonococcal urethritis.

According to Wehrbein (7) one to three per cent of all gonococcus infection lead to the metastatic infections of one or more joints. Aside from the presence of the gonococcus, little or nothing is known about the various factors which are responsible for gonococcus arthritis.

Constitutional factors may be responsible to some extent but this has not as yet been demonstrated. Neither has it been shown that previous non-specific joint infections predispose toward gonococcus infection of the joint. Pathological considerations have proven that trauma can not be anything but a minor contributing factor.

It must be conceded that the arthritic or periartritic manifestations of gonorrhoea are the metastatic exponents of a blood borne infection. There are many instances in which the joint fluid is found to be sterile, here however a toxin is present in contradistinction to a bacterial synovitis. The bacteria probably localize temporarily or absolutely in the epiphysis of the bone, cartilage or synovial membranes, and their inflammatory reactions evoke a serous effusion into the synovial sac of the joint; in other cases, depending on such factors as virulence of the infection and the vital resistance of the individual, bacterial evasion of the joint occurs practically at the onset of the development.

The diagnosis of a gonorrhoeal arthritis may be quite easy while in other cases it might be quite obscure. The majority of patients present one or more joints which are swollen and painful; active and passive motions are us-

ually impossible during the early days, and the pain may even be so great that sleep is impossible. The temperature is moderately raised and the patient may or may not have additional urological complaints, as urethral discharge, dysuria, or nocturia. No age seems to be exempt. Males are far more frequently affected than females, almost ten to one. The incubation period that is the time elapsed between the primary infection and the metastatic joint lesion, is most indefinite. The duration of the active stage, that is the stage of greatest pain and acute inflammation, may vary from a few days to several weeks. The complete recovery of the infected joint may require only one or two weeks or as much as six to twelve months. The outcome may be a normal joint or any degree of permanent change up to bony ankylosis.

Tuberculous arthritis.

There were five cases in their series distributed as follows: hip, two cases; wrist one case; elbow one case; and ankle, one case. These cases presented the typical clinical and x-ray picture of tuberculous joint disease.

Syphilitic arthritis.

In their series two cases were classified as syphilitic arthritis, but neither of them was typical of the

disease. Roentgenogram showed a destructive lesion of the joints, which was considered syphilitic in type. The typical syphilitic joint is usually monarticular and is caused by an extension of a specific periostitis into the synovial membrane. Anatomically they are: (1) enlargement of the capsule with thickening of the synovial membranes and effusion; (2) slight enlargement of the ends of the bones, with slight exostosis; (3) a dull velvety appearance of the cartilage, with atrophy in places. The knees are most frequently involved. The spine is affected in rare instances usually in the lumbar region. Trauma, with loss of pain sense, is an important element in the causation. A striking feature is the usual absence of pain. Occasionally there is pain from the distended soft parts and skin but not from the bones. Suppuration may occur, also spontaneous fractures.

Arthritis deformans.

Eighteen cases in their series were classified as arthritis deformans. This is the type spoken of by Barker as "primary progressive polyarthritis" and, as he says, is "the most malign of all arthropathies". English writers refer to this rare disease as "rheumatoid arthritis". This type is considered by many to

be nothing more than an extremely severe grade of chronic infectious arthritis. Certainly in the early stages it presents very much the same clinical picture. Its chief characteristic is its steadily progressive course. It is sometimes referred to as atrophic arthritis. Usually there is considerable periarticular infiltration, and later on an actual thickening of the capsule. Ankylosis occurs early, and there is marked destruction of the articulating surfaces, with telescoping of the joints and ulnar deviation of the hands and fingers. The process tends to be symmetrical. The temporomaxillary joints are frequently involved.

The average age of the eighteen patients in this group was 44 years. Fourteen were females and four males. It was very significant that the average duration of the disease on admission to the clinic was seven years. Most of these cases, if seen during the first years of the disease, would probably have been classified as infectious arthritis. However, in nine out of the eighteen cases no foci of infection could be located. In five cases the tonsils showed evidence of infection and in two other root abscesses were found. Only one of the group showed any improvement on treatment which consisted of removal of

foci, vaccine therapy, colonic irrigations and physiotherapy. This one patient was found sensitive to a number of articles of food and when these were removed from the diet, the patient showed marked improvement. They were not able to duplicate the result in any other patient.

Degenerative Arthritis

Degenerative arthritis is usually a milder disease than proliferative arthritis. The lesion originates in the bone and cartilage and in the majority of cases the soft parts are never seriously involved. For this reason degenerative arthritis is usually less painful than the inflammatory type already discussed.

Some writers describe degenerative arthritis as occurring in those who are "physiologically old". It is usually associated with arteriosclerosis, obesity, gray and falling hair, and other stigma of somatic deterioration. For this reason, this type of arthritis is usually looked upon as noninfectious. This is difficult to prove, but the character of its pathologic changes, its association with other sclerotic and degenerative processes in the body, the absence in most cases of definite foci of infection, and the clinical course of the

disease (absence of fever and inflammatory reaction about the joint), all speak rather strongly against the infectious origin of degenerative arthritis.

One hundred and eighty-two of their cases fell into this group. These were subdivided clinically as: arthritis of the menopause, 145 cases; degenerative non-articular arthritis, 30 cases; and senile arthritis, 17 cases.

1. Arthritis of the menopause.

Next to infectious arthritis, this was the most common type of arthritis seen in their clinic. More than twenty-five per cent of the whole series fell into this group. As previously stated, arthritis of the menopause is a chronic degenerative polyarthritis occurring in obese middle aged women at, or just after the menopause. In a series of fifty cases that they studied, the average age was fifty-two years. In almost every case the patient was considerably overweight. Symptoms usually appear during the first two years after the menopause. Sometimes the arthritis occurs simultaneously with the menopause, and in a few cases the rheumatic symptoms have preceeded the change of life by a short interval.

Foci of infection are rarely demonstrable, and for

this reason, the infectious theory of this type of arthritis is greatly questioned. The morbid changes are those of a degenerative osteoarthritis. The cartilage becomes thin, and there is lipping and spur formation of the bone at the margin of the joint involved. Occasionally there is a secondary thickening of the synovial membrane.

The onset of the disease is insidious. The first symptom is a slight stiffness in the knees, which gradually becomes more noticeable, especially in walking or bending. In their series of cases both knees were usually involved. The lumbar vertebrae and the bones of the feet are often involved. In a large percentage of patients there are well developed Heberdens nodes on the distal phalangeal joints. At times, a shoulder or hip joint may be implicated.

The physical appearance of these patients are quite characteristic. They are almost always overweight, sometimes to a marked degree. The posture is faulty, and there is usually some degree of flat foot. Examination of the joint ~~is~~ shows little, if any, swelling, but in cases of long duration, the head of the bones adjacent to the joints may be enlarged. On flexion a certain

amount of crepitation is usually detected. Roentgenograms show distinct lipping and spur formation. True ankylosis does not occur.

The progress of this type of arthritis is very slow, but with the passing years the patients discomfort becomes more marked. There is little tendency toward involvement of other joints. On the other hand, spontaneous recovery seldom, if ever occurs.

2. Degenerative monarticular arthritis (morbus coxae senilis).

This is another form of degenerative arthritis which occurs most frequently in the hip, in which it is spoken of as morbus coxae senilis. Occasionally it is seen in the shoulder or the knee. Twenty cases of this type occurred in their series. The distribution was as follows: hip, 16 cases; shoulder, 2 cases; and knee, 2 cases. This type of arthritis occurs in late middle life. The average age in this group was fifty-eight years. Fourteen were men and six women. Twelve of the fourteen men were outdoor workers. Eight of the twenty patients gave a definite history of injury. The pathologic changes in this group of cases are more marked than those occurring in the menopause arthritis. The lipping is more obvious, destruction of the articular surface. In fourteen cases,

no focus of infection could be established. Six patients had dental treatment for pyorrhea, and in one case the tonsils showed evidence of infection.

In a middle aged patient with chronic monarticular arthritis of the hip, the presumption is that the lesion is of a degenerative type. It must be remembered, however, that infective arthritis is occasionally monarticular and that it may involve the hip joint. The possibility of tuberculous arthritis must also be considered. The removal of foci of infection does not result in any benefit to the patient's condition. This condition does not progress to ankylosis.

3. Senile arthritis

Seventeen of thier series were classified under this heading. This form of arthritis is also a degenerative type, but has a somewhat different distribution from the two forms already discussed. The average age of the patient was sixty-seven years. Three of these were men and fourteen were women.

Definate foci of infection were noticeably absent. This form of arthritis may attack almost any joint in the body. It is always polyarticular. It is almost physiologic in the spine and also in the distal phalangeal joints, in which it shows itself in the form of

Heberden's nodes. The knees, knuckles, feet and shoulder joints are also frequent sites of involvement.

The lesion here, as in the other two types, is essentially an ostioarthritis, manifesting itself as a new growth of bone and cartilage around the edge of the joint. As in the other forms of degenerative arthritis, true ankylosis does not occur.

Gout

In their series they had four cases of gout, three men and one woman. The average age was thirty-four. Only one of their patients showed involvement of the great toe, but the others gave a history of previous attacks in the great toe. Three cases showed involvement in other joints. Only one showed tophi in the ear. The average uric acid content of the blood was 6 mg. per 100 c.c.

Gout is a disorder of metabolism associated with retention of uric acid and of other purine bodies in the body. There are a number of predisposing factors which seem to play an important part. Heredity is probably one of the most important. In from, 50 per cent to 75 per cent of all cases the disease existed in their ancestors, and the transmission is more marked on the male side.

Males being more subject than females.

Alcohol is an important factor. Therefore the disease is more common in England and Germany where a large amount of beer is consumed.

Food also seems to play a role, especially overeating without exercise. Occupation plays a large role, and the disease is much more common in workers in breweries, and in persons who deal in any way with alcohol.

Among the direct exciting causes of an attack is a meal with large quantities of rich food and alcohol; worry, or a mental shock, and in sensitive persons a slight injury or accident may be followed by an acute attack.

There are usually a few premonitory symptoms as twinges of pain in the small joints of the hands or feet, nocturnal restlessness, irritability of temper and dyspepsia. The attack sets in usually in the early morning hours. The patient is aroused by a severe pain in the metatarso-phalangeal articulation of the big toe, and more commonly on the right than on the left side.

The pain is usually quite severe. The joint swells rapidly, and becomes hot, tense, and shiny. They usually run a temperature from 102 to 103 degrees F. The pain

may subside by morning but the swelling remains for a few days. The inflammation never goes on to suppuration. Recurrences of attacks are frequent. With an increased frequency in the attack, the articular symptoms persist for a longer time, and gradually many joints become effected. Deposits of urates takes place, at first in the articular cartilage and then in the ligaments and capsular tissue; so that in the course of years the joints become swollen, irregular, and deformed. The feet are usually effected first, then the hands. Tophi may appear in the ears.

