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Gout

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Introduction

Gout was called podagra originally, a Greek derivation from "Pous," foot and "agra," attack. The term today has been adapted from the Latin, "gutta," which refers to a drop as a result of "a defluxion of the humors." This broad reference is not surprising since the visible tophus is a massive precipitate of salts or uric acid. Several adjectives have been employed to qualify the derivative gout or have been used in the description of the clinical syndrome and its presumed variations. In spite of the persistent confusion between gout and gouty arthritis with the consequent interchangeable use of terms, this inaccuracy is not serious.

The clinical manifestations of the disease are restricted to four terms. (1) Gout is the parent term without reference to acute or chronic joint distress. The term is justified in the case of any individual who has suffered one or more attacks of acute gouty arthritis. (2) If the patient is on a uricosuric regimen, a patient may show a concentration of urate in the serum within the normal range with an increased excretion of uric acid in the urine as the only sign of the abnormality. Regarding the appearance of an attack of acute gouty arthritis, these attacks should occur only during a small portion of the time of the natural history of the disease. (3) The intercritical period is the period between the acute attacks of gouty arthritis. Freedom from

acute joint symptoms should be anticipated in the intercritical periods in all patients during the earlier years following the initial attack of acute arthritis, and in most patients, throughout the natural course of the disease. While patients with gout may experience acute attacks intermittently between the attacks the afflicted show no articular symptoms or any chronic deforming joint manifestations. (4) Actually, chronic deforming gouty arthritis, the fate of only a small number of patients afflicted with gout, is a late manifestation of the disease, and several decades usually elapse following the first attack of arthritis before this stage appears. The earlier in life the first attack of acute gout appears, the greater is the tendency for the development of irreparable chronic deforming changes.

History

Gout not only received recognition as a clinical symptom before the birth of Christ but also has afflicted many eminent persons throughout history as Hippocrates (460-370 B. C.) and Hieron of Syracuse (fifth century B. C.).

In the early centuries of the Christian Era, several physicians described articular symptoms, very probably referring to gout. Among them are Galen, Seneca, Aretaeus the Cappadocian and Caelius Aurelianus. Aretaeus noted the higher incidence in the male and the greater susceptibility of the great toe as the site of the attack, but with the possible involvement of hands, elbows, knees, and hips as well as the appearance of subcutaneous tophi. Although Alexander of Tralles in the sixth century A. D. is accredited with the specific identification and use of colchicum in gout, Paul of Aegina confirmed the clinical value of colchicum in gout and noted that emotional factors may incite an acute attack. Paul expressed some misgivings concerning the drastic purgative effect of colchicum and, in the search for a less violent purge, may have contributed to the loss of prestige of colchicum in clinical medicine for several centuries, dark ages for gout and colchicum. In fact, not until the thirteenth century did medicine pick up these threads.[1]

Other noteable events of gout were recorded as the Khan of Mongolia suffered from gout, and in the year 1267, the King of Korea provided the Emperor with fur boots to protect the sensitive parts.

The marriage of Henry VII to Lady Margaret was postponed because of his Majesty's gout. Hertzog Christian von Wurthenberg, a sufferer from severe gout, wrote a treatise on the subject in 1537 and gave instruction to Martin Luther, a fellow sufferer. Horace Walpole confessed that he could talk about gout by the hour and so he does in his letters.

The rediscovery of colchicum in the treatment of gout is credited by historians to a French army officer, Nicolas Husson, but some consider him a "quack." Husson's secret preparation is known by the nonspecific term "eau medicinale." Colchicum was the chief constituent of other patent medicines, including Wilson's tincture, Portland powder, Laville's tincture and Reynold's specific. Ambrose Pare used colchicum for gout in the seventeenth century. In 1814, Want identified colchicum as the active ingredient of the secret preparations. Six years later, Pelletier and Caventou isolated the alkaloid colchicine from the meadow saffron, or Colchicum autumnale.[2]

Gout occupies an important place in the history of medical art, especially in the caricature. One of earliest caricatures appeared in Petrarch's "Trostspiegel" in Frankfort, Germany, 1572. The comics in the daily or Sunday papers today which make light of gout include "Bringing Up Father," "Major Hoople," "Grin and Bear It," "Brother Juniper," and the "Katzenjammer Kids."

