Gonococcal arthritis : its treatment by artificial fever therapy

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GONOCOCCAL ARTHRITIS
ITS TREATMENT BY ARTIFICIAL FEVER THERAPY

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INTRODUCTION

The disease gonorrhea has been known from time immemorial. The exact period at which it began to afflict man is unknown. The earliest records make mention of it. Wherever civilized man has penetrated, gonorrhea has been prevalent. However it was not until Neisser's epochal discovery in 1879 that the disease was first placed on a scientific basis. It was he who first called attention to the constant presence of a peculiar coccus in gonorrheal pus. He observed and described the organism naming it the gonococcus. His efforts to discover a medium upon which it might be cultivated failed and according to Jordan (2) it was Bumm, in 1885 who first obtained the organism in pure culture upon coagulated human blood serum, and then after cultivating it for many generations to prove its infective virulence inoculated it to man. Thus through the researches of these two scientist, Neisser and Bumm, the organism which they had so carefully described and cultured established beyond doubt that it was the specific cause of gonorrhea in man.

The secondary extragenital complication known as gonorrheal arthritis, without doubt had been thought of and considered a part of the disease by early investigators but it has only been known and appreciated that it was a metastatic manifestation since 1883. At this time Petrone first discovered the gonococci in a joint exudate. Blummer (1) who reviews Rendu's work found that this morphological demonstration was not substantiated until Rendu cultivated the organism from an infected joint. Jordan (2) stated that Neisser was aware of the gonorrheal metastases for according to Neisser statistics "gonorrheal metastases occur in about 0.7 per cent of all cases of gonorrhea coming to the know-
Since the time of Neisser, medical science has made great strides in the treatment of gonorrheal diseases and its complications. Osler (4) stated of gonorrheal arthritis "It is the most damaging and disabling of all the complications of gonorrhea." This statement has been amplified by numerous investigators. In a high proportion of cases permanent deformity and disability, affecting one or several joints, is the end result, Cooperman (12). The fact that so many different methods or treatment have been employed provides evidence of the inadequacy of most or all of them. It has only been since the advent of fever therapy that the medical world has come to acknowledge that in this type of treatment may lie the solution to the problem of therapy for gonorrheal arthritis. Now that fever therapy is being used the outlook for patients with gonorrheal arthritis has been enormously improved.

What comment the men, who first observed and described the gonococcus would say if they could now see the machines used in the destruction of that organism and the eradication of the disease from the human, would be a difficult thing to say. Without doubt they would be amazed to see the huge hypertherm, ten feet long and six feet high that is now used in the treatment of gonococcal infections and gonococcal arthritis. What an important organism—a microscopic creature one-tenth the diameter of a red blood cell, requiring such a large machine to combat and annul its disastrous effects.

Today, gonorrheal arthritis is no longer the dreaded complication that it was ten years ago. The authority to make
such a statement as this, has been made possible by those investigators who have treated gonorrheal arthritis by means of fever therapy.

These men have lifted the veil of ignorance and the light of scientific understanding has been placed in its stead. This disease has been conquered and it is serving as a incentive to further advancement in the field of fever therapy. The field of fever therapy is a relatively new one--many advancements are yet to be made. "Hope springs not from what has been done, but from the work that is just begun". 
INCIDENCE

The prevalence of gonorrhoea is universal. Geiringer and Campuzano (3) find that it has been variously estimated that from 50 to 90 per cent of the adult male population has had a gonorrhea infection at some time during their life. However no accurate figures covering the incidence of gonorrhea among the general population are available. This is due Jordan(2) believes, to the fact that physicians are unwilling to report cases by name, and many patients never consult a physician, but instead are treated by quacks and druggists. Gonorrhea is without doubt more common in the male than in the female(16)

When we consider the complications of gonorrhea--namely gonorrheal arthritis we find a better agreement among the investigators. This is one of the most frequent and important complications of gonorrhea, according to Stevens(18). It has been estimated by various authors(1,3,4,5,8,12 and 29) that from 2 to 9 per cent of all patients with gonorrhea develop gonorrheal arthritis. Thus when we consider the prevalence of this disease and the incidence of the complication of arthritis--the number of patients suffering from this type of arthritis becomes a very appreciable number.

MORBID ANATOMY

The mode by which the joint becomes infected is generally supposed to be via the blood stream or the lymphatics. That is to say a gonococcemia actually takes place(6,9,10 & 11). Cooperman(12) states that the urethra and the cervix uteri are the common foci, although cases of arthritis have been reported in new-born infants afflicted with gonorrheal opthalmia and in children suffering with gonorrhea of the rectum.
Somewhat late in the course of an acute urethritis, according to MacCallum(6), after the inflammation has reached the posterior urethra and has lasted several weeks, there often arises a painful involvement of a joint. This joint involvement varies considerably. Slight infiltration and swelling mark the mildest forms whereas in the more severe forms erosions of the cartilage and refraction of the cancellous bone may occur, and fixation of the joint with ankylosis. Blumer(1) is in agreement with this observation for he finds the joint cartilage may be slightly congested in mild cases but in severe ones, erosion is not uncommon. He further states that the inflammatory exudate within the joint cavity varies from slightly cloudy serum in very mild cases to purulent or hemorrhagic exudate in the more severe ones. The synovial membrane may be merely congested in mild cases but in further advanced cases it may be hemorrhagic or even necrotic. Cooperman(12) believes that this protean nature of gonorrheal arthritis is dependent upon the strain of the infecting organism and the susceptibility of the individual. Periarticular fibrosis with matting together of tendons and fascias, resulting in flexion contractures were found in the extra-articular morbid changes were noted by this investigator. Further pannus formation, erosions shredding and fibrillation of cartilages were frequently noted in advanced cases of intra-articular pathology.

MICROSCOPIC PATHOLOGY

Ghormby and Deacon(13) have investigated synovial membranes in various types of arthritis and have found that the synovial membrane in gonorrheal arthritis is essentially like that of the pyogenic arthritides. At first, a thickening of the
synovial membrane with edema and rapid infiltration of polymorphonuclear leukocytes takes place. As time goes on a more advanced stage is reached and this is characterized by an increase of fibroblasts and capillaries, and by the infiltration of plasma cells and polymorphonuclear cells. From this stage the condition progresses to the advanced stages of fibrosis and bony changes.

Why such a predilection for the joints on the part of the gonococci has never been fully explained. Kapo(11) reviews this interesting problem and he believes that the synovial fluid acts as an ideal medium for which the gonococci have a peculiar predilection. Key(14) who has studied the normal joint fluid and the lymphatics and capillaries of the joint, has demonstrated the ready passage of carbon particles into the subsynovial tissues. It is highly probable that the gonococci have little difficulty in obtaining entrance into the joint cavity and once there find a reservoir of nourishment in which affords a ideal culture medium.

CLINICAL PICTURE

Osler stated, "Variability and obstinacy are the two most distinguishing features". Emphasis was first placed on the monarticular feature of neisserian arthritis. Kendell et al.(50) find that 74% of their patients suffering from gonorrheal arthritis had polyarticular involvement. Leading clinicians(4,8,7,10,12&15) believe that it is more of a polyarthritis with later localizations in a selected joint than a primary monarticular affair. Cecil(5) in his monograph on arthritis gives a condensed summary of gonorrheal arthritis. He states, "Manifestations in the joints may be either monarticular or polyarticular. According to most authorities, the polyarticular form is more common in the male and the monarticular in the female. The joints most frequently
affected are those of the lower extremities, particularly the knees, the ankles and the joints of the feet. Next in frequency come the shoulders, elbows and the joints of the hand. The vertebral joints are not often attacked. In the polyarticular form, the disease has a tendency to concentrate itself on one joint, the symptoms in other joints subsiding rapidly."