The diagnosis is usually made on the basis of recurring attacks of arthritis, limited to the big toe or tarsus, occurring in a member of a gouty family, or in a man who has lived too well.

Intermittant hydrops articulorum

In their group only two instances of intermittant hydrops articulorum were encountered. Both patients were men around forty-five years of age. In both, the attacks come regularly every ten days. The duration was two or three days in one case and one day in the other. Both patients showed infected tonsils and one an infected prostate. One patient had a tonsillectomy and prostatic massage with some improvement, the other was not

treated.

In intermittant hydrops articulorum there is a periodic swelling of one or more joints without fever. The effusion, which may take place rapidly, is accompanied by stiffness, but not necessarily pain. The interval between attacks may vary from a few days to several months. In some instances attacks are accompanied by edema of the face or erythema. Generally the disease can not be arrested.

Spondylitis

The vertebral joints, like other joints in the body, are susceptible to the various types of arthritis. Infectious arthritis may occur in a single vertebral joint, but more frequently it involves several vertebrae. It occurs more frequently in the cervical and dorsal region of the spine. In severe cases, however, it involves frequently the whole vertebral column, producing considerable periarticular reaction of spasm of the dorsal muscles. Fibrous ankylosis may occur early, with production of the so-called poker spine. Like other forms of infectious arthritis it is amenable to successful therapy if the foci of infection, usually in the tonsil, are removed early.

True arthritis deformans frequently attacks the spine

and progresses rapidly to complete ankylosis.

Degenerative arthritis usually occurs in the lumbar spine and is frequently seen in association with arthritis of the menopause and senile arthritis. Lip-ping of the lumbar verebrae is almost a physiologic process in late middle life.

Heberden's nodes

Heberden's nodes are present in practically every case of menopause arthritis. They may develop independently, however, of any other joint involvement, when they fall in the category of senile arthritis. In their experience, they were found more frequently in people who work hard with their hands and are exposed to the cold weather.

In a comment of their series of cases they state that the division of arthritis into two groups rests on definate pathologic and probably etiologic, grounds. The three subdivisions which they have made under each group are based largely on clinical manifestations. In the proliferative type, however, different infectious agents are probably responsible for the different clinical groups. The three subdivisions of degenerative arthritis are largely a matter of clinical convenience, though here also a variety of etiologic factors may play a part. It

seems quite possible, for example, that menopause arthritis is dependent in some way on endocrine disturbance which as yet is not thoroughly understood.

The significance of this division of chronic arthritis into two groups is of the greatest clinical importance, if the proliferative type is infectious and the degenerative type non-infectious. The failure to make a correct distinction between the two classes may lead to much unnecessary surgery. This applies particularly to the indiscriminate extraction of teeth in middle aged and elderly people with degenerative arthritis.

In matter of treatment we must make sure of our diagnosis, for in the infectious type, too much emphasis cannot be placed on a complete elimination of all sources of infection. In the degenerative type the problem of focal infection is of secondary importance in the general management of the case.

In a summary of their article they report 612 cases of chronic arthritis, approximately two-thirds (68%) were of the proliferative type and one-third (30%) were of the degenerative type.

Proliferative arthritis occurs most frequently in young people; degenerative arthritis is more often seen

in the middle aged and elderly.

The commonest form of proliferative arthritis is associated with focal infection about the teeth or tonsils. The commonest variety of degenerative arthritis is the arthritis of the menopause.

The proliferative type of chronic arthritis is presumably an infectious process. Degenerative arthritis has not been proven to be of an infectious nature. It appears more likely that this form of arthritis, as the name implies, is a degenerative process analogous to arteriosclerosis and the other degenerative changes that ~~attack~~ various organs of middle age.

Differential diagnosis-

The differentiation of the two groups of arthritis is a very important problem, especially in the matter of treatment. In the rheumatoid arthritis; focal infection plays an important role, so that removal of all probable foci of infection is the first step in treatment, while in ostioarthritis, focal infection plays but a secondary role. Therefore it is very necessary that a differential diagnosis is made between the two groups.

The two major groups of patients represent entirely different clinical and pathologic states and the first

step toward a more intelligent appreciation of the arthritic problem lies in a more universal recognition of the distinction. For the sake of clearness and conciseness the differential diagnostic points have been arranged in tabular form (8).

| | Rheumatoid Arthritis | Osteoarthritis |
|------------------------------|---|---|
| 1. Family history | Not infrequently a history of rheumatic fever in a member of the family | Frequently a history of a similiar form of arthritis in older member of family |
| 2. Past history | Occasionally a history of rheumatic fever, tonsillitis or sinusitis. | Not characteristic |
| 3. Age of onset | Any age; over 80% between 20 and 50 yrs. | Rare before 40; Most frequently 40-55 yrs. |
| 4. Mode of onset | Rarely acute; usually subacute or insidious; often accompanied by migratory pains. | Insidious; not accompanied by migratory pains |
| 5. Patient general condition | Usually undernourished anemic and chronically ill | Well nourished, frequently obese, not anemic |
| 6. Evidence of infection | Slight fever (99) and slight leucocytosis, foci of infection usually present | No fever, no leucocytosis. Foci of infection less common |
| 7. Joint involvement | Symetrical and generalized: proximal interphalangeal joints especially involved | Usually symmetrical; less generalized; larger joints; particularly knees; but also distal interphalangeal joints may be involved |
| 8. Appearance of joints | Early: periarticular swelling, fusiform fingers. Late: ankylosis, extreme deformity, ulnar deflection | Early: Slight articular enlargement Late: pronounced articular enlargement: ankylosis slight, never complete: Heberden's nodes |

| | Rheumatoid Arthritis | Osteoarthritis |
|-----------------------------|--|---|
| 9. Muscular atrophy | Often marked, particularly in late stage | Not characteristic |
| 10. Cutaneous changes | Extremities cold and clammy; skin atrophic and glossy; redness of thenar and hypothenar eminences. Psoriasis occasionally present. | No characteristic features. |
| 11. Subcutaneous nodules | Present in 15 to 20% of cases | Not present |
| 12. Sedimentation rate | Greatly increased; values above 30mm. in nearly all active cases | Normal or only slight increase, only rarely above 30mm. |
| 13. Roentgenologic findings | Early: no bony changes; slight narrowing of joint spaces; periarticular swelling. Late: Osteoporosis, bone destruction with new bone formation; ankylosis and deformities | Early: Slight lipping at joint margins. Late: Marked lipping, osteophyte formation and hyperostosis. |

Pathology

There has been a great deal of work done on the pathology of chronic arthritis. The first large amount of work was that done by Nicholas and Richardson in 1909 (9). This is recognized today as probably the most complete work on the pathology of chronic arthritis.

The following pathology was taken mostly from Nicholas and Richardson's original work (9). The pathology of chronic arthritis may be divided into two large groups,

that of proliferative and degenerative arthritis.

1. Proliferative arthritis

In all cases the most marked change is seen in the synovial membrane, with usually secondary changes in the capsule. The synovial membrane proliferates and forms a layer of vascular granulation tissue. This change is at first most marked at the periphery of the joint near the attachment of the synovial membrane to the articular ends of the bone. This proliferation causes thickening of the synovial membrane, and in most cases produces a thin layer of synovial pannus, which advances from the margin of the joint over the surface of the articular cartilage. In some cases the cartilage beneath the pannus does not disintegrate and adjacent cartilaginous surfaces are merely united by fibrous adhesions. But usually when this synovial pannus comes in contact with the underlying cartilage, it extends downward into the cartilage and causes the cartilage to disintegrate and disappear. In many cases the entire thickness of the cartilage is destroyed down to the zone of provisional calcification, so that the bone is entirely denuded of cartilage. Unlike the degenerative type, however, this denuded bone is not directly exposed to joint friction

but is covered with a layer of pannus varying in structure from vascular granulation tissue to dense non-vascular fibrous tissue. This destruction of cartilage is not uniform throughout the joint; in the early stages it is most marked at the periphery, and only in the extreme cases results in complete destruction of the cartilage, and in all cases for a long time considerable areas of unaltered joint cartilage remains. This synovial pannus may extend over the surface of each bone in the joint without the formation of adhesions, leaving the ends free to move upon each other, and this condition is most common in the large joints; or may form a thick layer which binds together adjacent bones of the joint. In the first case, two surfaces, each covered with synovial pannus, are free to move one upon the other; in the second, the two adjacent bones are firmly bound together by the intervening layer of pannus, while the joint cavity undergoes a corresponding diminution of mobility.

In addition to this peripheral ingrowth of pannus the entire synovial membrane of the joint may proliferate, and if, as often happens, the central portion of an articular cartilage of a bone is held in contact with any portion of this proliferating synovial membrane, adhesions

may form between the synovial membrane and central portions of the articular cartilage. By the formation of such adhesions the original joint cavity may be divided into connecting localized cavities.

Besides this destruction of joint cavity from peripheral ingrowth or from central adhesions of proliferating synovial membrane, there also may be marked destruction of the joint cartilage from its epiphyseal surface. Frequently there arises early a proliferation of the connective tissue of the marrow spaces of the epiphysis just below the zone of provisional calcification; this proliferation results in the formation of a zone of edematous granulation tissue in the marrow spaces, and this zone as a rule is quite vascular, and in most cases infiltrated with lymphoid and plasma cells. This layer of sub-cartilaginous granulation tissue may come in contact with the epiphyseal surface of the cartilage, may extend into the cartilage, after penetration of the zone of provisional calcification, and may cause destruction of the joint cartilage from below. This process may begin quite early at the periphery of the joint just as the synovial pannus does, or may begin at a more central point beneath the joint cartilage. If it begins at

the central portion of the epiphysis it may cause at first a thinning, later a complete perforation of the joint cartilage from below, even in those instances in which peripheral ingrowth of synovial pannus is not marked.

In most cases the peripheral ingrowth of synovial pannus is the most marked feature, rarely the destruction of cartilage by epiphyseal granulation tissue predominates, often the two destructive processes go hand in hand, and ultimately, by destruction of cartilage the two layers may coalesce; in the latter case the ends of the bone may be covered with a thick layer of granulation or fibrous tissue in which islands of the original disintegrating cartilage still persist.

In addition to these two destructive processes there is often a proliferation of the perichondrium of the articular cartilage and of the endostium of the epiphysis, and by the proliferation of these two layers new cartilage or bone may be formed. The proliferation of these two layers may be synchronous with the proliferation of the synovial pannus and of the epiphyseal connective tissue, but generally it arises subsequent to the synovial proliferation, and sometimes precedes it.

