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## Arthritis and rheumatoid conditions

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## ARTHRITIS AND RHEUMATOID

### CONDITIONS

#### Introduction

Arthritis is a diseased state characterized by disability and usually, by structural changes in one or more joints, the word being derived from the Greek "arthron", meaning joint, and the ending "itis", meaning "of the nature of", and now signifying inflammation. The subject of arthritis can be sub-divided into a number of sub-divisions such as traumatic, tuberculous, and the like, but the present work deals essentially, with that large group which does not come within any of these categories and has been associated for centuries, by the profession as well as the laity, with the term rheumatism.

It is doubtful whether any disease or group of diseases has such a complicated and contradictory nomenclature as the forms of chronic non-tuberculous arthritis under consideration. By the earlier writers the conditions we are considering were usually considered manifestations of rheumatism or gout. As early as 1881, Charcot described the conditions as "chronic articular rheumatism", sub-dividing them into a "polyarticular type", and a "monoarticular type". The first more rapid in its course, affection younger persons and with but little tendency to formation of new bone, and the second type more gradual in its onset and course, affecting older persons and associated with periarticular bony outgrowths. A long step toward escape from this chaos was taken when Nichols and Richardson published their exhaustive monograph "Macroscopic and Microscopic Morbid Anatomy of Arthritis Deformans", in 1909.

The work of Nichols and Richardson referred the matter solely to the basis of morphological changes actually occurring and as a result they brought the subject of arthritis down to the simple basis of two main types which they call respectively proliferative and degenerative. These types have also been referred to as the atrophic and hypertrophic and at a meeting of the newly created American Committee on Rheumatism, Philadelphia, March 17, 1928, these terms were officially chosen as those to be used by the Committee in its work.

This is essentially the classification adopted by the British Ministry of Health in 1922, although atrophic arthritis is called by the English rheumatoid arthritis, and hypertrophic

arthritis is called by them osteo-arthritis.

Arthritis is one of the oldest diseased states of which there is any historical record, and dates back to the Mesozoic period, long before the advent of man. The preservation of such evidence is due to the fact that arthritis produces lesions which frequently involve the osseous structures and persist long enough to permit of being transformed into fossil form.

The oldest pathological manifestations, such as dental caries, pyorrhea alveolaris, fracture, osteomyelitis, callus etc., appear in the age of amphibians during the latter part of paleozoic time.

In the next era, the mesozoic, during the age of reptiles, various lesions appear in fossil remains, including hemangiomas, osteomas, the arthritides and others.

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.

Subsequent to this and after the arrival of mammalia, we find the cave bear of Europe and the ~~sabre~~-toothed tiger of California, especially subject to it. It is not surprising, therefore, to find that the early evidences of man show that he suffered from arthritis.

There is no question, therefore, that arthritis has been a cause of human suffering since time immemorial, and as one writer has put it, it was the disease par excellence of the ancient Egyptians. The great emphasis that the Greeks and Romans put upon physio-therapy, is evidence of the prevalence of the disease at that time, and there are resorts of spas in Europe, such as Aix les Bains, which have been frequented continuously for two thousand years.

#### Arthritis as an Economic problem

The extent of arthritis as an economic problem in this country, is beginning to be appreciated by the profession, although there has been somewhat earlier recognition of this abroad. Thus, in England before the war "The Cambridge Committee for the Study of Special Diseases", selected arthritis, as the medical and economic problem most needing investigation.

Since the World War, another great movement for the prevention and treatment of arthritis, has been launched by the International Society of Medical Hydrology. The profession in twenty-four countries, has lent support through the cooperation of representative men; and in some countries, notably Sweden, Holland, Germany, England and France, organized activity is well under way.<sup>2</sup>

In Sweden we find that artaritis comes first on the list of disabling diseases causing "permanent pensionable invalidity", aside from cardiovascular and senile conditions. It accounts for 9.1 per cent of cases as against 5.8 per cent for tuberculosis.

In England, using the word rheumatism to include lumbago, we find that it causes nearly one-sixth of the total industrial disability, with an estimated expenditure of £2,000,000 for sick benefit and a loss of 3,000,000 weeks of work per annum.

Creation of an American Committee to cooperate with the International Committee, was accomplished chiefly through the efforts of Dr. Louis B. Wilson, Director of the Mayo Foundation.

For decades, arthritis has been regarded with relative indifference by the medical profession. The disease no doubt, constitutes one of the most difficult fields in medicine, and carries with it, therefore, a fatalistic attitude of hopelessness in the profession, which has driven the discouraged sufferer to commercialized institutions.

In the last few years, however, an increased interest has been aroused in arthritis and it is taking its place as one of the great chapters of medicine, along with tuberculosis and syphilis.

### The Etiology of Arthritis

The etiology of arthritis has long been and still is a matter of dispute. No single factor can be looked upon as the cause of the disease. As yet, no single organism is looked upon as the specific etiological factor. It is possible to show that arthritis is a systemic disease. We must take a wider physiological concept of the disease, considering in each individual case, the role of infection, the influence of heredity and constitutional make-up, the neurological factor, the metabolic disturbances, and the altered peripheral of capillary circulation.

One of the great advances in our knowledge of the etiology

of arthritis came in connection with the theory of focal infection. To Billings<sup>3</sup> of Chicago is commonly attributed the credit for calling to our attention the relationships of dental, tonsillar and other infections to the arthritis complex. However, we are still far from being able to offer precise information as to when an infected tooth, for example, is or is not responsible for systemic effects. Consequently, great numbers of perfectly sound and healthy teeth have been removed and the comfort as well as the health of many persons has been impaired through failure of satisfactory mastication. On the other hand, the practitioner is behind the times who does not study his arthritics, for evidences of focal infection.

Certain precipitating factors usually precede an attack of arthritis. It is well recognized that arthritis may follow attacks of ill health, periods of fatigue, and periods of great physical or mental strain. In the Army during the World War, in a series of 400 cases,<sup>4</sup> the most conspicuous precipitating factor was exposure to wet and cold or both. It played a leading role in 60 per cent of all cases. It is surprising to note that this is in keeping with the ideas of people at large, that exposure is often followed by stiffness or painful function of the part concerned. In these 400 cases studied in the Army, the four leading precipitating factors were; exposure 60 per cent, dysentery 9 per cent, injury 8 per cent and flu 7 per cent.

Recognition of the importance of foci of infection in the production of systemic disease, has been responsible for an intensive study of sites of infection and the bacteriology thereof. Rosenow<sup>5</sup> and his co-workers at the Mayo Foundation and Haden<sup>6</sup> at Kansas City, have been able to induce arthritis in experimental animals following injection of the organism isolated from patients suffering from the disease. It is the contention of these men, that an "elective affinity", exists, by virtue of which an organism obtained from a focus of infection, or an infected joint of a patient suffering from arthritis, will, upon reinjection into an experimental animal, tend to produce an analogous lesion in a comparable joint in that animal. Haden has been able to demonstrate a remarkable elective affinity in cases of eye infection, kidney disease, peptic ulcer, onychia and other conditions.

Various explanations have been advanced to explain this tendency to selective localization. Haden believes, that the degree of clumping, the state of the blood supply of the part, the food supply and the resistance of the tissue are important in determining the site. A more important factor seems to be some peculiar property, probably chemical in nature, inherent in the organism.