Pepper(15) finds that the temporomandibular and the sterno-clavicular joints are often involved in this type of arthritis and uses this clinical fact to diagnose cases together with other findings.

**SYMPTOMS**

In the acute type the onset is sudden, the temperature rising to 103 to 104 (5). The joint involved is swollen, hot and red, and on palpation there may be distinct fluctuation. Extreme tenderness and loss of joint function is common(15). The course of the disease, according to Keefer (16) may vary tremendously, depending upon the severity of the infection, the joints involved, whether or not reinfection occurs before recovery takes place and the mode of treatment employed. In any event, the illness may last for several months, causing great economic loss and in not a few cases, permanent damage to the joints results. The onset may be subacute, with local pain and tenderness and edema. The duration of the attack is variable.

Cooperman(12) gives an excellent example of the average case. The symptoms are as follows: "There is usually an initial chill, rapidly developing swellings in several joints successively, severe pain, marked sensitiveness to passive motion and the like. Patients are markedly prostrated but the temperature is usually only moderately elevated. In the course of a week or ten days,
local symptoms clear up but one articulation still remains bearing the brunt of the infection. Here it merges gradually into a chronic lesion which after prolonged interval of time changes with considerable pain and disability."

CLINICAL CLASSIFICATION

There are numerous classification of gonorrheal arthritis. Some are made upon purely clinical grounds, other bacteriological or pathological evidence.

Keyes(16) who makes a bacteriological classification finds that there are essentially two types. These are

(1) Gonorrheal arthritis, in which the organisms are located in the joint itself.

(2) Gonorrheal osteo-arthritis, in which the gonococci are localized in the articular extremities of the bones, and any effusion into the joint is secondary.

Geriringer and Campuzano(3) make a classification on clinical appearance in which they enumerate four groups.

(1) Arthritic, in which one or several joints may become involved.

(2) Hydrarthrosis, usually monarticular, particularly liable to involve the knee.

(3) Bursal or synovial form, in which the tendons and their sheaths, bursae(e.g., of the patella, olecranon or the tendo-achillis) and periosteum are involved. The articulations may not be affected.

(4) Arthralgic, in which there are wandering joint pains with or without redness and swelling.
Blumer's classification seems to be the most likely and understandable. He leaves aside the arthralgia group and confines the arthrities to more definite forms. He recognizes

1. Acute Gonorrheal Arthritis:
   (a) Serofibrinous
   (b) Phlegmonous

2. Chronic Gonorrheal Arthritis:
   (a) Hydrops
   (b) Ankylosing form

He considers the most common type is that of the acute serofibrinous form. It usually occurs as a polyarthritis affecting most commonly the joints of the knee, foot and hand. The affected joints are painful, swollen and often fluctuant, with reddening of the overlying skin. This form may gradually develop into the chronic type with hydrops or more rarely by suppuration. The phlegmonous form is rare and is characterized by the severe pain and with little or no effusion. A prominent feature is tissue destruction.

Chronic hydrops is often insidious and painless in onset but may follow an acute arthritis. Large joints are apt to be involved more frequently and there is little loss of motility. The ankylosing form resembles infectious deformans arthritis and this is very common.

Other portions of the locomotor system which may be affected by metastatic gonorrhea are the bursae, tendon sheaths, muscles, periosteum and bone. These complications, will not be considered at this time.
DIAGNOSIS
DIAGNOSIS

The diagnosis of a metastatic complication of gonorrhea depends upon essentially two factors—the history and the laboratory. Both are of equal importance. In the former we must consider the history of infection, the type of onset of the arthritis, the type of arthritis and the appearance of the joints involved. In the latter we have four factors.

(a) The bacteriology, which includes the demonstration of the gram negative organism and its cultivation from various exudates or from the joint fluid.

(b) Joint puncture—with examination of the fluid.

(c) Roentgenological findings

(e) and Immunological studies—the positive gonococcus complement fixation test.

HISTORY

The patient afflicted with a gonorrheal arthritis usually gives a history of a recent gonorrheal urethritis. In general this is the most important factor in diagnosis according to Blumer(1). Obviously this is a simple matter in many patients but under certain conditions, it is attended with considerable difficulty. In women the manifestation of gonorrhea often give rise to such trivial symptoms and signs that the patient may be entirely unconscious of the infection and the physician may have difficulty in demonstrating gonococci in the secretions.(5) In the male a good history is often difficult—this may be due to the fact that he wishes to conceal his infection.(10).

Acute arthritis may develop during any period of the active urethritis but Stevens(18) finds it is comparatively rare during the first week. MacCallum(6) states that it usually is
a period of several weeks before the onset of arthritis.

Chronic gonorrheal arthritis may follow an acute arthritis or it may develop insidiously, (10). This may be months or years after the primary infection. It may develop after an acute exacerbation of the chronic gonorrhea. Nevertheless it is difficult and inexact to base a diagnosis on history alone, for as Pepper (15) states, "even the discovery of a gonococcal infection does not prove its causal relation -ship to an existing arthritis anymore than does the finding of a peri-dental abcess."

Only when an acute arthritis develops during the phase of an acute gonorrhoea can one safely and easily make a diagnosis of gonorrheal arthritis. A clinical sign which may be of value is offered by Cecil (5). He finds when arthritis complicates acute gonorrhea, there is frequently a history of marked decrease or cessation of activity of the primary focus at the time of development of the arthritic symptoms."

Thus when gonorrheal arthritis develops during the course of an acute gonorrhea, it offers little or no difficulty—the presence of gonococci in the urethral or vaginal discharge is almost conclusive evidence of its etiology. However in chronic cases of gonorrheal arthritis where the etiology is not so apparent other measures must be resorted to. With this thought in mind we turn to the laboratory for additional help.

LABORATORY

Bacteriology: We have already considered the etiology of gonorrheal arthritis as that being due to the gonococcus. We have further indicated that the presence of this organism in the dis-
charges from infected organ presents almost conclusive evidence of the etiology of the acute arthritis, (5 & 12)

In view of the fact that occasional non-gonorrheal forms of urethritis exist and often a arthritis may develop concomit with this urethritis it becomes a matter of importance to be able to detect gonococci when present and to differentiate these from the non-specific organisms. If we confine this differentiation strictly to bacteriology we have two methods of approach. These are the microscopic and the cultural. Animal inoculations are of no value, as animals are not susceptible (6,19)

In the microscopic diagnosis it should be borne in mind that after the acute serous stage has passed, the specific gonococci in carefully made preparations are always found largely within the pus cells. When treated by Grams method, the gonococcus completely loses the stain. The cells occur in pairs, with the flattened sides in juxtaposition; the appearance in stained preparations is like that of a coffee bean. Both Jordan and Park and Williams (2 & 19) in their text books on bacteriology give excellent reviews on the morphology and cultural characteristics of the gonococci. Torrey (43) also gives methods of culturing the gonococci. In a more recent article Stunier (17) states, "We have been greatly helped in the last few weeks by a comparatively new method of culturing the gonococcus. McLeod and his associates devised a method, which has been improved and simplified by Luther Thompson of this clinic, by incubating the cultures in an atmosphere of carbon dioxide. We can find the gonococcus in discharges by the culture method when the organisms are not found in smears and we are relying more on culture determination of
cure than we are on smears."