The proliferation of the perichondrium results in the formation on the joint surface of a layer of fibrous tissue of variable thickness, which usually early undergoes a transformation into cartilage like that seen in callus formation in fractures. In many cases transformation into true bone also may occur. In the early stages of proliferation of the perichondrium the joint cartilage is covered with a thin fibrous membrane, which by gross inspection cannot be distinguished from a thin layer of synovial pannus; after formation of bone or cartilage begins, the surface of the joint may become much roughened from the projection of the cartilaginous or bony masses.

In addition to this proliferation of the perichondrium there often occurs a proliferation of the endosteum of the marrow spaces just below the joint cartilage. This proliferation of the endosteum always is accompanied with a proliferation of the connective tissue of the marrow already described which leads to the destruction of the cartilage. As a result of the proliferation of the endosteum new trabeculae are at first formed beneath the destroyed cartilage. These trabeculae at first are osteoid in character, and later may become true bone. At first these trabeculae appear beneath the level of the original

zone of calcification, but later they may extend upward into the cartilage, accompanying the ingrowth of the granulation tissue of the marrow. Ultimately, after perforation and destruction of the cartilage, the proliferating layers of the perichondrium and of the endosteum may become fused into one mass.

Hence, two layers of granulation tissue form in these joints, one derived from the synovial membrane, and one from the connective tissue of the marrow. Accompanying these two layers of tissue which produce new cartilage or bone, are the perichondrium of the joint and the endosteum of the epiphysis. All the four layers may proliferate together, so that within the joint, destruction of cartilage and new formation of cartilage or bone may take place, while from the side of the epiphysis likewise destruction of joint cartilage or deposit of new trabeculae may occur. After the original cartilage has been destroyed these two layers, at first separated by the articular cartilage, become united and fused into one; and it no longer is possible to distinguish from which of the layers any portion of the new joint surface was derived. As the same process takes place in both of the adjacent bones of the joint, the

two articular surfaces of bone instead of being covered with normal articular cartilage are covered with a layer of new tissue derived in the manner just described. The results of the approximation of two such surfaces varies in accordance with the character and origin of the new tissue. The synovial pannus may extend between two adjacent cartilaginous surfaces and become adherent to each, and more or less completely obliterate the joint cavity. If synovial pannus predominates the ankylosis usually is fibrous; if perichondrial proliferation predominates, cartilaginous or bony ankylosis may occur. In some cases the ankylosis by bone may be so complete as to obliterate the original joint surface completely, and the two adjacent bones may be united into one with a perfectly continuous marrow canal. In most cases all four of these processes are present at the same time in one joint, especially in the large joints, so that pannus, erosion of cartilage, either from above or below, with fibrous, cartilaginous, or bony ankylosis may co-exist in the same joint.

2. Degenerative Arthritis-

In this class of joint lesions, the earliest and primary change in the joints is a degeneration of the

hyaline cartilage of the articular surfaces. As a result of this cartilaginous degeneration, the cartilage becomes softened and eroded, and the underlying bone may become exposed so that instead of two cartilaginous surfaces being in contact the cartilage of one of the bones of the joint may be in contact with exposed bone, or two bony surfaces may articulate. Since the degeneration of cartilage usually is not uniform over the whole extent of any given joint, the areas of exposed bone at first generally are circumscribed. Whenever erosion of cartilage or bone occurs there practically always comes a compensatory growth of cartilage or of bone of the opposite articular facet so that the articulating surfaces of the two bones of the joint always are in contact, although as a result of the erosion of one bone and a corresponding overgrowth of cartilage due to proliferation of the perichondrium of the opposite articular surface, the line of articulation becomes very irregular and indented. In most cases the fibrillation of the cartilage at first affects only a portion of the articular facet of one bone, but ultimately may extend over the entire joint surface of both of the bones which enter into the articulation, so that ultimately the entire articular cartilage may disappear from both

bones. So that, finally, instead of two cartilaginous surfaces being in contact, two bony surfaces are in contact, but since this change is brought about gradually, and since in the early stages and erosion of one bone is met by a corresponding overgrowth of the opposite facet, the bony surfaces which result are very irregular in outline and in many cases present an extremely notched appearance.

Moreover, since in this type of joint change, the destruction of cartilage takes place gradually, and is at first confined only to a portion of the joint, motion continues for a long time. Under these circumstances it always happens that the articular surface of the joint, which has been denuded of cartilage and yet remains movable, undergoes marked thickening of the bony trabeculae, and the marrow spaces of the articular end of the bone may be nearly completely obliterated. As a result the exposed bone becomes extremely dense, and acquires a structure as solid as that of normal cortical bone, or may be even denser. This exposed dense bone under the friction of continued joint motion acquires a high degree of polish, and has an appearance closely resembling that of ivory, hence the term, "eburnation of bone".

While this process of fibrillation and destruction of cartilage with erosion of one portion of the joint and the corresponding overgrowth in the opposite portion takes place, secondary changes in the joint may occur. In the change in the shape of the joint; these sub-luxations come on gradually and may take years for their production. As a result of the changes in the shape of the joint surface the plane of the articulation may be changed, and the amount of joint motion may be very much diminished in certain cases, in fact, the irregularity of the joint surface may become so great that the two bones may become interlocked, and no motion may be possible, although there is no true ankylosis of adjacent joint surfaces. This sort of joint fixation is called "ankylosis by deformity". In some cases, however, even where the irregularity is very great, a considerable and surprising amount of motion may be retained.

Secondary changes in the shape of the bone entering into the joint which has been denuded of cartilage also commonly occur. The reasons for these secondary bony changes are not clear. The changes consist in an increase in the activity of the perichondrium at the periphery of the joint at the point where cartilage and cap-

sule come together. As a result of this perichondrial activity, resulting in the new formation of cartilage which may be transformed into bone, the head of the bone increases in size, but this increase in circumference as a rule is not a uniform one, but is irregular and nodular and produces marked changes in the articular ends. Such changes most commonly are seen clinically in the so-called "Heberden's nodes". This increased circumference of the affected bone gives on vertical section an increase in width. This deposit of new bone usually is within the attachment of the joint capsule, and leads to an actual increase in size of the articular surface. There may also be a formation of a new imperfect cartilage on the new bony surface, which, however, frequently is so irregular as to make the unevenness of the joint due to the primary cartilaginous degeneration and erosion even more marked. In some cases this peripheral perichondrial new growth may be so marked as to lead to more or less filling up of the original joint cavity, and in that way the head of a bone may be forced from its articular cavity and partial or complete dislocation may result. The newly formed perichondrial marginal bone as a rule is composed of very dense and thick trabeculae.

It has been said that the exposed articular ends become eburnated, if the joint motion persists as it usually does. This layer of eburnation, however, is relatively thin, and as a rule does not involve the entire underlying epiphysis. Beneath this relatively thin layer of eburnation the trabeculae of the shaft may remain unaltered, or in some cases may be diminished in number or in size, but in none of the cases which have been examined has there been any evidence of reabsorption of bone by osteoclasts. It is probable that the eburnation of the bone next to the articular facet is due to the development of new bone to replace the function originally taken up by the joint cartilage, or it may merely be the reaction of repeated traumatism from motion after the destruction of the cartilage occurs; while the diminution in the number of bony trabeculae of the shaft at a distance from the joint may be due either to the reabsorption of bone always seen in old age, or may be a reabsorption secondary to disease and diminished function such as is seen in the proliferative type of arthritis.

The capsule of these joints as a rule shows no great increase in thickness, although moderate thickening may

occur. In certain joints, however, notably in those associated with organic disease of the central nervous system, in which as a rule the destruction is marked and occurs comparatively rapid, the thickening of the joint capsule may be enormous.

The synovial membrane in many of these instances may appear normal; in some, however, there is marked thickening of the synovial membrane, especially of that portion which is thrown into folds at the periphery of the joint. Sometimes this portion of the synovial membrane shows marked proliferation, and may result in the formation of large papillary masses, either sessile with a broad base or pedunculated with a broad or narrow extremity. These papillary masses are frequently composed entirely of granulation or dense edematous connective tissue; sometimes by metaplasia such masses may be converted into cartilage or into bone, or into fat tissue, "lipoma aborescens". Pedunculated masses may be torn from their narrow attachments, and be set free in the joint cavity and so appear as loose foreign bodies, the so-called "joint mice". As a rule in this type of joint change there is very little or no tendency for the synovial membrane to extend over the articular surface, al-

though such a tendency in certain joints, notably the knee, may be present to a slight degree; in no case, however, does fibrous ankylosis occur.

Etiology of Proliferative Arthritis-

The etiology of chronic deforming arthritis has long been a subject for debate. Perhaps no disease in the whole realm of internal medicine has been more prolific of hypotheses and theories. It has long been recognized that there were many predisposing factors, such as fatigue, cold and exposure, which played an important part in the actual onset of symptoms; but the exciting cause or agent has eluded the most persistent investigators.

Probably the oldest theory that can be found on the etiology of chronic rheumatoid arthritis dates back to the sixteenth century. The physicians at this time thought that it was produced by harmful phlegm which flowed down from the brain and injured the other parts of the body. This theory had existed long before the sixteenth century and was even considered until the seventeenth century.

As far back as 1819 Dr. Benjamin Rush (10), an eminent American physician, was impressed by the possible relationship between infection and arthritis, since he had observed recovery from the disease in a case which

infection in the teeth had been removed. It was not, however, until within the last two decades that the importance of that observation became generally recognized.

The most important contribution to the etiology of chronic arthritis was made by Billings (11) and his co-workers nearly twenty-five years ago, when they pointed out the relationship which existed between focal infection and chronic infectious arthritis.

He divided his foci of infection into ten different sites: the tonsils, teeth, sinuses, bronchiectatic and pulmonic cavities, ulcers of the gastro-intestinal tract, chronic appendicitis, gall bladder, urinary tract, genital tract and local submucous foci. In all his arthritic patients all above sites were examined for foci of infection. If any possible foci were found, they were immediately removed.

Dr. Billings report was based up ten cases of arthritis. In the ten cases reported all showed infected tonsils, one was accompanied by infected teeth. The tonsils were removed in all cases and teeth cleaned up in the one case. In every case a streptococcus was isolated from the tonsils. In nine of the cases; the streptococcus obtained from the tonsils was injected into a rabbit and in

every case, arthritis was produced in the rabbit.