There were many treatises published on gout in England in the 18th and the 19th centuries as John Brown's Brunonian Theory which

was traced to an inspiration received during an attack of gout. Another treatise was William Cullen's First Lines of the Practice of Physic where he devoted thirty-five pages to gout, but he made no mention of colchicum although this had been described as anti-gout remedy for several centuries. William Cadogan, pediatrician of London in the 18th century, published a treatise on Nursing and the Management of Children and an essay on gout based upon his personal experiences. The Reverend Sydney Smith was a brilliant man of letters, and he came from a family of gouty ancestors and put great faith in the effectiveness of colchicum, noting that "On Sunday I was on crutches utterly unable to put foot on the ground, on Tuesday I walked four miles such is the power of Colchicum."[3]

The association of uric acid and gout dates from 1776, when Scheele identified this substance in urine. A few years later, Wollaston isolated uric acid from gouty tophi. In 1793, Forbes extended Wollaston's observation, when he speculated that gout might be associated with an increased concentration of uric acid in the body. Because of a lack of laboratory procedures for his hypothesis at that time, Garrod could not furnish convincing evidence of an increased concentration of uric acid in the blood of gouty persons until 1848. The famous uric acid thread test was described in 1856. The data were similar to results by current biochemical methods for the determination of the constituent in the serum of gouty patients.

The hereditary nature of gout has been recognized since the earliest description of the disease. Galen, Seneca, and others noted the familial affiliation. One of the first statistical tabulations was reported by Scudamore, who computed a familial incidence of 60 per cent in his series of 522 patients.

The exact mode of transmission of gout has not been determined, because of the insurmountable task of any one observer examining a sufficient number of patients with families large enough to accumulate sufficient data to justify treating the observations statistically. Scudamore observed that the father was afflicted in 87 per cent of the patients with a positive family history. Also noted was the tendency of an affected female to transmit the disease to her offspring.

A logical extension of the familial aspects of gouty arthritis has not been possible until the development of clinical methods for the determination of uric acid in serum. Folin, one of the fathers of clinical biochemistry, was among the first observers to report an increased concentration of uric acid in the blood in a non-arthritic relative of a gouty individual. More than two decades later there were reported similar findings in three nonaffected relatives of gouty persons.

Since the ages of the nonafflicted relatives cover a period of more than eight decades, it is believed that these data support the presumption that the disturbance in uric acid metabolism may be

present many years before the onset of acute gouty arthritis. It is equally reasonable to believe that the uric acid disturbance may be present throughout life, without the appearance of clinical signs of gouty arthritis. The hereditary factor is dominant in the cause of gout, while dietary reasons, as alcoholic intake and other factors, are of secondary importance only. It can be that one or more of these factors may precipitate an attack or augment the tendency to articular distress in an individual who might avoid development of clinical symptoms.

Gout has been found in lower animals. Finding of urate deposits, in and about the joints and in subcutaneous spaces, has been described in a number of animals, particularly birds and reptiles.

Clinical Aspects

Since an acute attack of arthritis of one or more of the joints of the extremities is the first conventional sign of articular gout, the diagnosis usually is not suspected until after this attack. A diagnosis of gout usually is not made until after the first attack except for the highly unusual development of subcutaneous tophi preceding the initial attack. Albuminuria, elevation of blood pressure, and the passage of a renal stone have been noted before the initial articular attack.

The typical onset of acute gout is sudden and may appear at any time during the 24 hours of the day on any day of the year. The metatarsal-phalangeal joint of the great toe usually is afflicted, but other peripheral joints of the upper or lower extremities may be involved.

The pain of acute gout is caused in part by effusion into the joint cavity as well as by edema of the surrounding soft tissues. The synovial capsule, somewhat inelastic, is sensitive to pressure and has tenderness usually on the lateral aspect of an involved joint. One or more joints may be involved simultaneously during an acute bout, or several joints may be involved successively. Also, the inflammation may extend beyond the joint at times, with involvement of the lymphatics similar to a cellulitis.

When a physician is trying to diagnose as to whether it is an infection of the joint or gouty joint, there are usually two points

of differentiation: (1) the skin is tense and shiny over a gouty joint, and (2) the color tends to be a cyanotic purple rather than a fiery red.