It is sufficient to say in the face of a clinical picture of gonorrhea if one finds a gram negative intracellular diplococci with the morphological characteristic typical to it, we can be relatively sure we are dealing with gonorrhea. However to make sure of this diagnosis we must resort to other measures including the culturing of the organism and the immunological studies.

**Joint Puncture:** In this procedure the joint cavity is entered under strict asepsis and a small portion of the joint fluid is aspirated for examination. Myers, Keefer and Holmes (59) have preformed a great amount of work on the characteristic of synovial fluid in gonorrheal arthritis. They find the most important examinations of the synovial fluid from the diagnostic point of view were the bacteriological, the cytological and the serological test. The chemical examination yielded very little significant information. The others will be considered shortly.

However in order to understand the significance of their work we must recall the normal characteristic of synovial fluid. According to Key (14) the normal joint fluid contains from one to three hundred living cells per cubic millimeter and also about an equal number of red blood cells and a small amount of fat and tissue debris. The percentage range of these cells are

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Percentage Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monocytes</td>
<td>42-84%</td>
</tr>
<tr>
<td>Indeterminate macrophages</td>
<td>3-29%</td>
</tr>
<tr>
<td>Primitive cells</td>
<td>0-10%</td>
</tr>
<tr>
<td>Leucocytes</td>
<td>0-12%</td>
</tr>
<tr>
<td>Synovial lining cells</td>
<td>0-7%</td>
</tr>
</tbody>
</table>

In contrast to these normal findings, Myers et al. (59) in a series of forty cases of gonorrheal arthritis found the total cell counts
of the fluids varied between 1,800 to 158,000 per cubic millimeter, and varying from 7,350 to 158,000 per cubic mm for infected fluids and for non-infected fluids from 1,800 to 78,250 per cubic mm. Thus while the variations in both groups were wide, it is true that higher cell counts were found more often in the infected than in the non-infected synovial fluid and both were enormously increased over the normal cell count. By infected fluids it is meant the gonococci are present in the joint fluid.

In another article, Myer et al. (28) state that if the organism can be cultured with ease, the surface of the synovial membrane was destroyed and it is the site of an intense inflammatory reaction. Therefore, they conclude, the organisms have extended from the periarticular tissues into the synovial cavities and destroyed the synovial lining of the joint; in those with non-infected fluids, the inflammation is confined to the periarticular tissues beneath the surface of the synovial membrane.

In conclusion these authors, after careful study found that the synovial fluid with a cell count of 40,000 or above per cubic mm., recovery of symptoms was not complete. On the other hand, of the 40 patients in their series, with synovial fluid cell count below 40,000 only 37% recovered completely. In other words a synovial cell count over 40,000 was invariably followed by some permanent change in the joint.

From these results it is apparent that the cell count is of more use in prognosis than diagnosis. They further were unable to demonstrate the gonococci in the synovial fluid only in a limited number of cases. Nevertheless they feel this is one of the surest means of making a diagnosis--the demonstration of the gonococci
in the joint fluid.

**Roentgen findings:** According to most investigators (11,23,24) gonorrheal arthritis yields a wide variety of roentgen appearances. These vary from a simple swelling of the soft parts to diffuse bony ankylosis (23). Finding of a honey-combed osteoporosis, spotty ground glass atrophy or calcaneal exostoses should create a strong suspicion of gonorrheal disease (11). Holmes and Ruggles (24) give two findings in addition to those of pyogenic infection which are very suggestive of Neisserian origin. These are-- a localized destruction of the cartilage in the knee on the under-surface of the patella, which sinks in toward the condyles of the femur. Then subsequently hypertrophic changes appear on its margins and on adjacent areas of the femur. The second is the occurrence of small localized areas of rarefaction in the bones, at the junction of the articular surfaces and the cortex. Harrison (26) finds that with destruction of the articular surface of the patella allowing it to approach more closely to the condyles of the femur and then a resulting ankyloses is almost pathonomonic of gonorrhea. Kerley (27) finds that gonorrheal atrophy closely resembles tuberculous atrophy and the differential diagnosis cannot be made by x-ray examination alone. Pepper (15) states, "With the aid of the judicious use of the history the x-ray may be of value--especially is this true if we distinguish between acute truly gonorrheal arthritis and other more chronic not strictly gonorrheal processes." In summary of this phase it may be said that the early diagnosis by roentgenogram appears to be of little value. Ghormly and Decon (13) believe this is due to the fact that changes occurring in
arthriti that can be recorded by x-ray appear relatively late. They further state, "Most patient who have arthritis are seen by some doctor before any diagnosis can be made roentgenologically." It appear likely to concluded that there are no specific roentgen signs of gonorrheal arthritis but the roentgenogram may render valuable assistance in making a clinical diagnosis. However in early cases of arthritis it seems advisable to make a diagnosis by other means than the x-ray. (13).

Immunological studies: Park & Williams (19) state that since the time of Bordet-Gengou in 1901 medical men have been interested in the phenomena of complement-fixation. It was Muller and Oppenheim who first applied it to the diagnosis of gonococcus infections. Since that time (1906) numerous investigators have worked on this problem. Although the gonococcal complement fixation reaction has been known since that time and it has been used in the diagnosis of gonococcal infections for many years, conflicting reports of its value are still seen.

The reaction depends on the production of specific antibody formation. According to Price (20) this is in turn dependent upon the

a. age of the infection
b. the anatomical spread of the disease
c. the reaction of the tissues to the presence of the gonococci
d. and the stage of the infection at which treatment was instituted and the efficacy of its therapeutic action

These postulates are supported by the observations that a large percentage of patient with early, localized anterior urethritis
show negative reactions, the more chronic and more systemic infections tend to give positive fixation. However in rare cases when the tissues do not respond to the presence of gonococci a negative fixation may result,(20). McCwen, Bunim and Alexander(21) state "Since joint involvement indicates that the disease has become systemic, it would be expected that cases of gonorrheal arthritis would show positive complement fixation, and this has been borne out by a number of our studies."

More recently the complement fixation test in synovial fluid has been studies. Kling and Pinkus(22) give a very concise account of the technic and mode of procedure. They find that 0.1 cc of the synovial fluid is the optimum amount to secure specific reactions. Inactivation of the synovial fluid is necessary to prevent anticomplementary reactions and also the fluid must be perfectly clear; it was found that slight turbidity or hemolysis interfered with the results. Their conclusion were

1) The presence of other infections do not interfere markedly with the specificity of the reaction.

2) A strong positive reaction in the synovial fluid was therefore considered as valid proof of the gonorrheal etiology of the arthritis--and more conclusive than the reaction in the blood serum where it only indicates the presence of an active focus somewhere in the body.

Myers and Keefer(25) are not in agreement with the latter statement. Their conclusions were, "The determination of the synovial fluid reactions can be said to add little information not obtainable from the study of the blood sera." Kolmer (58)
found that cases of gonorrheal arthritis yield from 80 to 100% positive reactions and the complement fixation test has considerable value in establishing the diagnosis of these infections. Other authors substantiate the view that it is helpful in diagnosis (20,22,23). Price(20) gives figures to show the longer the period after infection the greater the per-cent of positives; the 1st week after exposure to infection only 8% are positive, the 3rd week after exposure 80% are positive and after the 6th week 100% are positive. It thus becomes apparent after a period of three weeks the complement fixation test becomes of valuable assistance to the diagnostician, especially in those cases when it is difficult to demonstrate the gonococci and also in the cases of chronic gonorrheal arthritis.