Rosenow has stressed "the focus is of importance not only as affording the entrance way for bacteria, but also as a place where varying affinities (for certain tissues) may be acquired."

The sites in the body which most frequently harbor such infections are, the teeth, the tonsils, the accessory sinuses of the nose, the genito-urinary tract, especially the prostate. The organisms most frequently found are the streptococcus viridans, the streptococcus non-hemolyticus and the streptococcus hemolyticus. These organisms are also found in the other chief sites of infection, already mentioned.

Granting that bacteria are the cause of arthritis, we are still at a loss to explain the mechanism by which this pathology is produced. The influence of bacteria in the production of arthritis is in no way comparable to the evidence of bacterial activity as ordinarily understood in the pathological sense. One of the most characteristic lesions of arthritis is involvement of bony tissue, which may ~~become hypertrophic~~ become hypertrophic with new bone formation. It is more conceivable to believe that the bony changes are due to an altered physiology of bone rather than due to bacterial activity.

Zinsser<sup>1</sup> believes, for instance, that rheumatic fever represents an allergic state. Reasoning by analogy, knowing that some cases of arthritis are of bacterial origin, it seems highly probable that the mechanism of this disease may be sought along these lines.

Heredity and constitutional make-up play an important part in the etiology of arthritis. In a study of 1100 cases by Dr. E.G. Peirce and Dr. Ralph Pemberton,<sup>3</sup> hereditary influences, either direct or collateral, were observed in 58% of the cases studied. It does not represent a direct transmissibility from parent to child, but rather a predisposition or a general familial background on which the disease may develop. The proverbial relation of soil and seed is here exemplified, the soil being afforded by the constitutional make-up; the seed being represented by infection or some other exciting agent.

During the World War, a clinical study of chronic arthritis together with laboratory observations was carried out on 400 cases of arthritis. Prior to this time, and subsequently thereto, data have accumulated upon a series of 700 cases in civilian life. A statistical survey, based upon these 1100 cases, has been carried out by Dr. Ralph Pemberton and Dr. E.G. Peirce.

The following is a summary of the clinical data accumulated by these men.

1. In civil life the onset of chronic arthritis was gradual in a little more than one-half of all cases.
2. The knée is the site of most frequent involvement among all groups and in both sexes, although the hands are affected among women with equal frequency.
3. Foci are present in civilian arthritics with the same frequency as occurred among soldiers, viz about 70 per cent.
4. The most frequent sites of focal infection in civilian arthritics were dental, nose and throat, and genits-urinary in the order named. This is in contrast to the studies among soldiers who showed foci most frequently in the tonsils.
5. Symptoms referable to the nervous system were present with surprising frequency and demonstrate the widespread influence of the causes of arthritis.
6. Malignant neoplasms are very infrequent.
7. Active tuberculosis was very infrequent. Dr. Lawrason Brown, of Saranac Lake, found only 11 cases of arthritis among 4499 cases of tuberculosis.
8. Diabetes was met with only 6 of the 700 civilian cases an incidence of 0.85 percent.
9. The blood pressure tends to be mornal, or low among arthritics as a whole. In many cases it is exceedingly low.
10. The normal low hemoglobin and red cell count of women as compared with men may be an important factor in the predominance of the female sex (2 to 1) in arthritis.

The problem of infection, however, does not adequately explain the cause of a great many cases of arthritis, espically of the hypertrophic type. In fact, the English, believe that infection is of no etiological importance in the hypertrophic type. It is quite possible that focal infection is the result of the background rather than the cause of it.

The derangement of function which we now recognize as constituting a background of the rheumatoid problem is one that has to do with the disturbance of the finer blood supply to various parts of the body. Definite proof of this conclusion is to be found in studies of the blood gases, studies of the rapidity with which the circulation in arthritic patients takes care of substances absorbed into it from the digestive tract, and in the study of the blood count, in the blood first issuing from the capillary beds at the periphery in the arthritic patient. Direct study of the capillary beds under the microscope shows them to be the seat of irregularity and a general decrease in blood content and blood flow.

In a series of experiments conducted by Dr. Ralph Pemberton, Dr. Hendrix and Dr. Cronter<sup>1</sup> it was observed, that during the conduction of a test revealing a lowered sugar tolerance, there takes place in most cases a rise in the percentage saturation of that blood with oxygen. The ratio of the oxygen content to the

oxygen capacity increases, which means that more oxygen is left unutilized. Knowing about the beneficial results of heat upon the rheumatic syndrome, they proceeded to test the oxygen percentage of blood, after the patient was subjected to heat applied in the usual therapeutic manner. They observed, that the oxygen saturation of the peripheral blood tends to rise, as the result of application of external heat. This rise in the oxygen saturation is presumably due to the acceleration in the circulation that occurs. These factors suggest that in the arthritic patient there is a change in the circulatory conditions or rate, such that the tissues do not extract from the blood the usual amount of oxygen.

It had been an observation of Pemberton,<sup>10</sup> Cecil,<sup>11</sup> Fletcher,<sup>12</sup> Archer and others, that in a considerable number of arthritics, a lowered caloric intake was followed by undoubted benefits. In view of the evidence, suggesting an increased circulatory rate, it seemed possible that the "lowered glucose tolerance" in arthritis might be referable to an unduly rapid absorption of glucose. Pemberton,<sup>13</sup> in collaboration with F.A. Cajori and C.Y. Crouter, determined to test this, by feeding urea and potassium iodide coincidentally with glucose, in the conduction of a test for lowered sugar tolerance. In their series of experiments it was found that there was no increased rate of absorption, but ~~at~~ a failure of the blood to adequately reach a certain area. Therefore, they determined, by another set of experiments, to reduce the blood flow in some part of the body in such a way as to simulate the arthritic condition and then to conduct the sugar tolerance test in the usual manner. In summing up the results of their experiments, they believe that the evidence strongly indicates, that denial to the muscular tissues of their usual degree of contact with the circulating blood interferes with the withdrawal of glucose, so that when sugar is fed a "lowered sugar tolerance", results. This clearly suggests that circulatory changes contribute to the pathology of arthritis and focal infection with which a lowered sugar tolerance is so closely associated.

Carrying out a similar set of experiments, they were able to show that in normal persons the red cell count of the first drop of finger blood was frequently higher than the count of the freely flowing blood. The majority of patients with arthritis showed the opposite condition and had a lower count in the first drop of finger blood than in the freely flowing blood. The explanation for this phenomenon is again, in accordance with the previous studies, indicating a disturbance in the peripheral blood flow of arthritics. It is, probably, the case in constricted vessels, that fewer cells issue forth following a stab.

- This is further borne out by studies of the surface tem-



perature of arthritics, by means of the thermocouple. Arthritics, as a whole have lower surface temperatures than do normal persons because of the decreased blood flow in the tissues concerned. The capillary bed is in a state resembling vasoconstriction, and is unresponsive to those adaptations which changes in environment impose upon it. This is probably the explanation for the added discomfort that arthritics experience from changes also account for the lowered metabolic rate so often observed in arthritic patients.