Acute attacks of gout tend to involve articular structures only, although nonarticular tissue may be affected independently of a neighboring joint. A subcutaneous tophus, a burse or a tendon infiltrated with urate, may be acutely involved and extremely painful. A fever with temperatures as high as 104° F. is usual in a severe articular attack and may confuse the physician. The urine output may be scant, especially with high temperature, if abundant quantities of fluids are not taken.

The first attack may be of short duration and subside, or without medical attention the attack may persist for several days or even several weeks. With proper diagnosis of the acute attack, the patient should make significant improvement and partial rehabilitation within 24 hours and essentially normal function not more than 72 hours after beginning therapy. Patients with advanced gouty changes and extensive urate deposits are more prone to prolonged bouts of articular attacks. Anti-gout agents, prophylactic and therapeutic, are important factors in preventing an attack, as avoiding mild ones and markedly shortening the duration of severe ones.

The site of acute gouty arthritis is relatively constant, the metatarsal-phalangeal joint of the great toe, right or left. The interval between attacks varies considerably. Several years may

elapse from initial attacks but as the disease progresses, the frequency of attacks tends to be increased. Patients who show large deposition of urates in and about the joints of the extremeties are prone to suffer greater incapacity from acute gouty arthritis per year unless prophylactic therapy is followed.

Between the acute attacks in patients without articular deformities, there are no clinical symptoms or findings. The intercritical period between attacks in some patients may be several years. Patients in later years may suffer the first few attacks during the remainder of their lives. Chronic deforming joint changes are observed in only a small number of the total gout population.

Diagnosis

Gout is not readily diagnosed by the physician although theoretically it should not be difficult to diagnose. Gout should be differentiated clearly from the other articular disorders. This advice offered by Llewellyn on the diagnosis of gout a generation ago continues to be good. "Confronted then, with the suspected case of gout, whether acute or chronic, what shall be our way of approach? Not the easy and hazardous path of lightning diagnosis affected by those who plume themselves on their so-called clinical 'instinct,' but the slow, laborious route of clinical 'observation,' that leads more surely to the vantage ground of the truth; this assuredly in all disease, but in none more so than in joint disorders, whose outward resemblances so often hark back to inward disparities."[4]

Careful inquiry should be made into the family history of every patient with unexplained acute arthritis. If a family history of gout is obtained even though it is one or two generations removed, this information is significant.

An increased concentration of serum urate in a nonaffected relative of a gouty patient increases the probability of acute arthritis at some future time. It is believed to be desirable for each member of a gouty family to undergo tests for such a determination periodically. The individual should be recorded as a potential gouty patient.

A urate calculus may precede the initial attack of gout. The practice of determining the chemical composition of each primal renal stone is highly desirable. Formerly it was believed that determination of uric acid content of the serum should be restricted to those who had passed urate stones. It is now believed that the concentration of serum uric acid should be determined in calcium stone formers as well as in urate stone formers.

Albuminuria is another sign of acute gout. Many patients have reported albuminuria, sometimes several years before the first articular attack. It has been recommended a serum uric acid determination in each patient with unexplained albuminuria be made. Also, hypertension may precede the first attack of acute gout.

The clinical characteristics of the acute attack are extremely helpful in suggesting the correct diagnosis. The sudden onset of severe pain in one or more peripheral joints of the extremities in a previously healthy male should imply gout.

The concentration of serum uric acid is another valuable aid. This elevation precedes the acute attack, is observed during the acute attack, and is present in the intercritical period unless uricosuric agents are administered. The increased concentration of uric acid in the serum persists throughout the natural history of the disease unless uricosuric agents are given.

Unfortunately the determination of uric acid presents certain technical difficulties in some routine biochemical laboratories. Most persons with a normal uric acid metabolism show a serum urate

level less than 5 mg. %. in contrast to most gouty patients with levels usually higher than 6 mg. %. It is interesting that many of the nonspecific anti-arthritic agents have a uricosuric effect as newer corticosteroids, ACTH, Butazolidin, Benemid, salicylates and cinchophen. If sufficient amounts of these drugs are taken prior to the collection of blood, the uric acid may be within normal limits. Thus, it is wise to withhold any uricosuric agent for a period of at least 48 hours before obtaining blood if a correct value is desired.

The response to colchicine may be of diagnostic value as well as of therapeutic aid in suspected gouty patients. Colchicine is specific for acute gouty arthritis and has little or no effect upon other forms of acute or chronic joint distress. In a suspected case of gout, a full course of colchicine should be administered, and most patients with acute gouty arthritis respond and the diagnosis is revealed. It should be stressed that if colchicine is prescribed as a diagnostic tool full therapeutic amounts must be given. Inadequate amounts of colchicine may provide little symptomatic relief and may give, therefore, a misleading diagnostic answer.