Following the tonsillectomy there was marked improvement in all ten cases. It is noteworthy that the streptococcus obtained in almost pure culture from many of the patients, when inoculated into animals, produced an acute arthritis either single or multiple, and in many of the animals produced an arthritis of deforming type. In summing up his article he states that there is evidently a definite relationship between foci of infection and chronic systemic infection. He believed that the joint manifestations were nothing other than metastatic infections.

Before going into any of the theories as to the direct etiology it might be well to consider a few of the predisposing factors.

Predisposing factors play a role in the etiology of chronic arthritis. Even the ancient Egyptians thought that the main factor was one of environment especially along the damp Nile valley.

Cecil (13) who is a strong advocator of the infectious theory of rheumatoid arthritis is of the impression that some predisposing factors play a large role. Of these sex has been regarded as a predisposing factor in

the causation of infectious arthritis, the frequency in females being stated to be something like four times that in males.

Race seems to be a factor for there is a lowered incidence rate amongst the colored than amongst the white race. The negro race seems to have almost a natural immunity.

Faulty metabolism and undernutrition also play their part. We quite frequently see chronic arthritis in patients who are underweight, though part of this may be due to the disease itself. Dietetic errors for many years have been suspected as an exciting cause.

Sudden or repeated exposure to dampness, rain and cold is probably one of the commonest predisposing factors in infectious arthritis. This was especially emphasized by Pemberton (13) in his statistical study of arthritis in soldiers. He states that a high percentage of the soldiers that developed chronic arthritis gave a history of prolonged exposure, standing in water or marching or sleeping in the rain. We also find chronic arthritis more prevalent in the temperate zone, especially along the Great Lakes and the Atlantic sea board, it is also very prevalent in London.

Wilcox (14) states that, although there does not appear to be any direct hereditary tendency, a family history of chronic arthritis is quite often obtained. We find that all ages are susceptible but infectious arthritis is rare under the age of twelve. From the age of twenty years infectious arthritis has a relatively large incidence for all ages.

Trauma also plays a part here, although not as pronounced as in degenerative arthritis. Arthritis may frequently be seen following a sprain, fracture or an injury to a joint. Here the local resistance is lowered so that bacteria may become localized at this particular point. This has been demonstrated experimentally but producing trauma to a joint and then injecting bacteria intravenously. The bacteria seem to have a strong predilection for the injured tissue.

Shock, fatigue, and mental strain lower the general body resistance and may act as a predisposing factor.

Pemberton (23), in a statistical analysis of 400 cases admitted to U.S. Army General Hospital, did considerable work in regard to the precipitating factor with the following results:

| | No. of cases | Percentage |
|----------------------|--------------|------------|
| Exposure | 232 | 58 |
| Dysentary | 33 | 8.25 |
| Injury | 30 | 7.5 |
| Flu | 28 | 7 |
| Gas | 23 | 5.75 |
| Drilling and hiking | 15 | 3.75 |
| Tonsilitis | 13 | 3.25 |
| Pneumonia | 6 | 1.25 |
| Neisserian infection | 4 | 1 |
| Unknown | 56 | 14 |

In relation to surgical foci, one hundred and seven persons (27%) were taken sick in the apparent absence of any demonstrable foci. Two hundred and ninety-three (73%) showed definite foci of infection and of these two hundred and eight showed foci in the tonsil. This was 52% of the entire series and 71% of all cases showing foci.

It was also noted that one hundred and eighty-four patients, or 46% recovered in the presence of demonstrable foci while only 8.5% recovered after removal of foci, and only 7.7% were improved after the removal of foci. This is considerable to the contrary as that reported by Lillie and Lyons (15) where they concluded that 79% of their series were improved by tonsillectomy alone.

Pemberton and his co-workers went further and tried to show if any relationship existed between chronic arthritis and metabolic functions. They finally concluded

that the basal metabolism, nitrogen and urea of the blood, carbon dioxide combining power, blood calcium, fat, cholesterol, renal functions and blood sugar all fell within normal limits except that one half the patients showed a high blood creatin. They also found a slightly lowered sugar tolerance, as measured by the glucose tolerance tests, and this they explained may be due to the fact that there seems to be some definite relationship of foci of infection to sugar tolerance, that is those producing systemic disease.

In dealing more with the direct etiological factor we find there are many theories as to the cause. In most of the workers, rheumatoid arthritis is considered as an infectious disease. The portal of entry and the organism causing the disease is of considerable debate.

Foci of infection has for many years been considered a problem of great importance in rheumatoid arthritis.

Lillie and Lyons some twenty-five years ago did considerable work to show the relation of foci of infection to arthritis and myositis. They performed tonsillectomies on two hundred consecutive cases of arthritis and myositis.

Their series was divided into two groups. In the first group they report 81.6% improvement following

tonsillectomy and 77.7% in the second group. He therefore states that it is justifiable to advise a tonsillectomy in every case of myositis or arthritis. He goes further and states that a marked improvement may be assured from tonsillectomy alone in 79% of the cases and that 40% of the patients with chronic myositis or arthritis who are invalids will respond favorably to tonsillectomy.

This would be probably contradicted by Pemberton (13) who states that removal of the foci of infection plays but a minor role.

Arbuckle (16) and Donelan (17) are of the belief that a great many cases of chronic infectious arthritis are due to a sinus infection. They believe that this is especially true in the insidious cases when the signs and symptoms of sinus infection are not so pronounced, for here there is more likelihood of toxic absorption and spread of the infection through the lymphatics.

Arbuckle is of the same belief as Rosenow (18) that the infection probable travels by way of the lymphatics and this is why we have so many negative results in blood cultures.

In two cases reported by Donelan, the foci of infection

were in the sphenoidal sinus in both cases. By clearing up these sinuses the arthritis soon cleared up. Two cases proved nothing in themselves but gives us some evidence that we may have a foci of infection in the sinuses as well as in the tonsils.

Stauffer (19) in a study of two hundred arthritic patients, found that forty-five had the posterior ethmoids and sphenoid involved.

Alexander (20) is a strong believer of the infectious theory of rheumatoid arthritis. He thinks that the true etiology may be due to a number of different organisms, although some strain of streptococcus is the most common cause. In his report he states that he noted a large per cent of his arthritic patients have shown an enlarged liver and on this basis, he believes that the liver may be one of the primary foci of infection.

Goldwait (21) was one of the early workers who thought that rheumatoid arthritis was due to some organism or to some toxin produced by that organism in some other part of the body. He thought that the arthritis may result from practically any of the infectious or pus-producing organisms.

Hastings (22) did considerable work on blood cultures

and complement fixation tests as early as 1910. In a series of twenty-four cases of arthritis deformans, blood cultures were negative in every case. In twelve cases the complement fixation test was negative and in twelve it was positive. Four cases of typical arthritis deformans reacted to the gonococcus and the rest of the positive tests were for the *Streptococcus viridans*.

He therefore concluded that some cases of arthritis deformans were infective in nature and that the infecting organism may be a *Streptococcus viridans* or a gonococcus. This was further verified by treating the patients with specific vaccine with marked improvement.

Davis (34) was also one of the early workers who did considerable bacteriological work on culture inoculations from the tonsils of arthritic patients. In twenty-eight cases of arthritis, hemolytic streptococci were obtained in all and were predominate in twenty-five.

In two cases the pneumococcus was present and in one the *Streptococcus mucosus* was present. Blood cultures and joint cultures were also taken from these patients but they were all sterile.

Strains of streptococci from the various clinical groups were inoculated into animals. These streptococci

were obtained from patients with chronic arthritis, nephritis, endocarditis and from cases of chronic or recurrent tonsillitis. In all cases arthritis was produced in the rabbits. Hemolytic streptococci from the normal throat was also found to produce arthritis in the rabbit. It is possible that the reason why in one individual streptococci cause arthritis, and in another nephritis, lies in the varying local susceptibility of the organs of the individual rather than in any peculiar specificity of the infecting organism. In a conclusion of his article, he states that due to the fact that removal of tonsils produce very favorable results in arthritis and that the infected tonsils are very frequently found to contain hemolytic streptococci, it is justifiable to consider the streptococci a very suspicious etiological agent.

In another series of cases in which Davis (35) reported, he states that the probable atrium of infection was the tonsils. In almost all of his cases the tonsils were removed and cultures were made from the crypts. From thirty-eight of the forty-two cases a hemolytic streptococcus was grown almost in pure culture. Blood and joint cultures were negative in all cases. He states that this does not mean that bacteria can not be found in

the blood at times, or that bacteria are not present in or about the joints.

These streptococci obtained were inoculated into rabbits, producing arthritis and in many instances typical of arthritis deformans. Cultures were made from the joints of these animals early, and in most cases yielded a streptococcus. This may be referred to the human, that early in his arthritic condition the bacteria may be found while later, culture will be negative. In summing up his article, he states that the most common portal of entry is the tonsils; and that in almost every case a pure growth of hemolytic streptococci may be obtained from the tonsils. Removal of the tonsils shows marked improvement in many cases, therefore, this seems to point to the tonsils as a focus from which infectious material is being constantly disseminated.

We find a number of workers who believe that all types of arthritis are infectious in nature. The variations being due to the variation in the location, the intensity, the duration, the termination of the process and the stage in which the affected structures are examined.

In a considerable amount of experimental work done on dogs by injection of a hemolytic streptococcus, Nathan(26)

was able to produce, besides the epiphyseal and marrow changes, a intra and periarticular joint exudate. This exudate was very carefully examined bacteriologically; but in every case it was found sterile. In the neighboring epiphysis, the streptococcus could be demonstrated in almost every case. This was then tried with the staphylococcus pneumococcus and other strains of streptococcus. Aside from minor differences in symptoms and courses, the infection caused by these microorganisms were followed by analogous changes in the joints. This joint exudate, therefore, appears to be a symptomatic exudate. Therefore, he concluded that this exudate is symptomatic, and this probable accounts for the failure to recover microorganisms from the joint fluid in many cases of joint infection in the human being.

Margolis (27) has done some bacteriological study of the epiphyseal marrow in trying to find the offending organism more consistently. Thus in their series of fifteen specimen of epiphyseal marrow and bone from various types of chronic infectious arthritis, seven were positive and of these, four were positive for streptococcus and three for diphtheroids. Of fourteen specimens of synovial membrane, four were positive; in two

cultures the organisms were streptococcus and in two diphtheroids. In a series of forty control cases other than those of non-specific arthritis yielded organisms in twenty-one cases; but in no case was the streptococcus found. These were probably due to secondary infection or accidental contamination.

Therefore, they found that the epiphyseal marrow and bone yielded bacteria more frequently than any of the other tissues.