It has been possible to show by experimental interference with the blood supply to the patella of dogs, that the consequent reduction of the blood flow is followed by evidences of arthritis, chiefly of the hypertrophic variety.<sup>14</sup>

Dr. Ralph Pemberton<sup>15</sup> believes that the general disturbance in the capillary beds of arthritic patients, is apparently brought about through the intermediation of the nervous system, by virtue of inherent weakness in it, imbalance of it, or the influence of intoxicating factors operating centrally or peripherally on it. The influence of the nervous system in producing arthritis has long been observed in cases of Charcot's joints of tabes and syringomyelia. Recently there has come from the Mayo clinic, the operation of sympathectomy, the results of which in atrophic cases was striking.

Pemberton has long believed that the gastro-intestinal tract and food intake played a role in the etiology of arthritis. The dilated, elongated and distorted intestines found in some arthritics has been a common observation. Likewise, it has been known for some time, that cutting down the food intake and building up the general metabolism, was a valuable therapeutic aid. Recently, Fletcher<sup>16</sup> has shown, that concurrently with improvement along dietetic lines, the large bowel often returns to normal. Animal experimentation shows that this abnormal picture can be artificially produced by diets in which inadequate vitamins, a large carbohydrate intake and a deficiency of protein play a part. It has been shown that on this basis infection readily implants itself in many tissues.

## Pathology

One of the great difficulties, in the past, in the study of arthritis, has been an inadequate conception of the morphological changes taking place. Classifications of arthritis were based upon etiology, clinical manifestations, etc. A long step toward escape from this confusion was taken, when Nichols and Richardson published their monograph, "Macroscopic and Microscopic Morbid Anatomy of Arthritis Deformans", in 1909.

This paper was based upon a pathological and clinical study of sixty-five cases of chronic, non-tubercular, deforming arthritis.

From their studies,<sup>17</sup> they were convinced that these joint lesions can be divided with great definiteness into two pathological groups. 1. Those which arise from primary proliferative changes in the joints, chiefly in the synovial membrane and in the perichondrium. 2. Those which arise primarily as a degeneration of the joint cartilage. These two pathological groups are characterized by distinct gross and histological differences. These two pathological types, however, do not correspond to two definite etiological factors, or to two definite and distinct diseases. The tissues which enter into the joints of the body are bone, articular cartilage, synovial membrane, ligaments, capsule. These tissues are all of mesenchymal origin, although differentiated into tissues of very different histological appearance. The cells of which these tissues are composed either may proliferate if stimulated by any one of various irritants or may degenerate from the effect of any one of various agents. Yet the actual cell and tissue changes which may occur are limited in number, although the gross appearances vary with the special tissue which proliferates or degenerates. Hence the same end result may be produced in these joints by a variety of irritants or agents, and a given irritant or agent may produce a variety of gross appearances.

They believe that the original lesions arise either in the synovial membrane, as is the case in the atrophic or proliferative type, or in the cartilage, as we find it in the hypertrophic or degenerative type. Primary proliferation of the synovial membrane, as found in the atrophic type, may be caused by traumatism, acute suppurative infections, gonorrhoea, syphilis, and probably faulty metabolism. Primary degeneration of the cartilage, which constitutes the first change in the hypertrophic type, may be due to traumatism, dislocations, the presence of tumors of bone, gout, disease of the central nervous system and other causes suggesting deranged metabolism. One of the outstanding features of the arthritic process is

that whatever the original cause, the process once started tends to continue.

#### Artrophic or Proliferative Arthritis.

In this type of arthritis the primary change occurs as a proliferation of the synovial membrane and of the perichondrium of the articular cavity, combined in many cases with a synchronous proliferation of the connective tissue and endosteum of the epiphyseal marrow directly below the joint cartilage. The degree of involvement of the perichondrium is variable; in some cases it is markedly involved, in others it is negligible. The greatest change, however, is in the synovial membrane, and two kinds of changes arise within the joint. The proliferation of the synovial membrane produces a layer of granulation tissue, which sooner or later may extend over the joint cartilage as a thin pannus-like layer. Where this pannus comes in contact with the cartilage, it usually produces a destruction and absorption of the cartilage. Proliferation of the perichondrium, leads to the formation of a layer of specialized connective tissue, which readily transforms itself into cartilage or even bone. Consequently, two processes may go on in these joints simultaneously, namely, a destruction of the joint cartilage by synovial pannus and a new formation of cartilage or bone arising from perichondral proliferation. Analogous changes may be taking place within the marrow of the epiphysis of the bone itself. There may also arise a proliferation of the connective tissue of the marrow spaces of the epiphysis just below the zone of provisional calcification. A formation of numerous blood vessels accompanies this overgrowth of the connective tissue of the marrow. This vascular granulation tissue may extend through the zone of provisional calcification upwards to the joint, and cause a destruction and disappearance of the overlying cartilage, so that in joints where this process is marked there may arise a destruction of articular cartilage in two ways--from the joint surface by the action of the synovial pannus and from the perichondrium by the action of the granulation tissue of the marrow.

Besides this proliferation of the connective tissue of the marrow, there may be present a proliferation of the endosteum of the epiphysis which may result in the formation of new bone of cartilage along the epiphyseal margin of the articular surface.

Four general processes may thus be going on at the same time: (1) The formation of a pannus by proliferation of synovial membrane. (2) Proliferation of perichondrium of the articular cartilage. (3) Proliferation of the connective tissue of

the marrow spaces of the epiphysia, accompanied by the formation of numerous blood vessels and vascular granulation tissue. (4) Proliferation of the endosteum of the marrow spaces with the formation of new trabeculae.

These four layers, developing one-half above and one-half below the joint margin may in the later stages become fused into one mass.

The results of the approximation of two such surfaces varies in accordance with the character and origin of the new tissue. If synovial pannus predominated the ankylosis usually is fibrous; if perichondrial proliferation predominates, cartilaginous or bony ankylosis may occur. The end-result of such a process may be complete fusion of one bone with another.

T.P. Strangeways,<sup>18</sup> of England has divided the atrophic type of arthritis into the following six types: capsular, dry, adhesive, rarefying, villous and infective. However, this classification is based upon anatomical, pathological and etiological factors and therefore, is not as preferable as the classification of Nichols and Richardson.

#### Hypertrophic of Degenerative Arthritis.

The hypertrophic type of arthritis is characterized by an early degeneration of the hyaline cartilage of the articular surfaces. The dominating end result, however, is over-growth, or hypertrophy of the cartilage and bone of the joint as a whole. As a result of the cartilaginous degeneration, the underlying bone may become exposed, so that instead of two cartilaginous surfaces being in contact with each other, the bone of one may be in contact with the cartilage of another or two bony surfaces may articulate. The process, however, is not uniform and continues irregularly, so that the exposed areas of bone are fairly well circumscribed. Wherever erosion of cartilage of bone occurs there practically always comes a compensatory growth of cartilage or bone of the opposite articular facet. The changes are brought about gradually, and since the erosion of one is followed by compensatory overgrowth of the opposite facet, the two bony surfaces are very irregular in outline and present an extremely notched appearance. Motion in the joint, therefore, may be long preserved, and it is also to be noted, that bony ankylosis never occurs in this form of arthritis, although ankylosis by deformity may arise, due to impingement of one part against another.

With the above changes taking place, 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 may be completely obliterated. This leads to increased density of the articulating end of the bone, and may acquire a structure as solid as that of normal cortex. Under the friction of use, this bone acquires a high degree of polish and is then termed eburnated. Eburnation is pathognomonic of hypertrophic arthritis and never occurs in the atrophic variety.