DIFFERENTIAL DIAGNOSIS

In the differential diagnosis we are compelled to consider both the acute and chronic types of all arthritides, for it is to be remembered that gonorrheal arthritis is a disease of protean character and can simulate most any of the common arthritides.

Of the acute arthritides, Rheumatic fever is the most difficult to rule out. Stevens(18) states that gonorrheal arthritis is accompanied by less constitutional disturbance than rheumatism and further it shows little tendency to flit from joint to joint and it is extremely resistant to salicylic medication. Pepper (15) is in agreement with the latter statement. Osler(4) finds that there is usually some thickening about the affected joint in a short time which is usually not the case in Acute Rheumatic Fever. The type of joints involved are very similar but according to two investigators(18, 15) the temporomandibular and the sterno-
Clavicular joints are often involved in gonorrheal arthritis seldom if ever in rheumatic fever.

From the other acute specific infectious arthritis such as pneumococcal, staphylococcal and other less common forms of acute bacterial infection of the joint, the clinician must rely on the presence or absence of gonococcal foci, the history and above all the laboratory findings, Cecil(5).

In the chronic arthritis, the rheumatoid or infectious arthritis is very easily confused with gonococcal arthritis, particularly in women who have little or no vaginal discharge. The history is extremely important. Osler(4) finds that the small joints are usually not attacked so often, and after an onset with polyarthritis the majority of the affected joints clear, leaving one joint particularly involved in gonorrheal arthritis. This rarely occurs in arthritis deformans. The x-ray, according to Cecil(5) is of value in late casesy only.

The hypertrophic forms present some difficulty. The presence of Heberdên's nodes, the age occurrence, the x-ray and bacteriological studies serve to differentiate it, (2,5).

Pepper(15) finds that often it is impossible to distinguish on the basis of the arthritic picture, the so-called Neisserian arthritis from rheumatic fever; or other forms of non-gonorrheal infectious arthritis. "There is not enough difference in the onset, the order of involvement, the number of joints involved, those involved, the duration of individual joint involvement nor in the severity of the local symptoms to permit one to make a satisfactory differential diagnosis."
It becomes apparent from that quotation the need for a synchronous knowledge of the clinical picture together with the laboratory diagnosis if we are to make an exact diagnosis. How many cases of gonorrheal arthritis have been diagnosed as other non-gonorrheal infectious arthritis is difficult to estimate—likewise other specific arthritis have been mis-called gonorrheal arthritis. Perhaps this inexact diagnosis of gonorrheal arthritis is responsible for some investigators to report unfavorable results, when the condition was treated by some form of fever therapy.

We have stressed the importance of the diagnosis of this type of arthritis, for it is only when we learn the specific etiology of a condition that we are on a truly scientific basis. With this thought in mind we will consider one phase of treatment of gonorrheal arthritis, which has been said, in the past few years to be the specific treatment for this type of arthritis—that treatment being Fever Therapy.
TREATMENT
TREATMENT

It is not the purpose of this paper to consider the various forms of treatment and their relative merit. There have been numerous types of treatment and with varying results. We have gone through the ear of internal medication, orthopedic measures, physiotherapy, specific gonococcus serum therapy—that is vaccines of killed gonococci, the intradermal or subcutaneous injection of living virulent gonococci, and the administration of filtrate from cultures of gonococci. Serological treatment has proved successful in many cases and is still being used today. However since the advent of the foreign protein therapy with the resultant high fever and with the clinical observation that high fever seemed to benefit gonorrheal arthritis, the focus of attention has been drawn to this type of therapy.

The end result of gonorrheal arthritis before fever therapy was introduced was uniformly poor. However it is agreed among most of the leading medical men that all cases of acute gonorrheal arthritis do not end up disastrously. On the contrary, in a limited number of cases of gonococcal arthritis, require very little treatment(1,5,10) and usually recover with good joint function. However the suffering and disability during the course of the disease is usually not relieved by palliative measures. In contrast to this, if we treat all cases of arthritis of gonococcal origin, with fever therapy we not only can usually cure the arthritis but a extremely shortened course can be promised.

As late as 1928, Cooperman(12) in a series of 26 cases concluded that the end results in advanced cases were uniformly
poor. In his series (12) fourteen cases were of the acute type, seven were seen in the sub-acute stage and five came in with residual deformities of seven to eighteen months duration for correction of flexion deformities. It is of interest to note that of this series two patients died during the acute stage of the disease, this without doubt indicates the seriousness of the process. Cooperman (12) made the diagnosis of gonorrheal arthritis mainly on the history but also with the aid of the laboratory, namely the serology and the bacteriology so no doubt he was dealing with gonorrheal arthritis. He concluded "The terminal results are invariably associated with permanently stiffened and disabled joints, left as souvenirs of some sexual indiscretion." This statement seems quite appropriate and characteristic of gonorrheal arthritis.

Today Coopermans article is antiquated. During the past four or five years the outlook for patients with gonorrheal arthritis has been enormously improved. Hench (29) in a very recent article concluded if early and adequate treatment is given to a patient with gonorrheal arthritis, the patient has an 80 per cent chance of being promptly cured, and if not cured an additional 10 per cent of being markedly relieved. He further states "The fever therapy treatment is almost specific and is almost completely successful when bony changes have not occurred."
True fever therapy according to A.J. Desjardin, et.al (8) began in 1918 and was originated by Wagner-Jauregg. It was he who found that inoculation with malaria of a patient suffering from dementia paralytica was often followed by improvement or complete remission of symptoms.

The beneficial effects of fever were known to the ancients. Hippocrates, according to Cannon (20) held the idea that disease is cured by natural powers— that is fever exerts a beneficial effect upon the organism. This viewpoint held until the nineteenth century when a number of observers took an opposite stand. Claude Bernard, Leibermeister and others devoted much attention to fever and believed it to be harmful. Today we have swung back to the beliefs of Hippocrates. Most scientist and clinicians believe it to have a beneficial influence (8, 29, 31, 32, 37, 34 & 35). In the literature of the past twenty five years, over a hundred articles have appeared concerning the benefits of induced pyrexia in the treatment of various forms of disorder and disease.

Since the time of Wagner-Jauregg, numerous methods have been used in the elevation of the body temperature. According to Bennett (36) "The evolution of modern-day artificial fever therapy has come about by way of two routes of experimentation;

1. The so-called biological chemical or infectious fever method.

2. Physical agencies producing fever.

In the first group the foreign protein reactions and the malarial therapy are classified. The foreign proteins that have been used are crystalloid and colloid substances of
heteroproteins such as peptone, mild and casein, egg albumens, vegetable extracts and various sera, etc. Malarial therapy according to Bennett(30), is really a foreign protein reaction—the protein being set free in the blood during the segmentation of the plasmodium. For additional information concerning this phase of fever therapy, Desjardins(37) and Bennett(36) give excellent reviews.