Following an acute attack, normal appearance and normal function return to the afflicted joint. There are still remaining two points absent in the initial attack, but present during the intercritical period after several years' course of the disease. These are subcutaneous tophi and osseous tophi. The deposits of urate may be rather extensive in the patient with moderate or severe gout but are not susceptible of detection until they have reached large portions.

The urate tophus in the ear does not appear in every patient suffering from this metabolic change. One or more white nodules on the helix of the ear is good evidence of the disease for a number of years as well as of neglect of earlier diagnosis. Patients with the severe form of the disease may have subcutaneous tophi adjacent to and involving most of the joints of the hands and the feet. The metatarsal-phalangeal joints of the great toe, the terminal phalanges of the fingers, the elbow, the knee, the lateral aspect of the foot and the heel are especially susceptible to periarticular tophi which may be bruised and result in a draining sinus tract. The Achilles tendon is another area prone to attract urate deposits in the moderately severe case of gout.

If confirmation of the presence of urate crystals is sought from a suspected urate tophus, there are several procedures. (1) A tophus on the ear may be scraped by a hypodermic needle, or (2) suspected urates recovered from a discharging sinus by a sterile swab. If the recovered material is placed upon a microscope slide and viewed under a low power lens, the characteristic needle crystals are readily identified. A suspected tophus that is removed surgically may be examined chemically for urates. If the diagnosis is delayed until the development of subcutaneous tophi the patient suffers needlessly.

X-ray

A significant percentage of patients with clinical evidence of gout, even those whose symptoms extend over a period of years,

may show no abnormalities in a roentgenographic study of the articular structures between attacks. During the acute attack, there may be swelling of the soft tissues but no essential change in the hard tissues. Thus, roentgenographic examination may provide no diagnostic help at the stage of the natural history of the disease when diagnostic help is most welcome.

The changes that may be observed in the roentgenogram of the extremities are confirmatory at times, they are nonspecific. The metatarsal-phalangeal joint of the great toe is one of the first structures to show chronic changes by x-ray.

In the x-rays, the characteristic finding in the gouty joint represents circular or oval areas of decreased density, and of rarefaction. In some instances, the tophus appears to be unilocular and of the same density throughout.

Demineralization of affected parts may be extensive or localized in the x-rays thus the end result of demineralization of a circumscribed area is complete replacement by sodium urate.

Deposition of calcium in a urate tophus is an unusual finding in x-rays which is of little diagnostic value.

The progression of changes shown by x-ray film is unpredictable. It is reasonable to believe that it should be a function of the severity of the uric acid disturbance and the frequency of acute attacks of gouty arthritis. However, a more precise evaluation of the roentgenographic changes with magnification procedure has been perfected by Culver at the Buffalo General Hospital. The structural

details of bone and cartilage permit greater precision for inspection of films and interpretation of the findings.

Differential Diagnosis

In the differential diagnosis, several conditions simulating gouty arthritis should be considered. The commoner forms of articular disease present the principal diagnostic difficulties. Because acute rheumatic fever may resemble acute gouty arthritis, the physician may find the task of differentiation, especially of a young person, very difficult in the initial examination. Either condition has a marked tendency to appear in the peripheral joints, and symptoms may appear rather suddenly following a streptoccoccal infection. The major signs of inflammation of one or more joints may be present. Since gouty arthritis may appear in young persons, while acute rheumatic fever may appear in older individuals, the diseases are not determinable from age. A favorable response to ACTH or salicylates may not be diagnostic of either disease, nor the level of uric acid in serum determination.

In contrast, the articular distress usually is more acute in gout, and while acute rheumatic fever has a slightly higher incidence among females, gout is predominantly a disease of males. Major complaints and characteristic electrocardiographic changes likewise suggest rheumatic fever while a response to colchicine is characteristic of gouty arthritis. X-rays of the affected joints in acute rheumatic fever show soft tissue swelling only.

A history of acute rheumatic fever or the presence of rheumatic valvular heart disease in patients with well defined gouty arthritis has been of interest. According to the authorities on both of the diseases, it is believed that it may be only chance that an occasional patient with gout will have had rheumatic fever as a child.