In some previous work, Hadjopoulous and Burbank (28) did considerable work on complement fixation reactions in relation to chronic arthritis and come to the conclusion that although the antibodies worked with covered a wide field, they could be reduced to three major groups which in the order of frequency and intensity of reaction were: first, streptococci, various types; second, against staphylococcus aureus; and third, against the paracolon group of gram negative bacilli. They then did considerable work on rabbits by injecting these rabbits with different strains of streptococci. With the viridans group they were able to produce arthritic changes which closely simulated the human type of proliferative arthritis.

With this as a basis to the fact that arthritis was of bacterial origin, they next tried to isolate the pathogenic organism from the blood stream. In their series of cases almost all cultures were negative but on examination of hanging drop slides they were able to detect ill-defined streptococcus or diphtheroid-like forms which would not take stains and were not seen in dry smears. They then came to the conclusion that they were dealing with a viable streptococcus. They next had to neutralize this bacteriolytic action and then they were able to grow pure cultures of the streptococci from the blood stream.

In a series of one hundred and forty-five arthritic cases they were able to get positive cultures in twenty-nine cases or 30%. The streptococcus was isolated in 10%, diphtheroids in 8% and staphylococcus aureus in 5%. They then took the above strains of organisms and injected them into rabbits and produced a typical chronic arthritis. Therefore, they concluded that the main primary cause of chronic rheumatoid arthritis seemed to be a highly selective group of streptococci, and that a secondary role may be played by diphtheroid bacilli, bacilli of the paracolon group and staphylococcus aureus.

Lewellyn and Barker (29) believe that the most com-

mon cause of chronic arthritis is the hemolytic streptococcus. They also state that 75% of arthritis is due to some foci of infection in the head and that the mere removal of foci of infection in the tonsils is not sufficient. For once the infection has spread to the joints, the latter could act as a new foci where bacteria could be further disseminated or in other words each infected joint then becomes a secondary foci of infection.

Moon and Edwards (30) report a series of eighty-three cases in which blood cultures were taken in every case with the following results: non-hemolytic streptococci, 18; B. Mucous, 3; diphtheroid bacilli, 3; unidentified organisms, 1; and negative culture, 58.

The results in their animal inoculation with the organisms from blood cultures showed a localization of infection in tissues corresponding to those infected in the patient. They also are of the impression that the organism may be isolated from the blood stream more frequently in the early febrile condition and less frequently in the subacute and chronic state, probably due to the fact that the organisms are embedded deeper in the affected tissues. They found in their series of cases that the streptococcus was the predominating organism although

other organisms probably play a minor role.

Burbank (31) who has done considerable work on the etiology of chronic arthritis is a strong believer that the streptococcus is the most common etiological factor. It is very interesting to note that in his large series of cases there seems to be a seasonal influence on the bacteriological findings. He states that the best time to obtain positive cultures is the late fall and early winter months. In the latter part of October and early November the bacteria isolated usually belong to the diphthero-streptococci type of microorganisms. They found that even with a definite diphtheroid morphology repeated transplantations caused some of these organisms to change to a definite streptococcic type.

In the latter part of November, all of December and most of January, true streptococcic type appear, while during the spring and summer months most all the cultures are negative.

This seasonal appearance or influence on bacteriological findings may be an explanation to the reason why so many blood cultures are negative. In searching through the literature, I have not been able to find any other worker except Burbank who states any relation of seasonal

influences on blood cultures.

Burbank also made stool cultures in all of his arthritic cases and found that well over 90% of all definite arthritic cases had pathogenic streptococci in large numbers in the intestinal tract. Therefore he considers the intestinal tract as one of the main portals of entry.

Gray (32) and his co-workers did a considerable amount of work on blood cultures. In their series of one hundred and forty-four cases, eighty-eight or 61% of their cases yielded a growth of streptococcus from the blood or joints, and in a number of cases streptococci were isolated from both the joints and blood.

Clawson and Wetherby (33) in their series of fifty cases report a positive blood culture for the streptococcus in 50% while only one patient of a control series of fifty patients showed a positive culture for streptococcus and this patient had a pelvic infection.

Probably the most extensive work done on the etiology of rheumatoid arthritis was that of Nicholls, Cecil and Stainby (34). In a series of one hundred and fifty-four cases which were diagnosed as rheumatoid arthritis, blood cultures were taken from all cases. Of the one hundred and fifty-four patients cultured, ninety-six or

62.3% yielded a short chained streptococcus. To confirm this work, they ran a control group of one hundred and four patients obtaining four positive cultures, and of this group many had various diseases, including infections of various kinds and degenerative arthritis.

Joint cultures were made in forty-nine cases of rheumatoid arthritis. In thirty-three cases or 67.3% a short-chained streptococcus was recovered from the joint culture. A control group of eighteen patients was also run in connection with this and in every case the culture was negative.

An interesting part of their work was the correlation of streptococcus isolated from the blood with streptococcus cultured from the joints and from various foci of infection. In a number of cases streptococci morphologically, culturally and biologically identical have been recovered from the blood, the joint and some focus of infection in the same patient. In forty-eight cases cultures were made both from the blood and from one of the infected joints in the same patient. In twenty-one cases or 43.8% streptococci were recovered from both the blood and the joint in the same patient. Morphologically and culturally the streptococcus in each case appeared

identical.

They also did considerable experimental work on production of experimental arthritis in rabbits by the injection of streptococci obtained from their arthritic patients. They were able to produce a chronic arthritis which simulated that in man, also they were able to recover the same organism from the blood stream and from the affected joints of the arthritic rabbit.

This is the most definite proof we have that the streptococcus is the etiological factor in rheumatoid arthritis. From a summary of their work they state that the evidence for the streptococcal origin of rheumatoid arthritis, according to their work is as follows:

1. Almost constant presence of streptococci in foci of infection.

2. Streptococci recoverable from blood in 62.3% of rheumatoid patients; 3.9% in pathologic controls; and none in healthy controls.

3. Streptococci recoverable from affected joints in 67.3% of rheumatoid patients; from blood or joints in 77%; none from non-rheumatoid joints.

4. High agglutination of "typical strains" of streptococci with serums of 94% of patients with rheumatoid

arthritis.

5. Disappearance of agglutinins with recovery from symptoms of arthritis.

6. Biologic identity of streptococci recovered from blood, joint and foci of infection in the same patient, though there have been a number of exceptions to the rule.

7. Reproduction of rheumatoid arthritis in rabbits with "typical strains of streptococci".

8. Recovery of same streptococci from blood and joint of arthritic rabbits.

9. Striking similiarity of histologic changes in rabbits joints to those in human rheumatoid joints.

The streptococcus has been considered by most workers as most probable cause of rheumatoid arthritis. The biggest share of the work that has been done on the etiology of rheumatoid arthritis, has been on the streptococcus as the most probable etiological factor.

Traut (35) has recorded the highest percentage of positive blood cultures that I have been able to find. In cultures taken from 38 patients he was able to obtain twenty-one or 71% positive cultures. In a series of twenty controls which were run in identically the same manner, he did not get any growth. The organism which

he isolated was a colony showing diplococci or diphtheroid forms with bipolar granules. These bacteria had characteristics of enterococci. By this he meant a gram-positive capsulated streptococcus which may appear as a diplococcus or as a diplo-bacillus.

Richard (36) was not able to obtain this high a percentage of positive blood cultures. In his series of one hundred and four cases, he was only able to obtain fourteen positive cultures but all these were classed as the *Streptococcus viridans*. Control cultures were made from the blood of other patients but no growth of this organism was obtained.

He also ran a complement fixation test on every patient with *Streptococcus viridans* antigen and was able to obtain a positive test in sixty-eight cases.

Forkner (37) and his workers have done considerable work on the bacteriology of synovial fluid in chronic arthritis. In a series of sixty-three cases, they were able to obtain a positive culture from the joint in 23% of the cases and positive growth from lymph nodes in 48% of the cases with *Streptococcus viridans* as the most common invader and an occasional case of gonococcus and one of *staphylococcus aureus*.

Considerable work has been done on the agglutination test is trying to prove the streptococcus as a etiological factor in rheumatoid arthritis.

In a study of one thousand two hundred and five agglutination tests, made by Keefer, Myers and Oppel (38) on three hundred and thirty-two patients using four different strains of hemolytic streptococcus, they were able to show that 54.5% of the patients with rheumatoid arthritis had positive blood serum agglutination.

Working along this same line, Nicholls and Stainsby found that in a series of one hundred ten patients the serum of patients with chronic infectious arthritis usually gave a strong specific agglutination reaction with typical strains of streptococcus. In their control group this was not obtained. They also found that degenerative arthritis could be differentiated from infectious arthritis by the agglutination reaction and, therefore, were of the opinion that the two must have different etiologies.

Due to the report of Cecil, Nicholls and Stainsby (34) there was considerable experimental work undertaken by other men to try and reproduce their results. Dawson, Olmstead and Boots (39) did considerable bacteriological work on blood, synovial fluid and subcutaneous nodules.

But their work did not in any way correlate with the work of Cecil and his co-workers. In a series of one hundred five blood cultures on patients with typical rheumatoid arthritis, blood cultures failed to yield results which they could consider of etiological importance. They also did considerable work on joint culture also culture of subcutaneous nodules but in no instance could they culture organisms which could be considered of etiological significance.

They then followed up this work by running one thousand agglutination tests on patients with rheumatoid arthritis. They found that in the great majority of case sera of patients with rheumatoid arthritis possesses the property of agglutinating hemolytic streptococcus to an extraordinary high titre. Due to the correlation of their two groups of work they were of the impression that the majority of cases of rheumatoid arthritis represents the response of the affected tissue to products of *Streptococcus hemolyticus* absorbed from a distant focus.

Due to the fact that bacteriological examination of the blood and joint fluid have been negative in so many cases, Rosenow (40) conceived the idea of trying

to isolate an organism from the lymph glands draining the involved joint.

In thirty-eight cases, in which the regional lymph glands were excised and cultures made, organisms were found in all but three cases. In a number of glands several organisms were found at the same time. Streptococci were obtained in fourteen cases; a peculiar, streptococcus-like organism at first completely or partially anaerobic was found in nine cases while *Bacillus welchi*, staphylococci, *B. mucous*, and gonococci made up the remainder of the cases. In no case was the *Streptococcus hemolyticus* obtained. The *Streptococcus* isolated resembled that of the viridans more than hemolytic streptococci. The virulence of all the strains tested were slight and when inoculated into rabbits and dogs produced a chronic arthritis. They then made an autogenous vaccine from the organisms isolated from the glands, and when injected into patients produced a marked improvement. They therefore concluded that the organisms found in the regional lymph glands were the etiological factor of the disease.