While this destruction and ~~resorption~~ resorption of cartilage in one part of the joint, with corresponding overgrowth in another part takes place, secondary changes in the joint may occur. The changes in the shape of the joint may lead to extensive sub-luxations, and interlocking of the bones so that no motion is possible. This is called, "ankylosis by deformity".

Secondary changes, consisting in an increased activity of the perichondrium, occur at the periphery of the joint where cartilage and capsule come together. As a result of this perichondrial activity, new cartilage is formed which may be transformed into bone and the head of the bone increases in size, but this increase is irregular and nodular giving rise to lumps, commonly known as "Heberden's nodes". This deposit of new bone is usually within the joint capsule and leads to an actual increase in size of the articular surface. This perichondrial new growth may be so marked as to completely fill the original joint cavity, and in this way the head of the bone may be forced from its articular cavity and partial or complete dislocation result.

The dense layer of eburnated bone is relatively thin. The trabeculae of the shaft of the bone are diminished in size and number. This may be due to resorption of bone, as always seen in old age or it may be resorption secondary to disuse.

The capsule of the joint, usually, shows no increase in thickness. The synovial membrane in many instances may appear normal; in some, however, there is marked thickening of the synovial membrane, which may result in the formation of large papillary masses, composed of dense edematous connective tissue. These may be converted into cartilage, or bone, or into fat tissue, "lipoma arborescens".

It is interesting to note, that the degenerative process above described, reaches its highest degree of perfection in the Charcot's joints of tabes and syringomyelia. Further evidence, to show that osteoarthritis is caused by a variety of factors.

Knagg's, of England, in his monograph "The Inflammatory and Toxic Diseases of Bone", devotes very little space to atrophic arthritis, because he regards this condition as essentially a joint affection. He pays great attention to the hypertrophic arthritis which he regards as a true disease of bone. He described it as being characterized by "peculiar changes in the articular cartilage, the synovial membrane and the articular ends of the bone, particularly the formation of osteophytes. These changes are in the main hypertrophic and produced by the formation of tissues, but there are also degenerative atrophy of certain parts of the cartilage and rarefaction of the adjacent cancellous and cortical bone. The bone changes, eburnation and formation of osteophytes, constitute the distinctive and diagnostic feature of the disorder, and the hypertrophy so obtrusive in osteoarthritis contrasts with the atrophic changes seen in the atrophic arthritis."

Arthritis is merely one expression of the rheumatoid syndrome. Other structures are involved and the most conspicuous site of the rheumatoid disability, other than the joints, is found in the muscles. Fibrositis is the name most commonly given to this form of disability. It is often called myositis or myalgia. In general, muscular pain and disability are more common, especially upon active motion, in the atrophic type, but subjects of the hypertrophic type, may show great tenderness of the calf muscles and along the tibial surfaces, or even along the bone itself. Many people complain of intermittent attacks of myositis or myalgia, but mild disturbances of this kind would show no pathological change. However, in the arthritics who over a period of years have suffered from more or less continuous muscular disability, definite changes take place in the fibrous tissues. Llewellyn and Jones<sup>19</sup> have shown that between the muscle bundles, there arises a dilatation of the smaller blood vessels, together with minute hemorrhagic extravasation. The interstitial tissue then becomes invaded by cellular infiltration and leucocytes range themselves between the individual muscle bundles and fibrils. The nuclei of the connective tissue sooner or later undergo proliferation, and this newly-formed tissue then in turn infiltrates the muscles. As the process progresses, an interlacing character is acquired by the fibres of connective tissue which may then become so closely arrayed as to exert compression and separation of the muscle bundles and smaller muscular fibrils. This pressure induces degeneration of the muscular tissue, and late in the disease the latter becomes largely displaced and replaced by the newly-formed fibrous tissue. Obviously, the consequence of this process is loss of muscle bulk, and this atrophy is one of the characteristic later features of arthritis, especially of the proliferative type.

## Symptomatology and Diagnosis.

The symptomatology of arthritis can be fairly definitely divided into the atrophic and hypertrophic type, but it must be remembered that great variations occur and it is sometimes very difficult to distinguish, clinically, between the two great types.

### Atrophic Type

The first thing to bear in mind is that every stage may be encountered between the acute type associated with a sudden febrile onset, somewhat resembling rheumatic fever and tending to lead to ankylosis and the more chronic and afebrile type of less sudden onset which tends to merge into the osteoarthritic type.

<sup>20</sup>  
Cecil gives a very good description of a typical case: "The patient, usually a young person, pale, thin and rather prone to be of the neurotic type, gives a history of gradual development of pain, stiffness and swellings in several joints. He generally dates the onset of his symptoms to some disturbance in physical equilibrium, such as an acute infection, exposure to cold or a surgical operation. Many patients give a history of repeated attacks of tonsillitis. The symptoms may develop suddenly or gradually. When the onset is sudden the patient may run an irregular fever varying from 99 to 101 degrees Fahrenheit, but when the onset is insidious, the temperature usually remains normal. The disease is almost always migratory, jumping about from joint to joint. After several attacks, however, the joints chiefly affected become permanently injured and the process assumes a persistently chronic course."

Usually the disease makes its first appearance in the phalangeal joints of the hands. There arises a somewhat symmetrical enlargement of the phalangeal articulations, usually, at the mid-finger joint. This enlargement may consist in merely a slight thickening of the superficial tissues over the articulation or it may assume the characteristic fusiform shape, tapering both distally and centrally. The knees are involved almost as frequently as the fingers. As the disease advances and involves the larger joints, the patients become more uncomfortable.

Pain is a variable symptom. It is naturally, very marked in the acute cases, and occasionally absent in the more chronic cases. It may be due to inflammatory changes in the joint, pressure upon enlarged synovial fringes, stretching of scar tissue or adhesions, mutual opposition of articular surfaces with sensitive connective-tissue or to reflex muscular spasm. In addition, nerve pains may be encountered.

Another symptom which commonly precedes and accompanies an attack of arthritis is a sensation of fatigue. The patient may feel prostrated in the morning, even after having slept well. The desire to sleep is constantly present. A cervical type of headache of low degree, or even of frontal or temporal distribution, is a frequent symptom in such individuals. Many persons who develop arthritis have grown accustomed for years to mild discomfort of the muscular system, especially in the neck and back muscles.

There is usually a mild degree of secondary anemia, especially in the definitely infectious types. However, it is considered more as a complication than as a primary part of the arthritic syndrome. It is much more frequent in women, than in men, which may account for the increased incidence of arthritis in women.

There is comparatively little change in the blood chemistry in this disease. The non-protein nitrogen, the urea and the uric acid usually are within normal limits. Pemberton, and his co-workers have demonstrated a lowered sugar tolerance in a large proportion of cases. The lowered tolerance was roughly proportional to the activity of the arthritic process, and tending to return to normal with recovery.

The basal metabolism is usually normal or approximately normal. Pemberton<sup>21</sup> found the basal metabolism normal in 80 per cent of 29 cases studied. Cecil, Barr and Du Bois<sup>22</sup> found the basal metabolism normal in both acute and chronic infectious arthritis.

If the disease is arrested early the involvement of the soft tissue subsides and leaves no objective evidence of its occurrence. More frequently, however, the disease persists until cartilage and bone become affected and irreparable deformity had been produced. As the cartilage becomes destroyed a laxity of the joint develops. The phalanges tend to come nearer to each other, and the intervening tissue and skin undergo a sort of dimpling. Subluxation, finally, takes place and with it comes atrophy, from disuse, of the muscles and possibly other structures in the neighborhood of the joint.