Rheumatoid arthritis should not present a diagnostic problem except in unusual circumstances in the male patient. In the infrequent cases of the coexistence of gout and rheumatoid arthritis, the diagnostic problem becomes perplexing.

Roentgenographic changes in rheumatoid arthritis may be confused with those of gout. The cystic areas in rheumatoid arthritis, however, tend to be more centrally located, such as in the metacarpals or the carpals. The hands and wrists are affected more often than the feet and ankles. Frequently, generalized decalcification is apparent in rheumatoid arthritis, although generalized decalcification in gouty arthritis is unusual.

The differential diagnosis of rheumatoid arthritis versus gouty arthritis, or the coexistence of these two conditions may be resolved only by a biopsy of a nodule or the synovial membrane of the joint under observation.

In the differential diagnosis of sarcoid arthritis and gouty arthritis, there are several distinguishing features of systemic sarcoidosis which should leave little doubt regarding this condition. If in addition the family history for acute arthritis is negative and no tophi are discovered, the evidence surely points to sarcoid

arthritis. The response to colchicine cannot be used in differentiation since symptoms in sarcoid arthritis respond to this anti-gout agent. The incidence of sarcoidosis is considerably higher in the colored race, while the incidence of gout considerably less than in the white race.

McCarty has introduced recently the term "pseudogout," a clinical syndrome of recurring acute synovitis of the large joints, usually in males. X-rays of the affected joints show calcification of the articular cartilage. Confirmation of the diagnosis may be made by identifying intraleukocytic calcium pyrophosphate crystals in the aspirated fluid. The clinical features may suggest acute gouty arthritis where central joints as well as peripheral joints may be affected. The serum uric acid is not elevated. A negative response to therapeutic amounts of colchicine has been observed.

Although most references to menstruation and pregnancy in gout, including that of Hippocrates, usually imply that gout and menstruation or gout and pregnancy are incompatible, there are several statements to the contrary in the literature. There are a few isolated cases of gout and pregnancy, but it could be questioned if the diagnosis was valid.

Prognosis

The prognosis in gout is more satisfactory than in any other of the potentially crippling types of joint disease. Previously, it was generally accepted that the more frequent the acute attacks, the more rapid the progression of the disease and the greater the probability of the development of chronic deforming changes. This view was particularly applicable to the gouty patient in whom the onset of the articular distress occurred in adulthood. Patients who experienced the onset of articular symptoms in the declining decades of life usually escaped chronic tophaceous gout.

Critical renal impairment may be unrelated to the severity of chronic tophaceous arthritis and in a few patients, may lead to premature death. Many clinical cases lend little support to the belief that clinical evidence of renal impairment is a direct function of the severity of articular gout.

Almost 100 years ago, Thompson, in discussing gout in relation to insurance rates, supported the need for a substantial increase in premiums for the applicant with gout of not less than 20 per cent above the established for the healthy nongouty applicant.[5] Prejudice against the disease persisted until recent years, and now the medical department of insurance companies accept the gouty patient as a sound risk once the clinical course had been found by experience to be satisfactory.

Complications

Kidney impairment, with varying severity of hypertension and arteriosclerosis, is the only critical complication of gout. Although gout has this frequent complication only a small percentage of cases do result in uremia and premature death.

The detection of kidney involvement in the initial stages of the natural history of gout depends upon laboratory findings (1) albuminuria, (2) cells or casts in the sediment, (3) impaired concentrating ability, (4) increased concentration of urea in the blood, and (5) abnormal intravenous pyelography.

Renal stones constitute an interesting as well as important clinical complication in gouty arthritis. A renal stone may have a nucleus of uric acid and yet be composed principally of calcium phosphate during formation thus the importance of identification of the nucleus if uric acid is suspected as being responsible.

At present treatment upon the progression of the renal changes in gout cannot be determined. It is believed that patients on a daily dose of colchicine and Probenecid show no evidence of progression of renal dysfunction.

Hypertension and arteriosclerosis frequently seen in gouty patients are considered to be complicating factors of gout. There is a relatively good correlation clinically between hypertension and mild renal dysfunction.

The incidence of coronary sclerosis in patients with gout has been debatable. John Talbott does not believe that patients with

gout are more prone to the development of coronary artery disease than non-gouty individuals. Large vessel sclerosis appears to develop prematurely in some gouty patients. Deposits of uric acid on the pericardium, in the endocardium, and in the walls of great vessels have been reported in a small number of cases.