Poston (41), while working in the department of orthopedics of the John Hopkins Hospital, found that the

streptococcus was found most commonly in gland cultures from regional lymph glands of patients with rheumatoid arthritis. Her results showed that of one hundred and twenty glands cultured, growth was obtained from seventy two or 60%. The organisms recovered were Streptococcus viridans, sixty cases; Streptococcus nonhemolyticus, two; Staphylococcus aureus, two and gonococcus, one. Ninety per cent of the organisms grown belonged to the streptococcus viridans group.

Most of the workers on arthritis have considered the nose and throat as the primary foci of infection. The gastro-intestinal tract has also been considered by many men as a probable foci of infection either primary or secondary. Keating (43) is of the opinion that the gastro-intestinal tract is a secondary foci of infection with the nose and throat as the primary foci.

In a series of thirty-eight cases he was able to demonstrate streptococci in the feces in thirty-six cases, and all but two of these were hemolytic. Marietta, while working in the same hospital was able to culture forty-five positive stools in his cases, in all they were able to obtain a total of over ninety patients with undoubted chronic arthritis, which showed positive stool cultures

for either of the viridans or hemolytic group. They then took a series of one hundred sixteen cases as controls and were able to obtain only thirteen positive cultures for streptococci. He then treated his patients by use of autogenous vaccines and colonic irrigation with very good results. He therefore concluded that the most common foci of infection was the gastro-intestinal tract.

Fishbaugh (43) working along this very same line believed that there was a definite relationship between the colon and infectious joint disease. In his series of eighty cases he found they were free of any source of infection aside from the gastro-intestinal tract. By examination of the gastro-intestinal tract in these arthritic patients he found five conditions which he considered as etiological factors in chronic arthritis. They were chronic constipation, chronic or subacute colitis, bands and adhesions, diverticulitis, and rectal crypts and hemorrhoids. He considered these five factors as acting as direct foci of infection or by producing stasis of the gastro-intestinal tract which were inducive to bacterial growth. In his series of cases, treating them on these pathological conditions he obtained a cure or improvement in all but eight cases. Therefore he concluded that there

was a group of arthritic patients in which the large intestine was an etiological factor.

Probably the largest amount of work done on the relation of the gastro-intestinal tract to chronic arthritis was that of Smith (44) at least on the surgical problem. He states that the probable primary foci of infection is the nose or throat, but that the gastro-intestinal tract soon becomes infected and acts as the main foci of infection. The gastro-intestinal tract becomes infected, probably due to the failure of some part of the ilio-caecal coil to completely empty itself properly. With as a basis for his work, he examined the intestinal tract of more than one hundred patients with the x-ray and found a similiarity of the picture of the ileocecal coil. He then came to the conclusion that the typical soil for development of arthritis was a congenital mobile caecum producing a impairment of the physiological function of the colon so that the cecum became more of an inert sac and did not empty itself. With the cecum constantly filled with a culture medium, a streptococcus infection resulted, which in its turn, becomes the main foci of infection.

Therefore his patients were treated mostly by sur-

gery in freeing bands or trying to restore normal function of the bowel. In sixty-eight of his patients abdominal surgery was resorted to with very marked improvement. Most of his surgery consisted in removing or freeing bands, appendices, diverticuli; but in a few cases even the colon was removed. This work seems to indicate that there may be some relation between chronic arthritis and failure of some part of the ileocecal coil to completely empty itself.

From the work that has been surveyed we find most of the workers are of the impression that the streptococcus is probably the offending organism in chronic arthritis. There a number of men who think that other organisms are probably the etiological factors.

Lichtman and Gross (45), working with the streptococcus in rheumatoid arthritis were only able to obtain positive blood cultures in only 6% of their cases and thereby considered that the streptococcus was not present consistently enough to consider it as an etiological factor.

Bernhardt and Hench (46) were not able to obtain a single positive blood culture in this group of eighty cases. In a series of seven hundred eighty cases in

which he reviewed, sterile cultures were obtained in 74%; various organisms were isolated in 25%. Streptococci of various types were isolated in 18%, while numerous organisms made up the remainder of the group.

Some workers have considered other organisms as the etiological factor of chronic arthritis. The protozoan may even play some part according to Barrow and Armstrong(47). Out of two hundred forty-five cases of rheumatoid arthritis, 94% were found positive for protozoan infection. They stated that the protozoan could not be found in the joint and this was due to the fact that the joint infection is merely a manifestation of a systemic disease, and that the arthritis is probably due to a toxin absorbed from the foreign protein of the protozoan in the digestive tract. In their group of cases they used parasitic treatment and surgery where necessary to restore normal physiological function of the bowel. They report clinical benefits in 93% of their cases treated in this manner.

Holland (48) also reports that the protozoan may be a etiological factor. In a series of thirty cases of chronic arthritis he found six of them due to the presence of a parasite. The arthritic condition immediately cleared up by the administration of anthelmintics.

Dick (49) believes that other organisms besides the streptococcus may produce rheumatoid arthritis. In a number of cases, cultures were obtained from the infected tonsils which showed growths of Friedlanders bacillus and an occasional streptococcus. The streptococcus, when injected into rabbits and dogs, did not produce any arthritic symptoms. When injected intravenously the Friedlanders bacillus produced joint lesions in every instance.

Rosenow (50) reports that the diphtheroid bacillus may also be considered as a causative factor in chronic arthritis. In a number of cases he was able to obtain positive blood cultures for the diphtheroid bacilli. In the same patient he also found foci of infection in the teeth or tonsils containing the diphtheroid bacillus.

An interesting theory on the etiology of chronic arthritis was that ventured by Lintz (51) in 1924. He did considerable work on asthmatic patients and found that in a series of two hundred allergic cases in which he examined, seventy-seven cases showed a presence of arthritis. Therefore he considered it possible that some cases of arthritis might be on an allergic basis.

Turnbull (52) working at this same time reported an interesting article on the relation of anaphylactic dis-

turbance to arthritis. He states that the most probable cause is some infectious cause, but that sensitization to foreign protein may produce arthritic changes if allowed to act over any length of time. This foreign protein may be of bacterial origin or other proteins, so that first any foci of infection should be eliminated. If no foci can be found, then cutaneous tests should be made to determine what sensitizing proteins are being ingested in the diet which could be held accountable for the existing arthritis. He has obtained very good results in 60% of his cases. He also has noted that by eliminating the sensitizing protein from the diet, many cases have had their arthritic symptoms disappear, and by failure to adhere to their dietary limitation has immediately reproduced their arthritic symptoms.

The endocrine glands have long been considered as having some definite relationship to arthritis. This is most common especially in the ostioarthritic, but some men believe that the endocrines also play a role in rheumatoid arthritis. The thyroid is probably the most common gland showing any relation to arthritis, this was especially true in Fliegall and Straus's (53) series of cases. The favorable results of treatment in some cases

of arthritis deformans with iodine preparations support this view.

Llewellyn (54) published a very interesting article on the relation of endocrines to rheumatoid arthritis. He believes that hypothyroidism quite often is one of the etiologic factors, although some of the other glands at times show a definite relationship, especially pituitary, pancreas and the adrenals. The low sugar tolerance found in arthritis may be an indication of pancreatic involvement. The fact that so many of the arthritic conditions are found around the menopause or following delivery may indicate a pituitary involvement. The adrenals may show their presence by the low tension pulse quite often found in arthritis. Due to the fact that these endocrine disorders are found quite frequently in the arthritic patient, it may be the basis for the arthritic diasthesis. In England we find that rheumatism is more prevalent in the endemic goitre regions.

Ashworth (55) gives probably the broadest view, and also the view which seems most logical on the etiology of rheumatoid arthritis. He believes that chronic arthritis is a disease similar to pneumonia, where a fairly definite syndrome may result from one of several

organisms. The streptococcus being the most common organism although other organisms may produce the same disease, also we have a number of different types of the streptococcus; as in pneumonia the disease is usually produced by the pneumococcus and here we have several different types, also pneumonia may be produced by organisms other than the pneumococcus.

Etiology of Degenerative Arthritis-

Degenerative arthritis is a distinct disease entity and has nothing to do with infectious arthritis. Both the exciting and predisposing causes are different from those of infectious arthritis. Degenerative arthritis occurs in those who are physiologically old. It is, therefore, usually seen in people of middle age, or even older, but occasionally occurs as early as the forty-fifth year. It is usually associated with arteriosclerosis, obesity, gray and falling hair and other signs of tissue deterioration. In most cases, however, degenerative arthritis remains purely a degenerative process, and as such there is little evidence to show that it is infectious. The character of its pathological changes, its association with other sclerotic and

degenerative processes in the body, the absence in most cases of foci of infection, and finally the clinical course of the disease all indicate rather strongly that the condition is not of bacterial origin.

In regard to the exciting cause of degenerative arthritis, we may say it is trauma. This can be demonstrated in nearly every case. The trauma may be of an acute nature, but in by far the largest percentage of cases, it is chronic, and often rather insidious. With the advance in years we find the joints, particularly those subjected to the most usage and most strain may wear down.

We very seldom find this wearing down of a joint in early life unless some accident has produced some trauma to the joint or unless the strain has been excessive. However with the advance in age, we find the cartilage appears to lose some of its capacity for repair, and the degenerative process begins. Therefore some of the most common predisposing factors are as follows:

Old age- We find that any joint or joints that are subjected to excessive strain may begin to show a thinning of the cartilage and new growth of bone around the edge of the joint. It is quite possible that this decrease in the wearing quality of the joint is dependent

upon some disturbance in the local circulation. This may be in the nature of an endarteritis, or possibly capillary obstruction following compression of tissue. It is characteristic of senescence that it tends to manifest itself most in that organ or tissue which has been subjected to the hardest usage. Therefore, one would expect to find degenerative arthritis in middle aged laborers, and this is particularly true of morbus coxae senilis. The senile form of degenerative arthritis is almost a physiological process, and seems to develop at times in joints where no traumatic factor can be demonstrated.

Overweight- This is one of the most important causes of degenerative arthritis. Here we must consider that in obese patients the weight-bearing joints are being constantly subjected to trauma. The joints most commonly involved are the intervertebral joints of the lumbar spine, the lumbosacral joint, the sacroiliac joints, and the joints of the hips, knees, ankles and feet. In this type of arthritis, the trauma is slight but constant, due to the excessive weight of the patient.

Faulty posture- Faulty posture may predispose to degenerative arthritis by putting unnatural strain on a joint, or by bringing about an unequal pressure on the

joint surface. Incorrect standing or sitting, undoubtedly puts a strain on the lower spine, and improper standing or an improper gait puts an unnatural strain on the joints of the legs, particularly on the knee and ankle joints. Obese patients nearly all have a bad posture due to the fact that the lower abdomen is abnormally prominent, the upper back is rounded, and the shoulders pushed forward. The feet are abducted, producing a distinct tendency toward knock-knee. This posture produces a strain in the lumbar region, in the knees and in the feet, which, of course, is accentuated by the overweight, and these are the joints which show the characteristic changes.