With the advance of the processes just described, movement of the involved joints become less and less, until finally fixation results. The patient, naturally, assumes the position of greatest comfort, and we find that certain characteristic contractures usually result. In the case of the knee joint, the contracture is generally from 45 to 90 degrees. The patient finds that this position gives the greatest comfort,



and, therefore, the knee is held constantly at that angle. The posterior tendons, sooner or later becomes impossible to extend the leg without operative procedure. The patient, therefore, is forced to spend his life in a sitting posture, which progressively leads to secondary invalidism from disuse, inactivity, impairment of intestinal function, obesity, loss of appetite, together with deterioration or complete loss of morale.

Ankylosis may be either fibrous or bony in type. A fibrous ankylosis may result from thickening and contracture of the joint capsule and ligaments, or from fibrous adhesions within the joint cavity. More frequently bony ankylosis insues due to approximation of bone to bone. Actual bony union takes place, the marrow cavity of one phalanx becoming continuous with the marrow cavity of the adjacent phalanx and one bone exists where there were two before.

The course of the disease, varies greatly, depending upon the particular joints involved, the degree of maintenance of the general health and the stage of the disease. The course may be rapid, leading to great deformity, or, as in a small number of cases, the process may subside.

With chronicity, changes in the skin and nails occur. The skin develops a glossy or shiny appearance, sometimes accompanied by edema, due probably to a trophic disturbance. The nails become striated longitudinally, thinner than normal, somewhat flattened transversely, and brittle, so that they break easily.

#### Hypertrophic Arthritis.

The onset of this type of arthritis is more gradual, and the patient is nearly always middle-aged or elderly. Most of the patients are women. Hypertrophic arthritis is more frequently monarticular than polyarticular and differs in this respect from atrophic arthritis.

In the hands, the carpo-metacarpal joint of the thumb, and the distal inter-phalangeal joints of the digits are most frequently involved. The first objective sign is apt to be a slight enlargement of the bone on one side of the joint in the form of a circumscribed round projection. These projections have been known for generations as Heberden's nodes, after the physician who first described them.

The knee is the next most common site of involvement, and constitutes a much more serious course of the disease. Because the knee is weight bearing, the typical symptoms of pain, tenderness and stiffness, appear earlier than in the fingers.

Enlargement and alteration in the shape of the joint are due principally to changes in the articular extremities themselves, which usually take the form of periarticular "lipping". The arthritis is, as a rule, of the dry type, and synovial effusions are rare.

Changes in the capsule and ligaments are present, but less marked than in the atrophic type. However, quite frequently there is marked crepitus to the palpating finger, and occasionally it may be audible to others, when the patient mounts the stairs in the form of a grating or cracking sound.

In hypertrophic arthritis, muscular spasm is not a prominent feature and deformity as exists is largely due to alteration in the shapes of the articular surfaces due partly to absorption of bone, and partly to new formation of bone. Contact of bone to bone leading to eburnation and to more or less compensatory overgrowth, but never to merger of one bone with another as in the atrophic type.

The differentiation of atrophic and hypertrophic arthritis, in practice, is by no means always possible. The systemic evidences of the disease are often slight at the onset, and early changes in the joints are often not sufficiently characteristic to permit of clear-cut classification. In the larger joints superficial evidences may be very late in occurrence, because of the large mass involved. In those cases only X-ray studies have any definite value.

In view of the fact that the atrophic and hypertrophic type respond to the same treatment, there is room for argument that these types may have a common etiology. This implies the possibility of a common pathology. Perhaps, the underlying pathological processes in the two types of the disease, may depend upon a common alteration of physiology. Pemberton<sup>23</sup> believes that the two great types of the disease may be determined partly by anatomical or constitutional differences.

Cecil<sup>24</sup>, however, believes that the two types of arthritis should be definitely differentiated. He distinguishes differences in etiology, pathology, and in the course of the disease. The following table from Cecil gives a good differential diagnosis of chronic infectious arthritis.

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Atrophic arthritis	Hypertrophic arthritis
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	Atrophic arthritis	Hypertrophic arthritis
Average age of onset	Third and fourth decades	Fifty and sixth decades
Weight	Normal or underweight	Usually overweight
Blood	Low hemoglobin	Normal hemoglobin
Morbidity anatomy	Rarefaction of bone	Condensation of bone
Joints involved	Any joint in body	Chiefly knees and fingers
Type	Migratory	Localized
Appearance of joints	Periarticular swelling	No swelling
Special signs	Fusiform finger joints	Heberden's nodes
Roentgen-ray	Narrowing and clouding of joint space	Lipping of bony margins
Termination	Ankylosis and deformity	No ankylosis; usually no deformity.

Another common symptom of arthritis is myositis or better known as fibrositis. The muscles most commonly involved are the posterior muscles of the neck, the muscles of the back, the muscles of the shoulder and the triceps group of the arm. These may be tender on palpation, but usually hurt chiefly upon active use. In long standing cases, disuse will lead to atrophy.

Neuritis is considered by some authors to be more frequent than myositis. The two are often difficult to differentiate. In typical neuritis, however, the pain follows more closely the course of the nerve, which also shows tenderness over the same distribution, and there may or may not be loss of function of the structures supplied by that nerve.

Neurasthenia is one of the most common symptoms of the rheumatoid state. The patients are frequently refractory or depressed and consequently, fail to cooperate in the treatment. The physician in charge must have a wide experience in the rudiments of psycho-therapy and in the treatment of the milder expressions of the functionally unstable nervous system.

Skin diseases and involvement of the uveal tract of the eye are frequent concomitant symptoms of the rheumatoid syndrome. Of the skin diseases, psoriasis, herpetiform eruptions and urticaria are the most frequently encountered. The uveal tract involvements usually lead to iridocyclitis, which is most painful and needs instant attention from the ophthalmologist.

### X-Ray Findings

#### Atrophic type

In the early stages, there is no obvious osseous change, but the spindle-shaped enlargement of the soft parts may be demonstrated. Later on, as the process advances, there is haziness and narrowing of the interarticular space. Still later in the disease as the inflammatory tissue destroys the cartilage, the adjacent articular surfaces come into actual contact, so that the two bones appear to be fused together. There is, however, an absence of the lipping of the articular margins, as seen in the hypertrophic type. At this later stage there is considerable atrophy and rarefaction of the cancellous bone due to the diminished calcium content. Still later, when the bone itself has been destroyed and ankylosis has occurred, the markings of the joint are replaced completely by a diffuse shadow which merges with the adjacent bone.

#### Hypertrophic type

The first demonstrable change in hypertrophic arthritis is periarticular lipping. The later stages show a narrowing of the joint interval followed by erosion of the articular bone and alteration of the shape of the articulating surfaces. The articulating surface remains in most cases fairly well defined and sharp though presenting occasionally nodular eminences. Cyst-like spaces in the underlying cancellous tissue are commonly seen, as are also loose bodies, composed of cartilage, bone or of both, usually derived from detached periarticular chondro-osteophytes. Periarticular lipping is always the characteristic feature of osteoarthritis.