There are example of phlebitis associated with the acute attack of gouty arthritis, but there seems to be no close relationship.

Prevention

The practice of determining the concentration of uric acid in the serum of all relatives of a gouty patient is the first step in prevention of gout. Hyperuricemic individuals need no specific therapy prior to the initial articular attack. Probably the most important item is the identification of potential gouty patients so that the correct diagnosis will be made at the time of the first attack.

Treatment

Although gout is a chronic disease with articular symptoms, the prognosis and treatment of gouty arthritis is very optimistic. It should be impressed upon the patient of gouty arthritis that the persistence of the prophylactic treatment will void or reduce the incidence of acute attacks.

Although acute articular symptoms of gout have responded for centuries to colchicum or colchicine, some physicians shun its use in the treatment of acute attacks. One factor responsible in recent years for not using colchicine is the clinical trial of cortisone and adrenocorticotrophin and then the shift to phenylbutazone and Colcemide. While each of these has merit, it is the belief of John Talbott and others that no preparation has surpassed colchicine in the management of gouty arthritis.

Prophylactic Period

The greater portion of the time of the patients afflicted with gout should be intercritical, thus the treatment of the prophylactic period will be considered first. It is particularly important, therefore, to discuss the therapy of the intercritical period in terms of years rather than in shorter periods of time.

Considerable progress has been made in the understanding of the uric acid disturbance in the intervening years which has led to important changes in management and treatment. Furthermore, similar gain has been recorded in the prevention of recurring attacks

through better handling of the patient in the intercritical period. The direction of the prophylactic phase of gouty arthritis is concerned largely with the regular administration of two of the most effective anti-gout agents, colchicine and Probenecid. The combination of colchicine and Probenecid have given excellent clinical results. The combination has resulted in a further reduction in the incidence of acute attacks and improved state of well-being. In the discussion of colchicine and Probenecid, each will be considered individually despite their effectiveness together.

The daily use of colchicine in the intercritical period has been found to be extremely useful, although little or no effect upon uric acid metabolism may be attributed to colchicine. It is a good practice to recommend some colchicine regularly as a prophylactic to each patient with gout. One 0.5 mg. tablet is recommended three or more days each week in mild cases with a past history of not more than one attack per year. Intolerance to colchicine does not develop and when an acute attack appears, a full course of colchicine is maximally effective regardless of previous intake. This is an important clinical observation and should not be forgotten by patient or physician.

In the history of many patients regularly taking colchicine for two decades or longer, it has been observed that such a treatment is beneficial and associated with no undesirable features if gastro-intestinal symptoms are avoided during the prophylactic periods.

If acute symptoms should appear, the patient should start a course of treatment at the earliest possible time.

Colchicine stood alone as the prophylactic drug until the 1940's and then the combination of cinchopen, sodium salicylate, or acetylsalicylic acid with colchicine was used as a moderate uricosuric. They proved to be of little or no value between attacks.

Probenecid was first made available for clinical trial in 1950. Initially a few patients were placed upon 3 gm. of Probenecid daily, but this was soon found to be an excessive dose and produced gastro-intestinal distress. Therefore, those patients severely afflicted were prescribed 2 gm. of Probenecid daily, and patients moderately or mildly afflicted were prescribed 1 gm. a day. Gastrointestinal distress may be prevented by the ingestion Probenecid with meals.

There are two actions that may be attributed directly to Probenecid, and two actions to the combination of colchicine and Probenecid. The first effect of Probenecid is an increased excretion of uric acid in the urine and a decreased concentration in the serum. If the uric acid disturbance is milder and the serum urate concentration lower, the uricosuric action of Probenecid reduces the level to the normal range of 4-6 mg. %. The second effect of Probenecid is the decrease in the size of subcutaneous tophi and recalcification of the punched-out areas in the bone, areas of urate deposition which have slowly replaced calcium salts. If large subcutaneous tophi are present on exposed portions of the body, it is the usual practice to remove them surgically rather than

to wait for Probenecid to reduce them gradually. The most important effect of the combination of Probenecid and colchicine is the lessening or elimination of acute attacks of gout. The patients are cautioned that they might be more susceptible to acute attacks in the first few months of the treatment, but long term cases have proved the treatment very successful. Another effect of the combined medication is an improved feeling of well-being, not observed while colchicine was the only drug administered regularly.