In the second group we are dealing with physical agencies used in the production of fever. This dates back 4000 years ago, according to Desjardins(37), who found the Chinese used hot baths in curing many of their ills. Laymen have clung tenaciously to the curative merits of external heat. There have been numerous modes of inducing artificial fever by physical agents. Hot baths can be used effectively when the period of fever need not be long and unduly high. Other modes of producing fever by physical agents are, Radiant heat, Luminous heat cabinets, Non-Luminous heat cabinets, Electric blankets, Conduction heat methods, High frequency electrical methods, Short wave diathermy and Radio-Thermy. The latest development along this line has been accomplished by Kettering and Simpson. These men started using a air-conditioned cabinet with radio-waves to increase the body temperature. However in the summer of 1933, Simpson discovered that a patient's temperature can be raised and maintained consistently by air conditioning alone without resort to the radio-waves. This was truly a advancement. This cabinet, known as the "Kettering Hypertherm", will be described. For a complete and concise review on other types of physical agencies used in producing fever the reader is referred to the
works of Bennett(36 and Krusen(38).

In a brief comparison of the two it is to be noted in the former the elevation of the body temperature is at the expense of the body's own metabolism. Also it is not controllable—that is to say the desired temperature level cannot always be reached or kept at a constant level. In the latter group, the actual heat is not produced by the body but instead by some external source and the body only absorbs the heat. The temperature level can be regulated to the desired height and can be maintained at that point. However, there are certain complications which occur with the physical method of fever therapy. These however are of minor occurrence and will be discussed later. Today the majority of investigators feel that the present method of fever induction by the Kettering Hypertherm is by far the most advantageous method of induced fever.
RATIONALE OF FEVER THERAPY

Schnabel(17) found that for the past 40 years there have been occasional reports of cure of gonorrheal infections during a febrile illness. He quotes two investigators, Borgdan & Barthelemy who in 1893, told of a gonorrheal discharge which disappeared during an attack of pneumonia and recurred after the fever subsided.

In 1917 Culver(40) noted the cure of a urethral infection of Meissnerian origin after four days of Malaria. Luys(41) also in 1917 noted a case in which the urethral discharge subsided during an attack of mumps. Carpenter, Boak and Warren(42) review the literature concerning the effect of heat upon the gonococcus and they find numerous foreign workers who have noted the beneficial effects of heat on the disease gonorrhea and its lethal effect upon the organism itself.

The exact manner in which the beneficial influence of externally induced fever exerts its action is not clearly understood. Some believe it to be due to the increase in immune bodies and the increase in phagocytosis. Perhaps in the case of gonorrheal arthritis it is due to the specific lethal effect on the organism itself,(8).

Reimann(34) has shown that temperature at fever levels tends to influence the growth of bacteria adversely, to diminish the potency of toxins, to favor phagocytosis and to stimulate the development of immune bodies. He has classified the beneficial influence of fever as a defense mechanism against bacterial infection into four groups. The demonstration of--
(a) Antibacterial and antitoxic effects of fever in vitro.

(b) The enhancement of antibacterial and antitoxic ability of the host by raising the body temperature.

(c) The diminished resistance of the host to bacterial infection by lowering the body temperature.

(d) The beneficial effects of intercurrent infection and fever on other disease.

According to another investigator(?) the benefits of fever therapy presumably arise from

(1) A direct bacteriolytic or bacteriostatic effect due to the influence of heat itself on bacteria (without necessarily implying the formation of immune bodies.

(2) An indirect bacteriolytic or bacteriostatic effect resulting from increasing formation or mobilization of immune bodies.

(3) A local effect from vasodilatation, providing an augmented blood supply to inflamed tissues.

(4) A general effect from the heightened metabolism incident to fever.

Carpenter and Warren(44) who review Cammondon's work(47) write, "Cammondon made moving pictures of leucocytes and noted that they creep faster from 30-35 degrees centigrade than from 25 to 30 degrees centigrade. At 25 degrees centigrade he observed them to travel 9.6 microns per minute, while at 35 degrees centigrade they moved at 25.2 microns per minute. At the temperature of the..."
body becomes elevated above normal, the physical property of the leucocyte changes from the gel property toward the sol state, thereby becoming more permeable and able to ingest a greater number of bacteria or other foreign particles." It becomes apparent from this work that phagocytosis, one of the primary means of combatting infection and curing disease, is much more active during fever.

According to other authors(34,36 & 45) foreign authors as well as American authors have demonstrated an increase of agglutinins and hemolytic amboceptors by heating animals. Also the increase in titer of typhoid bacillus agglutinins as a result of fever due to other causes has been repeatedly shown both clinically and experimentally.

Tenney(45) has shown that the microscopic study of the capillaries of the nail bed showed an increase in the size and number of capillaries during the height of the temperature. Simpson(46) in a report on Artificial Fever Therapy given at the Mayo Foundation lectures states, "The evidence which has accumulated in the short period since the discovery indicates that fever exerts an adverse influence on the growth of bacteria, diminishes the potency of toxins, favors phagocytosis and stimulates the development of immune bodies." According to Hench, Slocum and Popp(29) an arthritis patient may be helped by any one of these factors acting alone or in combinations, But they conclude, "It must be admitted from data regarding all these factors particularly the augmentation of immune bodies, are meager and contradictory. Until more work is done conclusions are somewhat presumptuous."
Carpenter, Boak, Mucci and Warren (42) placed the treatment of gonorrheal infections by hyperpyrexia on an exact scientific basis. These investigators undertook the task of determining the thermal death time of the gonococcus at temperatures that can be tolerated by man. They subjected fifteen strains of Neisseria Gonorrhea to temperature of 39 C, 40 C, 41 C, 41.5 C and 42 C. (102.2 degrees Fahrenheit to 107.6 degrees Fahrenheit). The different strains which they experimented with had been under cultivation from one month to twelve years. The resistance of fever of the different strains was found to vary; the cultures that had been isolated ten or twelve years previously tolerated heat for a longer time than recently isolated cultures. When subjected to a temperature of 41.5 C (106.7 F) and 42 C (107.6 F), 99 per cent of the gonococci were killed in two hours, whereas the remaining 1 per cent required heating from seven to twenty hours at 41.5 C or from five to fifteen hours at 42 C. From these results they concluded that artificial fever might be valuable in the treatment of gonococcal infections.

From this last paragraph one is likely to conclude that probably the main benefits are due to the destruction of the organism by the high temperatures. This is not the case in the treatment of all disease by fever therapy but without doubt it is probably the major role in gonorrheal arthritis. Desjardins et al (8) state, "That fever therapy has no other basis than a knowledge of the temperature necessary to destroy other bacteria effectively and cure other disease--far from it, but in those disease one must depend on the indirect effect of heat, while in gonococcus infections the cure is mainly, if not wholly a question of degree
of temperature and duration of temperature. Consequently, the principle and perhaps the entire, effect is direct and specific."
Diagram of the Kettering Hypertherm: A, main compartment B, small compartment at front end of chamber, in which is mounted the mechanism for heating and humidifying the air and causing it to circulate through the main compartment C, the air channel between two layers of ceiling D, the vertical panel which closes the chamber during sessions of treatment E, the external, projecting portion of the rolling bed, on which rest the head of the patient F, the rolling bed on which the patient lies G, one of the sliding panels at the side of the main compartment which permits constant observation of the skin, the determination of rectal temperature, pulse and blood pressure and general care of the patient.
APPARATUS

The apparatus now used for fever induction and maintenance is an air condition cabinet developed at the Miami Valley Hospital and at the Research Laboratories of the Frigidaire Division of the General Motors Corporation, Dayton, with the collaboration of Mr. Charles F. Kettering and Mr. Edwin C. Sittler.