In the knee joint, early roentgen findings are to be seen at the upper and lower margins of the patella, in the form of projections of various sizes extending like beaks in a downward direction.

## PRINCIPLES OF TREATMENT OF ARTHRITIS

### GENERAL CONSIDERATIONS.

Treatment of arthritis is primarily preventive namely, the hygiene of the mouth and other sites of focal infection.

After the disease process has once begun, treatment is for less effective. In the past, the treatment of arthritis received very little attention, and consequently was notoriously unsatisfactory. With the increasing knowledge of recent years, the medical profession has come to look upon arthritis as a complex disease syndrome, and touching more fields of medicine than any other disease, with the possible exception of syphilis.

Much time is required for accurate study of every phase of the arthritis syndrome, in order to adequately comprehend the disease as a whole. The disease belongs within the realms of internal medicine. However, surgery, orthopedics, otorhinolaryngology, and many other specialities are called upon in the diagnosis and treatment. Many measures necessary in the treatment of arthritis, such as, heat and massage, constitute specialities in themselves.

Pemberton says,<sup>25</sup> "One of the first lessons to be learned in the treating this disease is the importance of maintaining a broad-minded attitude. There is no single panacea in the treatment of arthritis. In view of the wide disturbance of physiology and the secondary invalidism dependent upon it, it is obviously impossible that any single measures could be adequate to restore this state of affairs to normal." He also believes that the treatment for the two great types of arthritis should be the same. Each case of arthritis should be examined and treated, solely, upon its own individual merits.

The treatment of arthritis will be taken up under the following headings: treatment of focal infections, physiotherapy, vaccine therapy, diet, drugs and medicinal measures, and orthopedics procedures to prevent deformity.

#### Treatment of focal infections.

In few other diseases is the detection of foci of infection so important as in arthritis. Evidence has gradually been accumulating through the years to prove the contention of Billings, of the relationship of focal infections to arthritis.

<sup>26</sup>  
Rosenow and Nickel, working at the Mayo Clinic, have shown

that (1) foci of infection, wherever found, commonly harbor the causative organism of various systemic diseases (2) they afford favorable conditions for the entrance of bacteria and their toxic products where bacteria tend to acquire and maintain relatively high or peculiar invasive powers, and (3) the situation, depends on the specific or elective localizing power of the infecting organisms, in most instances streptococci. The disappearance of arthritic symptoms after removal of foci of infection, is a common observation. However, frequently we encounter a patient who fails to improve following the removal of several foci. Such failure should not be interpreted as nullifying the principle involved, for the disease may have existed for so long a time as to produce irreparable harm, or it may have become so thoroughly established as to continue independent of a primary focus.

<sup>21</sup> In a study of 400 cases in the Army by Pemberton and Robertson they found 293 persons (73%) who showed demonstrable surgical foci. Of this latter number 208 showed foci in the tonsils. One hundred and thirty-four persons (33.5%) were positive for a dental focus. Fifty persons or 12.5% were positive for a genito-urinary focus. Nineteen per cent showed a combination of both tonsillar and dental foci. One hundred and seven persons (26%) were taken sick in the apparent absence of surgical foci.

In a study of 545 cases of arthritis in civil life, Pemberton and Peirce found that infections of the nose, throat and accessory sinuses existed in 31 percent and infections of the teeth in 54 per cent .

In planning an attack upon toxic foci, it is best to proceed cautiously, and to deal with the primary focus first.

The treatment of diseased teeth must be carried out by a skilled dentist. The lesion that gives rise to the most serious consequence is infection around the root of the tooth, the so called apical infection. Caries alone does not seem to be a factor of very great moment. Examination should include testing the teeth for vitality. Crowned teeth are frequently dead teeth, and a dead pulp favors apical infection. X-ray of the whole mouth should be taken. Individual pictures of each tooth gives far better results than a single x-ray of the jaw.

The amount of infection necessary to give systemic symptoms is sometimes surprisingly small. Roentgen ray examination of the teeth may in one case show apical abscesses as large as a blueberry and yet produce no clinical evidences of harm. On the other hand infection causing symptoms may exist in a tooth that is roentgenologically negative. Every tooth, then should

be considered as a potential menace, until proven otherwise.

While it is true, that all dead teeth may become infected, it is by no means true that all dead teeth are infected. No vital, non infected tooth should ever be sacrificed. Provision of adequate denture is fundamental to the general health of the individual, and teeth which may serve as anchors to a bridge, may have an importance far greater than they had merely as individual members of a complete set.

When the tonsils are suspected of being the primary focus, removal is indicated. Small imbedded tonsils are often more potentially dangerous than hypertrophied ones, and tonsillar remains that have been left behind after an incomplete removal are capable of causing arthritis.

The appearance of tonsils productive of systemic harm is by no means constant or characteristic. They may be large, cryptic, inflamed or so inconspicuous as to be almost invisible. The appearance of the peritonsillar tissues, especially the anterior pillars, is of great value in reaching a correct opinion.

Another important site of infection in the mouth is the gums, which may be the site of a mild gingivitis or pyorrhea. In the milder forms, massage, stimulation and the cautery will suffice to clear up the infection. In the more severe cases, a radical operation is necessary, where a gum flap is laid back and the necrotic tissue excised.

Infection in the accessory nasal sinuses should be removed, as well as elsewhere. In the case of the maxillary sinus, adequate drainage can be instituted, but in the case of the other air spaces in the skull, the treatment is not so simple. They are less accessible and drainage is not easily obtained. The severity of the operation, may undermine the general health of the patient.

The problem here is one of the infection versus the mechanism of Nature to meet and overcome it. A great deal can be done by helping the patient to overcome the infection by stimulating the normal defensive reactions and by increasing the resistance of the patient.

The third most important site of focal infection in the production of arthritis is the genito-urinary tract. In a series of 700 cases, it was found to be involved in 14 per cent of the men, and 2 per cent of the women. The prostate gland, is the chief seat of a genito-urinary focus, in man. The infection may be entirely, non-venereal. The prostate upon examination may be found to be markedly enlarged, tender and even modular. The organisms present, are largely the same as are

found in other primary foci, namely, the several varieties of streptococcus and the staphylococcus. Treatment, consists in message, and removal of other foci of infection. Dr.P.S.Pelonze<sup>28</sup> of Philadelphia found that there was frequently an association of other foci of infection, such as teeth, tonsils etc, with prostratic infections.

A very frequent finding in women arthritics, is a cervicitis or endocervicitis. Salpingitis and oophoritis may exist, as a result of venereal infection. Pemberton, believes, that infections lesions of the genito-urinary tract in women have relatively little influence upon arthritis. He believes, that of much more importance are the more intangible influences of ovarian function of an endocrine nature and possible by some poorly understood influence of the uterus, dependent on the determination of additional blood to it.

The minopause is the general period of greatest incidence in women. Cecil<sup>29</sup> attaches great importance to the climacteric, and even makes a separate classification for what he terms "arthritis of the menopause."

Occasionally definite and localized foci are present in the gall-bladder, appendix or diverticuli, and these foci are best dealt with by surgical measures. The infection may be of a diffuse nature, involving the tubular glands of the colon and small intestine. Stasis may be present or various catarrhal or ulcerative conditions in the diagnosis of which radiography is of greatest assistance.