Presently, the combination provides the most effective treatment of any type of arthritis in present practice. Patients mildly or moderately afflicted lead normal lives in every respect. Patients with chronic deforming gouty arthritis continue to be handicapped in varying degrees but are not incapacitated.

The length of time that a patient should be on Probenecid daily has not been determined. It is believed that patients severely afflicted will be continued on Probenecid indefinitely while patients moderately afflicted probably may revert to smaller doses, meanwhile maintaining some colchicine daily as anti-articular prophlaxis.

In patients found to be unresponsive to Probenecid, or who belong to that small group of patients not suited to long term ingestion of Probenecid, another drug, sulfinpyrazone, is available. This preparation is administered orally, preferably with meals or milk, 50 mg. four times daily, and increased until a total daily dosage of from 400 to 800 mg. per day is reached. Treatment should be continued without interruption, as with Probenecid.

General measures during the intercritical period include attention to fluids, foodstuffs and exercise. A high fluid intake is desirable. Tap water would be fine, and fluids with caloric supplements are adequate, but since gouty patients tend to gain weight, the additional caloric intake may be undesirable. A patient with gout should develop the habit of drinking liberal quantities of tap water at mealtime as well as between meals. Most patients with gout are able to remain in a symptom-free state of gout, meanwhile enjoying a temperate intake of alcohol if they so desire and if other anti-gout measures are taken.

Gouty diets are probably as numerous as there are physicians. Each kind of foodstuff has been prohibited by some physicians and praised by others. The patient with gout should have a diet low in purine-rich foods to relieve the already overburdened mechanisms for the disposition of purines. Probably the most suitable diet for the gouty patient is a mixture of animal and vegetable foods. The caloric content is believed to be as important as the specific items. A few gouty patients tend to be overweight. This imposes a burden upon the cardiovascular system as well as upon the weight-bearing joints. Obesity is thought to be undesirable for the healthy as well as for those suffering from a chronic disease. The general rules for maintaining a normal body weight are believed to apply to gouty patients. Generally, patients who enjoy out-of-door activities should be permitted to continue them.

Acute Attack

It is believed that the most valuable drug in the treatment of the acute attack continues to be colchicine. This may be combined with phenylbutazone or adrenocorticotrophin, but it has not been replaced by them or any other anti-gout agent.

The amount of colchicine prescribed should be based upon the severity of symptoms. A mild attack may follow the dosage of not more than four or five single doses of colchicine 0.5 mg. (1/120 grain). A moderate or a severe attack requires the "full course" which is periodic intake of colchicine until the onset of gastrointestinal distress. The mild attack may be handled without interruption of daily routine, and probably without medical advice if the patient has been properly instructed.

A full course of colchicine may be ineffective because of one of several reasons: (1) The desired effect may not be achieved promptly if acute symptoms are permitted to persist for one or more days before beginning colchicine. (2) The course of colchicine may have been interrupted. (3) There may be some complicating factor which precipitated the acute attack and which persists as the causative agent.

The failure to appreciate the proper method for administering colchicine has been partially responsible for skepticism by some physicians and use by their patients. The apparent inevitability of gastrointestinal distress has contributed to the unpopularity

of colchicine. At the onset of nausea, vomiting or diarrhea, ingestion of colchicine is to be stopped and a gastric sedative ordered.

Phenylbutazone has been studied clinically and experimentally in the management of articular symptoms in the acute attack, and is an effective anti-inflammatory and analgesic drug. It is not specific for acute gout but valuable. A combination of phenylbutazone and colchicine has been very helpful in acute attacks. (1) If the patient has been on the colchicine-Probenecid prophylactic schedule for a relatively short period of time, the full effect of these agents will not have taken effect thus the acute attack continues to be a serious problem. In this situation, usually a less than a full course of colchicine is prescribed (2-3 mg.) together with 800 mg. of phenylbutazone during the initial 12 hours. This treatment may avoid the undesirable gastrointestinal distress and hasten rehabilitation. (2) An inadequately or poorly treated attack of gout that has not responded to a full course of colchicine may benefit from supplementary phenylbutazone. (3) Low-grade symptoms may persist for some unexplained reason after the full course of colchicine. Rather than give a second course of colchicine, from 400-600 mg. of phenylbutazone may be given for two or three days. It is very unwise to use phenylbutazone on a long term basis because of its possible toxicity.