Occupation- We find occupation has an important bearing on the etiology of degenerative arthritis. In morbus coxae senilis we have a disease of laborers and mechanics, which may develop either as a result of an acute trauma, or after long continued overuse, that is, chronic trauma of the joints. Chauffeurs quite often develop arthritis in the hip and back. Seamstresses and laundresses are very prone to Heberden's nodes.

Physical defects- Physical defects play a significant part in degenerative arthritis particularly of

the lumbosacral spine. In fat patients with pendulous abdomens, slight displacement forward of a lumbar vertebrae may lead eventually to bony changes. Subluxation of the sacro-illiac joint may predispose to degenerative arthritis. Flat feet may lead to arthritis in the feet themselves, but more often produces an improper distribution of weight, which in turn is instrumental in setting up arthritic changes in the knees. Fractures which involve the articular surfaces of the joint may be followed by ostioarthritis, particularly in middle aged patients.

Exposure- Exposure is a predisposing factor in degenerative arthritis, though probably to a lesser extent than in infectious arthritis. Everyone knows that damp, humid weather aggravates rheumatic conditions, and that a dry, sunny climate with moderate altitude favors improvement. Therefore people who live hard and exposed lives are more prone to degenerative arthritis than those whose circumstances are more fortunate.

The pathology of the joints, at least of the extremities, that has been studied and the clinical signs and symptoms indicate a noninfectious etiology. Many theories have been advanced as to the etiologic agencies that might explain degeneration of cartilage, which is the outstanding

pathologic findings.

Some of the older theories as to etiology were brought forth by pathologists. One being that the primary change was an inflammatory osteoporosis in the subchondral bone, which was followed by a sclerosis with secondary degeneration of the cartilage. Another theory was that the primary pathologic change was an atrophy of the subchondral bone and that this was followed by a loosening of the articular cartilage. Another theory was that the cartilage changes were secondary to an abnormal calcification in the border zone between the bone and cartilage. Still another theory was that the arthritis was a nutritional disturbance in the hyaline cartilage.

Some of the more recent authors have brought forth other ideas. Wollenberg (56) modified one of the above theories that the disease is due to a nutritional disturbance in the joint cartilage to the extent that this nutritional disturbance is in the nature of an ischemia, due to local arteriosclerosis and that the arthritis is primarily a vascular disease in which the joint changes are secondary to the local vascular sclerosis.

Axhausen (57), as a result of some experimental work, concluded that cartilage necrosis is the primary cause of

the disease and that the presence of dead cartilage in the joint exerts some influence, possibly chemical in nature, which leads to the development of the classical disease picture.

Goldthwaite (58) has been the chief exponent of the mechanical theory in this country and attributes the development and progress of the disease to faulty body mechanics and abnormal strain on the involved joints.

There has been a great deal of experimental work done on the production of hypertrophic arthritis. Axhausen (57) probably did the first experimental work. He destroyed a portion of the knee cartilage in a rabbit with iodine or ammonium hydroxide and later when the rabbit was killed, pathologic changes were found in the joint which resembled those found in osteoarthritis in man. Others have obtained similar results by impairing the blood supply to a portion of the cartilage or by traumatizing the joint. Key (59) has produced osteoarthritis 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 also produced mild arthritic-like changes in the knee joints of rabbits by the injection of mild irritants.

Treatment-

In the treatment of chronic arthritis we must consider it an individual problem. The following is just a survey of the most important methods used in the treatment of chronic arthritis:

Diet:

According to Pemberton (13) diet is one of the most important factors in treatment of chronic arthritis. Due to the fact, that in his experimental work on glucose tolerance test he found a low glucose tolerance in chronic arthritis, he advocates a low carbohydrate diet with a slightly high fat. He is of the opinion that chronic arthritis may be often markedly benefited and in many cases arrested by the institution of a low caloric intake, and of this he reduces carbohydrate most, the proteins somewhat less, and fat least of all. This low caloric intake is of great value especially in the obese patients and this is particularly seen in the osteoarthritides. In this restricted caloric intake we must be sure we are not dealing with an anemic or emaciated person, for here it would not be worthy of the sacrifice.

Some authors believe that the abnormalities observed in the colon in rheumatoid arthritis are manifestations of malnutrition and that malnutrition frequently plays a part in the development of arthritis. They have found that these abnormalities in the colon are markedly improved by high vitamine diet with co-incident improvement in the arthritis. Therefore, they advise a high vitamine diet consisting of cod liver oil, wheat germ or baker's yeast, and fruit juice.

Focal Infection:

Probably the most important single factor in the treatment of rheumatoid arthritis is the removal of foci of infection. The most common sites of focal infection are the tonsils, teeth, and sinuses, though, of course, a focus of infection may exist in almost any part of the body.

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. When infectious arthritis is allowed to run along for two or three years before the foci are removed, the results are usually most disappointing. We can easily see that a foci of infection of a year or two duration

may be responsible for secondary foci, so that mere removal of primary foci may have but a slight effect on the disease for we already have a secondary foci acting in the same manner as the primary foci.

The tonsils and teeth are the two most common foci of infection and it is usually after examining the teeth and tonsils, that a search for foci infection is given up. We should remember that the accessory sinuses of the head are common foci, and here we should be very careful for infection of the sinus is probably missed more than any other focus.

Due to the discussion under etiology of the colon and the intestine being a common etiological factor we must not forget that the intestine and more particularly the colon may contain, or itself constitute, a site of infection or intoxication. Ulceration of the colon, diverticuli, and even appendix may also act as a foci of infection.

The gallbladder should not be overlooked, and in case no other foci of infection is found, an investigation by the Graham dye method may be indicated.

We should also always keep in mind the genito-urinary tract as a foci of infection. The most common

type of arthritis found due to genito-urinary infection is gonorrhoeal arthritis, but we must also remember that a foci may be in the bladder, seminal vesicle, prostate and even in the fallopian tubes producing a chronic infectious arthritis. In removal of foci infection we find that there is considerable disagreement, Pemberton (13) is of the belief that removal of foci of infection does not play a very important role; while Cecil (60) states that the prognosis depends on the promptness with which foci of infection are discovered and removed.

Non-specific Protein Therapy:

This form of treatment has been used for over twenty-five years with some good results, while in other cases seems to be of no benefit.

Miller and Lusk (61) were the first to introduce the use of foreign protein in chronic arthritis. In a series of eighty-five cases they reported in 1926, treated with typhoid vaccine, improvement was shown in fifty per cent of their cases. Cecil (62) in his series of forty cases also reports good results by foreign protein therapy.

In using this form of therapy we must first consider

it is quite unpleasant for the patient and also we must first consider the patient. It is unsuitable for the old or feeble or those suffering from myocardial disease.

Various protein substances are injected intravenously, such as peptone, milk, or T.A.B. vaccine in increasing dosage. If the vaccine is to be used, a preliminary injection of thirty million may be given, and the dose be increased every fifth day until at the sixth and the final injection a dose of two hundred million is administered. A somewhat severe reaction occurs within a few hours after the injection. There is a rise of temperature often associated with a rigor and focal reaction in the affected joints. This is followed by perspiration, and on improvement not only in the condition of the joints themselves, which become less painful, swollen and stiff, but in the patients general condition.

The way in which protein shock therapy acts is not clear in the present state of knowledge. It has been suggested that the resulting improvement is due to increased lymph flow, to the perspiration, or to alteration in the ferment and anti-ferment action of the blood serum.

Vaccine Therapy:

Subcutaneous injection of a streptococcic vaccine has been used extensively for many years in the treatment of arthritis. Both autogenous and stock vaccine have been tried. Some of the larger series of vaccinated patients have been those of Billings, Coleman, and Hibbs (63). In their series of cases in 1917, they reported three hundred nine cases which have received vaccine therapy, and of this group one hundred forty-two or 46% were improved and seventy-one or 23% recovered. In a second series of two hundred and twenty-five cases reported in 1921, 19.6% were improved and 40.5% had recovered.

Burbank (64) reports good results by the use of vaccine therapy. In his series of one thousand sixteen cases of chronic arthritis all were treated by intramuscular vaccine therapy. Of the total number 7.5% were worse or unimproved, 10.7% slightly improved, 8.5% moderately improved, 56.6% very markedly improved, and 16.7% were symptom free.

Gray and Gowen (65) vaccinated patients having chronic arthritis by combining subcutaneous and

intravenous injections and reports very good results. Their best results, being from intravenous injections.

Clawson and Wetherby (66), at the University of Minnesota have done a great deal of work on vaccine therapy lately. In a series of three hundred sixty-five cases of chronic arthritis treated intravenously, with a streptococcic vaccine, 80% were clinically improved.

As shown in previous work that subcutaneous streptococcus vaccination does not desensitize the hypersensitive chronic arthritic patient but tends to increase the hypersensitiveness. The subcutaneous method of giving a streptococcic vaccine increases protective immunity only slightly. They also found that intravenous streptococcic vaccination desensitizes the hypersensitive patient and also brings about a high degree of protective immunity.

The following is the most accepted method of vaccine therapy and that employed by Clawson and Wetherby: Intravenous injection of a streptococcic vaccine is given at weekly intervals for at least eight weeks in the average case. After eight injections the interval

is usually extended to two weeks for several more injections and later extended to three or four week intervals. The extension of treatment should be guarded by clinical improvement.

The initial dose is 100,000,000 killed organisms. This should be increased by 100,000,000 at each weekly injection, if no marked reaction has occurred. If a disagreeable reaction follows the previous injection, the dose should be kept at the same level in the following injection. The maximum usually should not exceed 800,000,000 killed organisms; though this may be exceeded in some cases in which the reaction is slight. Reactions of some sort are usually experienced in about 50% of injections. In most cases reaction comes from two to ten hours following treatment. It usually consists of chills of varying degree and duration, followed by fever. The chill only lasts an hour or two and fever usually does not go above 100 to 101 degrees.

Colonic Irrigation:

This procedure has been found beneficial in arthritis, whether it is due to the removal of toxins or merely to stir up a sluggish intestinal circulation by

the application of heat and massage is not determined. It is particularly indicated in cases with ptosed colons, of sluggish action. It is best to have an x-ray study of the colon before beginning colonic irrigations to determine possible contra indications as diverticuli etc.