Mutch<sup>30</sup> believes, that stasis often occurs in the colon although there is a daily evacuation; stasis often occurs in the ileum, even when the patient does not refer any symptoms to the alimentary tract; streptococcal infections are often present in the bowel, although there are no symptoms of irritation of the colon, and extensive infection of the ileo-cecal region does not always lead to the excretion of living streptococci in the feces.

Pemberton has not found the gastro-intestinal tract to be the source of focal infection, nearly as often as Mutch and other investigators.

Investiative work in recent years, has shown that there exists a relationship of the intestinal tract to arthritis in a sense other than that of harboring focal infection. Pemberton believes that malfunction of the intestine, as a whole, plays a much more frequent and important role in arthritis than do the various surgical foci.



Pemberton and Newcomet,<sup>31</sup> at the Presbyterian hospital in Philadelphia, have made a long series of roentgen-rays of the intestinal tract in arthritis. They found that the type of colon, most commonly met with in arthritics is characterized chiefly by a tendency toward greater caliber, greater length, a more convoluted appearance and sometimes reduplication.

Snyder and Fineman<sup>32</sup> in a series of 235 patients, found that the majority of the colons were very redundant and showed very acute flexures. In many, pouch-like dilatations of the cecum and ascending colon were noted.

Dr. A.A. Fletcher<sup>33</sup> of Toronto Canada, gives a very good summary of the situation. In a personal communication, with Dr. Pemberton, he has expressed his tentative views, as follows: "In chronic arthritis, the lesions of the cecum and colon are similar to the changes found in experimental animals suffering from certain forms of deficiency disease. The cecum, and the proximal part of the colon, may be much dilated and atonic and there may be a decrease or even an absence of the haustral markings. Rowlands produced dilatation of the colon in rats by restriction of vitamin B in the diet. Diets liberal in vitamins and protein and low in carbohydrate favorably influence the course of arthritis and patients seem to do badly when excess of carbohydrate is given. Deficiently fed animals rapidly develop both acute and chronic infections. Observations such as these tend to support the belief that nutrition may actually play a part in the causation of the disease."

As a result of the above observations, colonic irrigations have been tried by various men and some good results obtained. However, there is still a great deal of controversy over the question of "intestinal putrefaction", so it is difficult to evaluate the results of these experiments. Cruickshank<sup>34</sup> does not believe that as a result of bacteriological activity in the intestine, toxic substances are formed which by gaining entrance into the tissues induce a state of chronic intoxication. He says that the several types of intestinal flora probably result from abnormal intestinal conditions and are not the cause of them, and furthermore that many varieties of ordinary intestinal bacteria can be cultured from the stools of normal people.

Keating,<sup>35</sup> on the other hand, believes that the most frequent area of focal infection in arthritis is the gastrointestinal tract, and he reports the culture of streptococci from the stools of the great majority of his arthritics.

Snyder and Fineman found that the addition of colonic irrigation to the older well-known therapy of arthritis, defin-

itely improved the clinical results. They also found that soap-suds enemas produced the best results. However, in 64 per cent of the constipated individuals and in 36 per cent of the patients who gave no history of constipation the soap-suds enema failed to cleanse the bowel completely. In these cases, irrigations produced a complete and thorough cleansing of the bowel in almost every case.

Colonic massage is almost as important as colonic irrigation, but it must be given by someone familiar with the principles of massage, as a whole. In the absence of indications to the contrary, massage may be carried out, beginning in the left lower quadrant and progressing distally, after which another point is selected 3 inches higher up, and the process repeated. In this manner 8 to 12 points are selected in turn, until the final massage begins at the caput coli. The patient, can usually be taught to do this himself.

#### Vaccine Therapy and the Use of Non-Specific Protein.

The use of antigens in the treatment of arthritis, is often of great value in increasing the natural powers of resistance, and thus helping the patient to overcome any residual infection. Antogenous vaccines are preferable in acute cases, but in old chronic cases mixed stock vaccine may be used.

The initial dose should be small, and gradually increased, depending upon the severity of the action induced. The initial should not exceed one million and at first the succeeding doses should be 25 or 50 per cent of the previous dose, and be at intervals of 5 days. These doses may be increased until 2,000,000,000 are given at a dose.

Keating reports, that antogenous streptococcic vaccine, by its specific action is of great value as an adjunct in the treatment of arthritics.

In the opinion of Kolmer, who has had extensive experience in this field, the results of vaccine therapy have not been encouraging. This is also the opinion of Pemberton.

It is interesting to note, that Kolmer<sup>36</sup> believes that the anatomical structure of the joints and synovial membrane, favors bacterial embolism, and that gonorrhoeal arthritis, for example is produced in this manner rather than by the elaboration of toxic substances at some removed focus.

Miller and Lusk were the first to use non-specific protein in the treatment of arthritis. Various protein substances may

be injected intravenously or intramuscularly, such as peptone, milk, or typhoid vaccine. Within a few hours, after injection, there begins a rise in temperature, followed by a chill, fever, sweating and a focal reaction in the affected joints. This is followed in 24 hours by an improvement not only in 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 known. It has been suggested that the resulting improvement is due to the increased lenkocytosis, to increased lymph flow, to the sweating, or to alteration in the ferment and antiferment action of the blood serum.

The intravenous dosage of non-specific protein at the beginning should be comparatively small. It is well to begin, with an initial dose of about 30,000,000, increasing every fifth day until at the sixth and final dose, 200 millions are administered.

The results of non-specific protein therapy in arthritis is not very encouraging. It is of value only as an aid in the treatment of the acute atrophic cases. In a report from England,<sup>27</sup> out of 70 cases treated by Campbell in a period of five years, 16 showed no improvement, 54 were improved, and of this number 38 had been able to carry on their work.

#### Treatment by Drugs.

It can be definitely stated in the beginning, that there is no specific drug for arthritis, comparable to the action of quinine in malaria. Perhaps in no other disease have so many drugs been advocated with so little success.

Llewellyn<sup>33</sup> lays stress upon the fallacy of placing complete reliance upon any one drug in the treatment of this disease which presents such varied characteristics, and states that it is far wiser to treat cases on general principles, noting any indications for special lines of treatment that may present themselves.

#### Arsenic.

The value of arsenic is mainly as a reconstructive tonic and hematinic. It is indicated chiefly in the cases of secondary anemia. Pemberton believes it is of valuable aid in a great many cases. He advocates beginning with small doses of Fowler's solution, such as 1 drop three times a day and increasing 1 drop daily until 5 drops three times a day are being given. Part of the secret of the use of arsenic consists in being able

to administer it continuously over a long period of time.

#### Iodine.

Iodides have been used in arthritis for a great many years. Potassium iodide is usually used. Recently oxyl-iodide intravenously has been used extensively. The real mechanism of action is not known, but it is thought that the iodides exercise their influence upon the thyroid gland, and so possibly upon metabolism.

#### Salicylates

The chief value of the salicylates is in their analgesic properties. They are particularly valuable in the early acute cases. There is no evidence, however, that the salicylates exercise a curative influence upon the rheumatoid syndrome. The great disadvantage of the salicylates lies in the fact that they frequently produce marked gastro-intestinal derangement, chiefly in the form of loss of appetite and indigestion.

#### Strychnine.

The use of strychnine is chiefly as a tonic. Many arthritics are characterized by "ptosed" body habits, general prolapsus of abdominal viscera, asthenia and muscular weakness. These individuals can be kept on a higher plane of physiological efficiency by the cautious use of strychnine.