Desjardins et al (8 & 31) and Simpson(39) have given excellent descriptions of this apparatus. It is from them that the following description is taken.

If the reader will refer to Figure 1 it will become evident that the chamber consists of a horizontal box, the base or bed of which can be rolled in or out at will. The patient lies on this bed, resting on a comfortable air mattress which is rolled into the chamber proper and the chamber is then hermetically closed by means of a sliding vertical panel, through which the head of the patient projects. Sponge-rubber insulation is utilized in the neck region to permit the patient to shift his position. Thus, when the chamber is closed, the patient's body is within the chamber while the head is outside, resting on a shelf provided for the purpose. At the foot of the chamber is a small insulated fire-proof compartment in which the air conditioning apparatus is housed. The dry bulb air temperature is controlled by a thermostat. The wet bulb temperature which governs the percentage of relative humidity, is controlled by a humidistat or by a wet bulb thermostat. The air velocity within the cabinet is controlled by blowers of fixed speed. Dry bulb and wet bulb temperatures within the cabinet are indicated on large dials, equipped with warning pilot lights, on the top of the front end.
of the cabinet, where they may be constantly observed by the nurse technician. The temperature-humidity factors may be controlled by the turning of a single knob. The average set of air conditions to which the patient's body is subjected is as follows: dry bulb air temperature of 130°F to 150°F, relative humidity of from 35 to 50 per cent, and air velocity of 425 cubic feet per minute. The elevation of the rectal temperature to 105°F is ordinarily accomplished in from forty minutes to one hour. The column of heated and humidified air is thus made to circulate around the patient about ten times a minute. The air is constantly conditioned by continuous passage through the air conditioning compartment. The patient's body is entirely free within the chamber, and no electrodes or other electrical gadgets of any kind come in contact with the patient at any time. This is one of the chief advantages of this method of fever therapy over any method that involves diathermy or short wave radiations with their electrodes or condenser plates. With this chamber the temperature can be raised more rapidly than with radiant light chambers and every degree of fever can be maintained for as long as the condition of the patient allows or requires. Moreover another important advantage is the facility with which the patient can be examined, the rectal temperature taken and all the physical needs of the patient attended to throughout a session of treatment. This is made possible by sliding panels on each side of the chamber; these can be opened any time for the supervising physician to examine the patient's temperature, to change the single blanket that covers the patient when it becomes
soaked with perspiration, for the introduction of a bed pan, or for any other purpose. Furthermore, in case of emergency, the chamber can be thrown open and the patient with drawn in a few seconds.

**TECHNIC**

Patients to be treated with fever therapy should be selected with as much care as are patients who are to undergo a major surgical operation (38). A careful physical examination should always be made and only those who are able to withstand such a vigorous treatment are selected. Usually in gonorrheal infections we are dealing with a group of patients who are in the most active phase of life and therefore contraindications are in a minimum,(8).

After successfully qualifying as a candidate for treatment the patient is given instruction to drink excessive quantities of water and milk the day before he is to enter the cabinet (48). The morning he appears for treatment he should not eat breakfast. Immediately he is placed in the previously warmed cabinet.

It is essential that a well trained personnel be in complete charge of the work; that skilful nurse technicians, who have had at least one months supervised training, administer the treatments, and that a physician be in constant attendance, (38). As stated before this is to be considered a major procedure and fever therapy should always be confined to hospitals.

The temperature and blood pressure reading are recorded, the extremities are encased in cotton blankets to protect the skin. During each session of treatment the condition of the skin is
frequently observed and if an area of erythema appears, it is first covered with a towel in order to prevent the impact of hot air. If the temperature of the patient is allowed to rise too rapidly, the skin may not have time to adapt itself and may show signs of overheating. Desjardins, et.al(8) further state that the skin of some patients is more sensitive than that of others. On this account, at the 1st session or the second it may be difficult to raise the temperature to the required level. When this difficulty arises from a tendency to diffuse erythema from an extensive functional inefficiency of the sudoriferous system, the problem may solve itself. One or two session of moderate fever, in their opinion(8) may so increase the functional capacity of the perspiratory mechanism that more effective treatment may subsequently become feasible.

A need for a sedative is usually apparent. The patient may exhibit signs of nervousness. During the induction period when the temperature of the body is rapidly rising there occurs a time which is known as the hurdle period. At this time the patient may be exceedingly uncomfortable. A sedative often tides them over this period. Various sedatives have been used. Owens(48) uses pentobarbital sodium 1 1/2 grains at the start of the treatment. He finds that after the temperature has reaches a stationary level, the patient may go to sleep for long periods. Other will require hypodermic injection of one-third grain of pantopon to allay their restlessness.

Atsatt and Patterson(49) are using dilaudid 1/32 grain and scoploamin 1/100 for the same purpose. Some authors, Desjardins et al.(31) finds that dilaudid is unreliable and may lead to collapse. Further any morphine sedation should be avoided because
of its tendency to induce nausea and vomiting, which in turn may interfere with an adequate intake of fluids and chlorides during the treatment. In general of the sedatives codeine, pentobarbital sodium and sodium amytal have been found most satisfactory.

Following the knowledge that a chloride loss from the body takes place during a session of fever therapy which in turn causes the patient to exhibit a considerable degree of weakness, Simpson(33) and Kendall et al (50) advocate that the patient drink throughout each session, from 1 to 4 liters of 0.6 per cent solution of sodium chloride. This not only replaces the chloride loss but also the water loss. Desjardins et al.,(52) estimates in the course of a five hour session a patient loses from two to five pounds of water.

The pulse, temperature and respiration should be carefully recorded every fifteen minutes during the early stages and oftener as the treatment progresses,(50). Atsatt and Patterson(51) find that indications of circulatory collapse such as intense facial cyanosis, circumoral pallor rapidly increasing pulse rate or markedly falling blood pressure are sufficient points of evidence on which to terminate the treatment.
CONTRAINDICATIONS

Most investigators give the same contraindications, namely advanced age with its cardio-vascular changes, organic lesions of the heart at any age are outstanding and formidable handicaps to fever therapy according to Desjardins et al. (8). Popp (29) feels that a patient of more than sixty years of age should not be subjected to the treatment. Functional disorders of the heart may or may not interfere with treatment and also severe renal disturbances may make fever therapy difficult or impossible (31). Pulmonary tuberculosis per se is not a contraindication, but the resulting impairment of respiratory function may make it impossible to raise the patient's temperature to the required level or to maintain it at this level for a sufficient period, (8). However it is to be noted that advanced vascular and renal changes, cardiac weakness, chronic debilitating diseases, chronic alcoholism and marked nervous and emotional instability the usual contraindications to fever therapy are not commonly associated in patients who contract gonococci infections (48).

COMPLICATIONS

Various complication may develop during the course of fever therapy. However there have been no really major complications (48). Minor disabilities such as first degree burns, nausea and vomiting, facial herpes, generalized erythema, exhaustion, abdominal cramps, transient headaches and occasional vertigo are not uncommon.