The procedure usually advisable is to begin with a ten-minute abdominal massage prior to irrigation, commencing on the left side and working downward. Each application of the hands starts about two inches further, from the rectum and works down towards the rectum until finally the massage begins at the right iliac fossa and follows around the entire course of the colon. General kneading movements should also accompany the inflow and outflow of the water which should be introduced in amounts large enough to give the patient the sensation of distension. The solution to be used for irrigation may be ordinary tap water, normal saline or a 5% solution of soda bicarbonate and should be slightly above body temperature, 40 degrees C. A colonic irrigation should always be followed by at least an hour and a half of absolute rest and usually no other vigorous treatment should be given on that day. The usual frequency of irrigation is every other day.

Drugs:

The frequent failure of all types of medication or treatment in chronic arthritis has led to the view that medical agents of whatever kind, have little or no value. Perhaps in no other disease have so many drugs been advocated with so little success. There are, however, a few drugs which have withstood the test of time and are of some value.

Arsenic is probably the most useful of all drugs having application to the arthritic syndrome. Given as sodium cacodylate in $\frac{1}{4}$ grain doses, three times a day, it may be continued for several months and then reduced to twice a day for another month under careful observation. There are apparently two chief influences exercised by arsenic. The first is in connection with a regeneration of the blood elements; the second is in regard to the influence it apparently exerts on metabolism.

The type of case in which arsenic has its most benefit is probably that accompanied by secondary anemia. Fowler's solution may be used but probably is not as beneficial as sodium cacodylate.

Probably the most widely used drug in relation to

arthritis is salicylic acid or one of its derivatives. The salicylates have their most useful field of action in acute inflammatory arthritis but is also useful in the chronic forms. The most common form used is sodium salicylate; in doses of from ten grains two or three times a day, to fifteen or twenty grains or more, every two or three hours. Sodium salicylate may cause some gastric upset with loss of appetite so that acetylsalicylic acid has been used a great deal of late.

Salicylates probably have very little beneficial effect except for the relief of pain, therefore, the drug is best used in beginning treatment and also acute exacerbation of chronic arthritis. There is some question as to whether constant use of salicylates is not even deleterious. Some believe that there is slight kidney impairment, also recently there is some evidence that salicylates may impair antibody formation. Therefore, probably the ideal use of salicylates is in beginning treatment and acute exacerbations.

Iodine is another drug that has followed arthritis down through the ages. It is probably used most commonly in the form of potassium iodide. In the light of recent studies upon the thyroid, it appears that iodides

exercise their benefits largely or entirely through their influence upon this gland and so possibly on metabolism at large. It is useful as an alterative, especially when the use of arsenic is temporarily discontinued.

Ortho-Iodoxy benzoic acid is a drug which was introduced by Young and Youmans (67) in the treatment of arthritis. The composition of this substance closely resembles that of salicylic acid. The basis for using it lay in the fact that it had been shown to be an antiseptic, upon intravenous injection in animals.

Millard Smith (68) has made a thorough study of the drug and as a result of his experiments he places ortho-iodoxy benzoic acid among the most important drugs available in the treatment of arthritis. Other workers have reported that it is merely a superior salicylate with a larger amount of analgesia over a period of time longer than occurs following the usual salicylates.

This drug may be used orally in doses one gram three or four times weekly. Intravenously its initial dose is .5 gram increasing upward to 1.5 grams depending upon the reaction. Usually about ten grams in all are given over

a period of three weeks.

Nitrites have been used with varying results. In view of the pathology, that is a disturbance in the finer blood vessels in arthritis, and in view of the influence which vasodilators, such as the nitrites have been shown experimentally to have upon some consequences of this disturbance, it would appear that the administration of vasodilators might conceivably have a beneficial clinical influence as well. This has been verified by Pemberton, who states favorable results with its use.

There can be no question that in the hands of many observers, thyroid extract has produced beneficial results. Some observers believe there is a definite relationship between the thyroid and arthritis. Thyroid extract may be beneficial in those cases with a lowered metabolism, but may also be quite harmful if used indiscriminately. When thyroid extract is administered the dose should be small and only cautiously increased.

Physio-therapy:

Physical therapy holds a very important place in the

treatment of arthritis. This is being especially recognized in the last few years due to the activities of the Council on Physical Therapy of the American Medical Association.

Under the heading of physical therapy are included various measures such as hydrotherapy, massage, passive motion, dry heat, in the form of baking, electricity in its various forms, and local applications.

The effect of systemic heat is to increase the pulse rate, induce hyperpyrexia and, in consequence, over-ventilation of the lungs. Carbon dioxide is washed out of the lungs in undue amounts and also escapes from the body in the urine and sweat. Other organic acids, together with phosphates and sulphates from the increased metabolism, also leave the body, and the net result is to induce a relative alkalosis.

The physiological changes induced by local exposure of a part to heat are along the lines just described, but more intensive treatment is obviously possible because the process can be longer continued. Relaxation of tissue is induced, especially of the muscles, together with a hyperemia probably due to dilatation of blood vessels

and a greater total flow in the area concerned. Local sweating also takes place, and the tissues are put in a condition to benefit more than they otherwise would by such measures as massage and passive motion or even active motion. If the local use of heat is continued too long a systemic response may take place, dependent on a general hyperpyrexia, comparable to that following systemic exposure.

Dry heat may be applied in form of the common hot water bottle, but the most common mode of application of dry heat is that afforded by the electric-light bulb. For systemic exposure lights are usually placed in a cabinet or large box containing a reflecting interior surface and large enough to allow the subject to sit in a chair, the head emerging through the door or other covering at the top. The number of lights in such an apparatus may be from twenty to fifty or more, subject to control in small groups.

In some of the larger institutions dry heat may be administered in the form of hot air, but this usually requires elaborate equipment for the purpose of heating the air. Electrical resistance coils placed within a box-like

container also afford a useful means of obtaining dry heat, especially for application to limited areas, such as a knee or ankle.

Probably the oldest form of the systemic application of heat is the hot bath. The presence of thermal springs scattered throughout the world has given rise to elaborate establishments for their utilization, but as far as heat is concerned about as good results may be obtained from the ordinary bath tub. The water may be pure or may contain various salts or other substances, such as magnesium sulphate or carbon dioxide.

Next to the hot bath, the most frequently employed form of moist heat is that afforded by the so-called hot pack. This consists, in principle, in wrapping the body in a sheet or blanket made hot by being dipped in hot water of about 82 degrees C. and subsequently wrung out more or less thoroughly. Obviously the severity of application will depend upon the temperature of the enveloping sheet or blanket, and this effect will be further influenced by the number of blankets superimposed on the subject to prevent evaporation and cooling.

Another form of exposure to moist heat is the steam

bath, although this is not used so frequently due to the fact the patient usually has to breathe the hot moist air, also there is some danger to this procedure from burns.

The full benefits to be derived from the systemic use of heat alone are not always so gratifying, and sometimes depend on the contrasting and accessory applications of cold. Usually following the hot bath a shower follows which begins considerably above body temperature, and shortly reduced to slightly below body temperature. If a shower is not accessible, a cool sponge bath may be sufficient.

The application of external heat locally to a joint is of great value. It must be considered in conjunction with other principles of treatment of the disease as a whole, and the joint in particular. The measure most often used in conjunction with local external heat is massage. Application of heat should not be carried to the point of irritation and should depend for its effects on repeated use, once or twice a day, for a time varying from about ten minutes to one-half an hour.

Probably one of the most valuable measures in the treatment of arthritis is massage. Recent work in

physiology, has shown that massage may stimulate some of the finer capillaries to open which are normally closed, thereby increasing circulation to the effected parts. Massage may also substitute for mild exercise, and theoretically it is superior for massage of the voluntary muscles, even though vigorous, is not accompanied by the presence of lactic acid and production of acidosis, which accompany relatively mild exercise.

There are four major indications for the use of massage in arthritis. These are respectively: (1) To prevent or delay atrophy of muscle tissue and to help to restore tissue when atrophy has taken place. (2) To improve the local metabolism. (3) To increase the degree to which the circulating blood reaches certain tissues and to increase the return to the circulation of many corpuscular elements tucked away in inactive organs. (4) Massage also keeps the venous channels in better tone so that the return flow is better accomplished. Massage also is of great value in the relief of pain of myositis.

Massage should not be confined to the limbs alone, but should include all superficial muscles of the body.

General massage in arthritis should be given at the outset only every other day. One should very slowly increase the vigor and frequency of the massage. We should be careful about the patient we pick for massage, for massage should never be given to a patient with an acute painful joint. Arthritis varies so much in its severity, and the patient's resistance is so variable, that the use of massage in every case of arthritis is entirely an individual problem.

Rest and Exercise:

The question of rest and exercise in the treatment of arthritis is a very important problem. This is an entirely individual problem. In a broad sense, the rule upon which the decision is based is the degree of activity of the disease. Thus, in acutely inflamed joints, the strain of exercise must be temporarily relieved. We must also remember here that over-indulgence in rest is one of the frequent causes of ankylosis so that passive motion should not be neglected too long.

Probably the best guide to the extent of motion

which is permissible is the amount of pain which exercise produces. Passive manipulation of the joints is begun first and gradually increased until the patient can carry on active exercise.

Roentgen Ray:

This has been used considerably in the last few years with good results especially in proliferative arthritis. Roentgen-ray may be used in two methods; one in fairly large amounts. Here the benefit is derived partly by the nature of a non-specific protein reaction. Immediately following we may see a severe systemic reaction, fever, heightened metabolism, and greatly increased output of phosphates, uric acid, and other products of nuclear breakdown. This is usually followed by clinical benefits both objective and subjective.

The other method of administration of roentgen-ray is wide-spread exposures of short duration. Here the patient does not suffer any systemic reaction, and the benefit is probably derived from a mild stimulus to metabolism. The benefits are probably derived more quickly in this method than in long exposures.

Orthopedic and surgical treatment:

One of the greatest dangers in chronic arthritis is the development of ankylosis and contractures. This is one of the main factors which one should strive to prevent in the treatment of infectious arthritis. The use of physiotherapy is one of the greatest aids in preventing deformities. Rest in a position least likely to cause strain or contracture should be secured when the joint is not in use, particularly at night. Therefore, it may be necessary to apply light splints during the hours the patient is in bed. The correction of postural deformities is also a point that should not be overlooked. In some cases mechanical devices such as braces or other orthopedic appliances are of considerable benefit.

Surgery may be resorted to in some cases. There has been some very good results reported by sympathectomy. In this procedure the nerves are cut controlling the walls of the blood vessels which supply the arthritic joints. This produces an increase circulation to the joint.

We find ankylosis will develop in a certain percentage of cases despite all efforts. Therefore, orthopedic surgery may be of considerable benefit to correct the

deformities ; this is especially true in cases where ankylosis has resulted in positions where the extremity is of minimum use to the patient.

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