Intravenous colchicine has a definite place among the anti-gout preparations. Intravenous colchicine should be used to complement, but not to supplement the oral dosage. There are some patients

with an irritable gastrointestinal tract who tolerate oral colchicine poorly and who profit from the intravenous preparation.

Adrenocorticotrophin and the adrenal steroids are of restricted value in the treatment of acute gouty arthritis, but adrenocorticotrophin has been found more effective in acute attacks of gout than the corticosteroids. Probably the most important use of adrenocorticotrophin is in the case of the patient whose acute distress fails to respond to a full course of colchicine.

Colcemide, which was introduced several years ago, has been effective in treating the acute symptoms although it has a few undesirable effects. Trimethylcolchicine, another colchicine derivative, is undergoing experimental trial. The use of codeine and other hypnotic drugs during the acute attack is not usually prescribed for gouty patients. Intravenous heparin has been credited with anti-gout properties. General measures for the treatment of the acute attack include a light diet, an abundance of fluids, and rest for the affected joints. No useful purpose is served if severely affected joints are kept active or subject to weight bearing so long as acute symptoms persist.

Surgical Treatment

The surgical treatment of advanced tophaceous gout has much value and may rehabilitate a partially incapacitated individual. When large subcutaneous tophi which have become unsightly, as well as smaller tophi of the hands and feet which interfere with the

wearing of gloves and shoes, surgery is recommended. Surgery has several advantages: (1) removal of large amounts of urate deposits to ease the load of the kidney, (2) minimization of the danger of necrosis of the skin and formation of ulcers when distention by tophi occur, (3) correction of deformity of fingers and toes, (4) stabilization of painful joints, particularly the weight-bearing joints, and (5) decompression of nerves which had been secondarily involved from pressure of adjacent tophi.

Most helpful in the medical handling of a gouty patient undergoing surgery is the preoperative administration of 1.5 mg. of colchicine daily, if the patient is not already on dosage of this magnitude in order to minimize the tendency for the development of postoperative gouty arthritis. Intravenous colchicine may be used in the postoperative period.

Summary

Gout has had a glorified history and has influenced many historical events through the ages. The therapy of gout has filled literature as well as the disease itself, and despite the present day medical knowledge the treatment and therapy have not advanced as other medical phenomena.

Gout is a metabolic disturbance which generally presents with the following clinical aspects: (1) mostly in men past 30 years of age, (2) most frequently in the great toe, but may occur elsewhere, around other small joints especially, (3) markedly painful, red and swollen, and (4) the joint may return to normal between attacks.

Laboratory findings show a serum uric acid elevation to as high as 25 mg. % (normal, 1 to 4 mg. %), while the urine uric acid is normal or only slightly elevated.

The pathology present in gouty arthritis is represented by the deposition of monosodium urate crystals in the bone in the immediate neighborhood of the affected joints. Urate crystal deposits, tophi, may also occur in cartilage of ears, tendons, bursae, muscles, heart valves, and subcutaneous tissues.

Radiographic changes are noted in only one third of gout cases. In these cases asymmetrical, periarticular swelling with small, punched-out, joint marginal defects are noted, especially in the first metatarsophalangeal joint. Occasionally these are infiltrated with calcium.

Although gout may not be a disease of major importance among the many arthridities, it has peculiarities and is intriguing to the investigator. Articular gout is relatively easy to diagnose especially in studying a group of gouty families. There still is lacking a complete knowledge on the mechanism of hyperuricemia or on the development of articular symptoms, and changes which follow a slight excess in body fluids. No one has discovered a cure for gout. Until such a time as more effective drugs are discovered or more effective means of correcting the disturbance of uric acid metabolism are devised, it is believed that colchicine and Probenecid should be the main drugs for the prophylactic period. These drugs provide periods of freedom from acute symptoms. Therapy for gout has been introduced, but no new ideas in the management appear to be in the near future.

Conclusion

Gout is one of the few chronic diseases in which the prognosis is very optimistic. Although the attacks are very painful, the majority of the time the patient has freedom from acute symptoms. The patient can usually enjoy a normal routine with very few limitations with adequate therapy. The physician has usually many clues to the diagnosis of gout, especially the hereditary factor.

FOOTNOTES

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