Desjardins (52) found that headache was one of the most common complaints. However this usually abated in a few hours following the high temperature.
Popp (29) noted cutaneous vesicles developed while the temperature is being maintained at a high level (106-107°F). This usually occurred during the first treatment and rarely noted after that—this indicating the skin had accustomed itself to the treatment. In order to avoid herpes and cutaneous vesicles the first treatment should be given cautiously and not too much emphasis placed on maintaining a high temperature (29).

Muscular tetany (hands, feet and sometimes the abdomen) have been observed but these promptly disappear on the administration of CO₂ and O₂ or the intravenous injection of calcium gluconate (31). Following the use of large quantities of sodium chloride solution (29, 48, 50), the symptoms of exhaustion, abdominal cramps have largely disappeared.

Nausea and vomiting is not an infrequent complication. It usually will occur if food has been taken against orders (48). However some will vomit inspite of fasting. Hench (29) finds that this condition will ordinarily pass after one attack of vomiting and a series of eructations, but in some cases it has lasted as long as 24 to 48 hours. The use of from 500 to 1000 cc of 10 per cent dextrose in physiologic sodium chloride given intravenously will usually control it (29, 48).

TOLERANCE OF PATIENTS

The manner in which a patient behaves during the course of treatment is a faithful index of the character and temperament of the individual (52). Nervous individuals and persons without fortitude or self-control are prone to fuss more or less and to ask to be released from the chamber long before the session is scheduled to end. However the majority of workers (7, 8, 39, 46, 53) find that patients tolerate fever therapy
well. Nevertheless there are cases of gonorrheal arthritis which have not been cured and this often has been due to the failure of the patient to consent to additional sessions of treatment, (29, 50).

DURATION OF SESSIONS OF TREATMENT

The duration of the session of hyperpyrexia varies according to the relative resistance of the gonococcus. Carpenter, Boak, Mucci and Warren (42) have pointed out, the destruction of the micro-organism depends on two main factors: The degree of temperature and the duration of temperature. The relative importance of the two factors, in their opinion is approximately equal. Strecher (32) had good results using a temperature above 106 F maintained from five to seven hours. The average number of treatment being 1.5 per patient. Schnable (18) used a temperature of over 106 F and found that about three treatments were necessary in the acute cases of gonorrheal arthritis and three and one half treatments in the chronic arthritis. Kendell, Webb and Simpson (50) state, "For practical purposes, we have found that four or five treatments, each of five to seven hours intervals of three to five days, are productive of prompt and satisfactory results." Desjardins, Stuhler and Popp (8) in a very recent article review this subject most thoroughly. They conclude that if a sufficiently high degree of temperature is not attained, if this degree of temperature is not sufficient or the interval between sessions is too long the infection is not completely or permanently cured. They have outlined the following plan as an index to the duration of the treatment.
1. After the second session if the smears and cultures show no gonococci, two sessions of the same length and at the same interval—complete the treatment.

2. But if discharge continues or smears and cultures show gonococci—the duration of the treatment goes to eight hours.

3. Then, if one session of eight hours does not suffice to destroy all gonococci—extend the period to ten hours.

4. After three sessions of ten hours and persistence of symptoms and gonococci—the period of treatment may go to twelve or even fifteen hours.

Such a procedure is not often called for—the usual treatment of 5 to 7 hours as outlined by Kendall(50) usually gives the expected results.

DANGER OF THE TREATMENT

The danger that accompanies this type of treatment are practically nil, according to some of the workers(33,39) but it is indirect ratio to the skill and efficiency of the operators of the fever cabinet. Simpson et al.(37) has treated one hundred patients with syphilis, arthritis, gonococcal infection and vascular diseases of the extremities and these patients have been subjected to over 5000 hours of sustained fever therapy without evidence of injury, except for the minor complications already considered. In a more recent article they further sustain this view,(39). Desjardins(52) is not in total agreement with Simpson. He has treated 362 patients for various conditions for a total of 1,810 sessions of treatment. One of these patients
died under treatment. This single death among the 362 treated gives a mortality rate of less than 0.3 per cent. He states, "To say that fever therapy is entirely devoid of danger is contrary to fact."

Bennett(36) finds from a total of 4509 patients, treated by thirty-four physicians, twenty-nine deaths or 1.6% mortality was reported. However if we consider only the deaths from gonococcal infections as a result of the fever treatment, instead of all deaths due to fever therapy in general, it would be doubtful if the mortality is at all as high as 1.6%, for it is to be remembered that in gonorrheal arthritis we are usually dealing with patients in their physical prime and these patients are much more able to tolerate fever therapy.
RESULTS OF FEVER THERAPY
IN GONORREAL ARTHRITIS
RESULTS OF FEVER THERAPY IN GONORRHEAL ARTHRITIS

Kendell, Webb and Simpson (50) were among the first to note the beneficial effect of artificial fever therapy upon gonorrheal arthritis. It was purely a coincidental observation. It is of interest to repeat their first case history.

"In March, 1932, a thirty-nine year old man was referred to us for artificial fever therapy because of a resistant seropositive syphilis. The history and physical examination revealed that the patient also had active chronic gonorrheal arthritis of five months duration, involving the right wrist. Gram-negative intracellular diplococci were found in large numbers in urethral smears. After the third artificial fever treatment, each of which consisted of five hours of fever above 105°F at intervals of one week, all evidence of active gonorrheal arthritis had disappeared. The joint function, which had been practically nil, was restored to 90 per cent of normal. The urethral smears became negative for gonococci after the fourth treatment and have remained negative since that time."

Since 1932 various articles concerning the favorable influence of high temperatures have appeared in the literature. An attempt will be made to review these articles in a chronological sequence.

Carpenter and Warren (44) in September 1932 published an article concerning the treatment of disease by artificially induced fever. They noted that particularly in gonococcal arthritis, high temperatures gave exceedingly good results. In only one case did they record complete failure. The treatment given to this patient was seven hours at 41.5 degrees centigrade.
It was later determined that the thermal death time of the gonococcus, isolated from the joint in that case, was much longer than the fever given the patient.

Tenney(45) in the same year noted that if a temperature of 106 degrees F. is maintained from two to four hours in cases of gonorrheal arthritis, and pelvic inflammatory disease, it acts almost as a specific. He concluded "As the thermal death point of the gonococci is supposed to be around 104, they are probably destroyed by the heat."

Bishop, Horton and Warren(41) also in 1932, using hyperthermia induced by high frequency currents found that acute lesions subsided rapidly, lost their redness and tenderness, and there was gradual recovery from the stiffness. The chronic gonorrheal arthritis became painless and there was gradual relief from the stiffness, with increased mobility. Nevertheless they concluded that it was too early to speak of permanent results in arthritis at this time.

In 1933 Kovacs and Kovacs (53) treated as series of all types of arthritis with high frequency fever treatment. In a limited series of cases the failures and the encouraging results were about equally divided but they particularly noted good results in Chronic gonorrheal arthritis.

Berris(54) in the same year, using a electric heating element in a air conditioned cabinet treated various types of arthritis. Among those were two cases of gonorrheal arthritis. He noted failure in one case and complete relief in the other case. His temperature range was not high being about 102 F.to 103 F. sustained from three to four hours.
Atsatt and Patterson (51) published an article also in 1933 in which a series of eight cases of gonorrheal arthritis which were treated by electropyrexia were reviewed. Their results were recovery in seven—little or no improvement in the eighth.

Markson and Osborne (56) treated two cases of gonorrheal arthritis by diathermy with the temperature to 104 °F for four hours and noted in both cases all pain was relieved but in one case a recurrence took place.