#### Digitalis

The use of digitalis in small doses of 3 to 5 min., three times a day, may be very useful in increasing the blood flow in the capillary beds.

#### Guaiacol Carbinate

Guaiacol carbonate at one time was considered a specific for arthritis. It is of benefit in some cases. It probably acts as an intestinal disinfectant.

#### Cod-liver Oil

Cod-liver oil in connection with the restricted diet, is very valuable in rehabilitating, asthenic, emaciated and anemic persons.

#### Nitrites

The action of the nitrites is chiefly as vasodilators. In view of the fact that in arthritis we have a generalized

vaso-contraction of the capillary beds, it would appear that nitrites might have a beneficial effect on the peripheral circulation.

In a series of 32 cases studied by E.G. Pierce,<sup>39</sup> the nitrites showed a favorable influence in 12 cases. Further investigation and experimentation is necessary to prove the efficacy of the drug. Dosage should begin with  $\frac{1}{4}$  gr. of erythroltetranitrate and be increased slowly up to  $\frac{1}{4}$  gr. t.i.d.

#### Ortho-iodoxy Benzoic Acid.

In 1935 Young and Youmans<sup>40</sup> introduced ortho-iodoxy Benzoic acid, as a valuable drug in the treatment of arthritis. The composition of the substance closely resembles that of salicylic acid, the latter being o-hydroxy benzoic acid. In a series of 43 cases treated, twenty-four or 56 percent were markedly improved; ten or 23 per cent, moderately improved; six or 14 per cent, slightly improved; and 3 or 7 per cent showed no improvement.

In a subsequent study of the drug by Millard Smith,<sup>41</sup> the results showed few failures, and a fairly large per cent of partial benefits. As a result of his experiments he places ortho-iodoxy benzoic acid among the most important drugs available in the treatment of arthritis.

P Pemberton and his associates have reached the conclusion that the drug is in the nature of a glorified salicylate, in that there may be a large amount of analgesia over a period of time longer than occurs following the usual salicylates.

Stein and Tanbe<sup>42</sup> in a recent study on 102 cases, found that two cases of rheumatic fever were made worse by the drug, thirtyone of the 100 cases claimed temporary relief of pain, but all returned later with exaggerated symptoms, and that the drug has no effect on swelling or joint changes. They have, therefore, discontinued the use of the drug.

There are three methods of administering this drug: by mouth, by rectum and intravenously. The best results have been obtained by the intravenous method. The initial dose is 0.5 gm., depending upon reaction. Usually about 10 gms. in all are given over a period of three weeks, divided as follows: 0.5 gm. to 1 gm. three times weekly for four doses; 1 gm., 3 times weekly for four doses; 1.5 gm., at the same intervals for two doses. Seven to fifteen minutes should be allowed for the injection.

## Physiotherapy.

Physiotherapy is the oldest means of attack upon the rheumatoid syndrome. These measures are still about as valuable in the treatment of arthritis, as any at our disposal. Because of the indifference with which the profession has regarded these agencies, the laity have turned more and more to masseurs, osteopaths and others, who have offered relief through these means in a variety of conditions. Until the profession learns to make fuller use of these fundamental measures, the layman will be forced to continue to support these cults.

Heat constitutes the most valuable measure in the realm of physiotherapy. Dry and wet heat are used. Following local exposure, there is directed to the part an increased circulation of blood which tends to keep the temperature of the tissues constant. With each degree rise in body temperature, the pulse rate increases about ten beats. Local and general sweating also takes place, with resulting loss of water and salts. With the rise in temperature the general body metabolism is increased and carbon dioxide is formed in quantities larger than normal. The over-ventilation in the lungs, however, washes out the carbon dioxide in even greater amounts than normal. The result of loss of carbon dioxide is to leave an excess of alkali in the blood stream and tissues. The excess of alkali is eliminated through the urine and sweat until the normal acid-base equilibrium is restored.

Heat places the patient in the condition to respond better to effleurage and massage, in that dilated lymphatics and blood channels are probably able to remove more quickly than otherwise the fluids and metabolic end-products displaced by the massage.

Massage has been highly developed during the last century, at the hands of the Swedish school. Massage is a name, for a variety of movements which vary from light stroking and tapping to severe kneading. Its influence is direct, and, through the nervous system, also indirect. Krogh, Carrier and others have shown that large parts of the capillary system are normally closed and that a variety of stimuli may cause them to open. Among these stimuli, light and heavy stroking are conspicuous and they have also shown that following various degrees of such pressure the smaller vessels return with varying rapidity to their former state. It is obvious, therefore, that massage has an undoubted influence over large parts of the finer circulation in both superficial and deep structures.

The indications for massage are; (1) to prevent or delay muscle atrophy, (2) to improve local and general metabolism

and, (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 regions.

#### Diet.

Belief in the value of diet received great impetus about fifty years ago, when it became popular to ascribe the harmful role in rheumatism and arthritis to uric acid. This led to the curtailment of meats, which are known to break down, in the body, to uric acid.

The work of Whipple, Minot and Murphy has shown the great importance of meats, especially of liver substance, in contributing toward the regeneration of red blood cells. It would seem therefore, that to withhold meat in rheumatic conditions, may contribute to the secondary anemia which is so frequently present in arthritis.

As previously stated in this paper, Cajori, Crouter and Pemberton have shown that 75% of arthritics have a delayed rate of sugar removal from the blood after ingestion by mouth. They have shown that in the muscles there tends to exist a condition which approaches relative anemia or mild toxemia. It would seem, therefore, that reduction of the food intake might importantly cut down the metabolic load upon those structures whose physiology is handicapped during their effort to care for it. It has been shown, clinically, that arthritics on a reduced diet, show marked improvement, both subjectively and objectively.

Reduction of the total diet, then, is the first essential in the dietetic management. The balance of health of the individual as a whole, must be the guiding principle, upon which the dietetic restriction is based. In the obese, restriction is easily carried out without danger to the individual. If, however, the patient is underweight, or harbors an active focus of infection, underfeeding would be obviously improper and even dangerous.

In regard to fat, Pemberton has found that while it cannot be used with impunity, yet it plays a relatively harmless role in contrast to carbohydrates. It can be used in such increased amounts as to make up the caloric deficit, due to curtailment of carbohydrates.

No attempt will be made to enter fully into the problems of dietetics, which is in itself a special study. It is, however well to omit entirely potatoes and rice. Bread should be

limited as far as possible. One 30-gm. slice twice a day is sufficient. Fruits should play a large part in the dietary, contrary to the popular idea that they are acid producing foods. The acid or basic nature of foodstuffs is determined chiefly by the nature of the ash to which they give rise upon combustion. Many supposedly acid fruits and vegetables give rise to an alkaline ash.

The subject of prevention of deformities in arthritis, is one of inestimable importance. Great credit is due to such great orthopedic surgeons as Sir Robert Jones of England, Dr. Glodwaite and Dr. Osgood of Boston, in teaching the medical profession, the importance of preventing deformity. No attempt will be made to cover this large field, except to mention the general principles of treatment, which are: (1) to prevent deformity, during the acute stages when muscular spasm is prominent, (2) to place the joint in the optimum position, in case ankylosis occurs, and (3) to remedy as early as possible any deformity due to muscular spasm which already exists.



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