In 1934 but few articles were written on the results of fever therapy on gonorrheal arthritis but in the following year there appear numerous articles.

Atsatt and Patterson (49) essentially republished their former article and again concluded that 87 per cent of acute gonorrheal arthritis could be relieved by electropyrexia.

Hench et. al (7), in 1935, admirably reviews the previous work preformed on gonorrheal arthritis and its relationship to fever therapy. The table on the following page, has been taken from this work and it will be noted that it is in accord with the results of previous investigators as reviewed in this paper. They (7) also review 16 of their own cases of gonorrheal arthritis which were treated with fever therapy. Of these 16 cases 9 were acute and 7 chronic. Thirty-two percent of the patients (five) were completely relieved of all signs and symptoms of arthritis. An additional 37 per cent (six patients) were also completely relieved except for rather insignificant residual stiffness, slight pain of a joint on motion or walking or a slight residual tenderness. Nineteen per cent more (three patients) were markedly relieved and in one patient (six per cent of the series) no benefit
was obtained. However this was a case of residual chronic gonorrheal arthritis of seven months duration. He further observed that patients with acute arthritis received somewhat more striking results than those with considerable residual striking results than those with considerable residual stiffness and destruction of joint tissues. Nevertheless, of the seven patients with chronic gonorrheal arthritis, whose disease was of three, six, seven, eight, fourteen and thirty-six months duration respectively, all were markedly relieved but the one previously mentioned. These results were not short lasting, for a latter check was made in eleven of the sixteen cases and from three to fourteen months had elapsed since the treatment. The result of this check up revealed that the status of the patient had changed but little and none of the improvement was lost. They concluded "Our results in sixteen cases of gonorrheal arthritis confirms those of others. About 90% of our patients were essentially cured or markedly relieved. Adequate fever therapy seems to provide a direct sterilizing action of affected joints."

Desjardins et al(8) also in 1935, using the Kettering Hypertherm treated twenty nine patients and with twenty five cures. They used an average of 5.4 sessions of fever therapy of 106.5 F to 107 F. temperature. Of the four patient who were not cured the believed that the failure was due to the fact that the required degree of temperature could not be attained or consistently maintained for a sufficient time.

Kendell, Webb and Simpson(50) had excellent results in a series of 31 patients afflicted with gonorrheal arthritis. Using essentially the same technic as others which consisted of four or five treatments, each of five to seven hours duration, at
a temperature range of 106°F to 106.8°F at intervals of three to five days. Of the 31 patients—19 had acute gonorrheal arthritis. Their ultimate average of improvement was 98.4%; 13 patients have obtained complete restoration of joint function. Of the 12 patients with chronic gonorrheal arthritis the average improvement in joint function at the conclusion of the course of fever therapy was 62.5 per cent; in four patients joint function was completely restored. The ultimate improvement in joint function in the cases of chronic gonorrheal arthritis was 88.3%.

Schnabel and Fetter(17) using the same technic as Kendall et.al(50) only the session are given weekly instead of every three to five days, treated 18 cases of gonorrheal arthritis. In nine of these cases, the arthritic process was acute of less than 6 weeks duration. The duration of the arthritic symptoms before treatment was three and one-half weeks and the number of treatments given each patient varied from 2 to 6. The average number of hours of treatment over 106 was 14.5 hours per patient, about 3 sessions per patient. The improvement in the involved joints was striking in all cases, and in some almost miraculous. Like former investigators they concluded that improvement was most rapid in the most recently involved joints. In only one case did the treatment prove disappointing and this was due to the lack of cooperation on the part of the patient. In their series of chronic gonorrheal arthritis, the average duration of symptoms before treatment was 7½ months. The earliest three months and the oldest 18 months. The average number of sessions was three and one half. The results were uniformly good. Of the nine—five were cured, three were markedly improved and only one did not respond to treatment.
During the past year, 1936, more articles concerning the treatment of gonorrheal arthritis by means of hyperthermia have been written.

Strecher (32) treated 21 patients with acute arthritis and 11 had prompt and complete remission of all acute symptoms. Pain and tenderness disappeared during the first treatment—joint swelling subsided in seven to ten days. Relief was so prompt and so nearly complete that an average of 1.5 treatments was all that was necessary. 6 Patients obtained marked relief of pain and tenderness but suffered from joint damage which caused some residual limitation of motion. Clinically they were scarcely distinguishable from the first group. Four patients, however, received little or no benefit. Strecher (32) concluded that fever cabinet therapy caused prompt and complete relief of the joint process in 52% of a series of 21 patients with gonorrheal arthritis and satisfactory improvement in 28.5%.

Trautman (57) had essentially the same results. Of 25 patients treated 16 completely recovered, five were markedly improved and four were moderately improved. These 25 patients all had the acute form of the disease. In his same article (57) he reviews a series of 15 patients with chronic gonorrheal arthritis treated with fever therapy and of this group—10 completely recovered, three were moderately to markedly improved and two were improved, but later had a return of their symptoms.

Owens (48) has performed considerable work in the field of fever therapy for gonococcal infections. He too, uses the Kettering Hypertherm with fever range of 106.5 F to 107 F.
He reviews a series of 22 cases of gonococci arthritis and of this number 14 were cured—the average treatment of 4.8 periods of 4.6 hours each were given per patient. Eight were improved with the average treatment of 2.8 periods of five hours each. Of this latter number one patients treatments were discontinued because of advanced age. Five discontinued when relieved of pain. Owens concluded that all had prospect of cure and in his opinion failure to cure these infections are to be regarded as due to insufficient heating.

In a very recent article by Desjardins et al (8) a good summary in regard to the treatment of gonococcal arthritis is made. He states, "The rapidity with which, in a large proportion of cases, the clinical manifestation of gonococcal arthritis subsides as a result of fever therapy is astonishing. In the course of the very 1st session of treatment the pain abates rapidly and the swelling diminishes a little more slowly. When the articular inflammation is acute the effect of fever therapy sometimes is really spectacular. In most cases through treatment is followed b, complete and permanent involution of the inflammatory process. When the inflammation is chronic, the clinical manifestations usually abate promptly and the infection is cured. But when the infection has already injured the bones, these as well as the resulting disturbances of function may be favorably influenced to some extent but cannot be expected to disappear completely."
SUMMARY

Gonorrheal Arthritis is a metastatic complication of the disease gonorrhea and its prevalence is universal. The clinical features of this arthritis are much the same as in other types of arthritis, but there are a few salient features which tend to differentiate it.

The diagnosis is made with the knowledge of a history of a gonorrheal infection together with the aid of laboratory findings. Of the laboratory findings the Bacteriology and the Immunological studies offers the most help.

Ten years ago the outlook for patients suffering with this type of arthritis was poor. Today, as the result of the development and use of induced fevers, the outlook is excellent.

In the treatment of this disease it has been found that the use of the Kettering Hypertherm is the method of choice. The basis of fever therapy, in gonorrheal arthritis, is thought to be the actual destruction of the organism by the high temperature.

Fever therapy is a costly and complicated treatment and requires the constant attendance of the operators at all times. The results of this treatment is especially encouraging. The majority of workers feel that when gonorrheal arthritis is adequately treated with fever therapy, 90 per cent of the patients can be cured or relieved of their symptoms. Some consider fever therapy in gonorrheal arthritis as specific therapy.
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