

one of the commonest manifestations of a general infection of the circulating medium with the gonococcus or its toxins. Other manifestations are endocarditis, myositis, disease of the tendons and fasciæ, and of the eye. According to Taylor, it is probable that septic absorption in urethritis does not take place until the infection has reached the posterior urethra. The gonococcus has been cultivated from the blood, first, I think, by Hewes in 1894, and later by Welch. Gonorrhœal arthritis, then, always implies infection of the circulating medium.

The joints show varying degrees of inflammatory change. There is first a simple synovitis with more or less fluid—serous or sero-fibrinous. Later the fluid may become purulent. The process tends strongly to extend to the fibrous and ligamentous structures about the joint, resulting in a periartthritis. Adjacent bursæ and tendon sheaths are very commonly involved.

Bacteriological studies, by the microscope and by cultures, give varying results. The gonococcus may be found alone or pus organisms may be found alone—the latter in cases with purulent exudation. The fluid may contain both gonococci and pyogenic microbes, or it may be sterile. It is probable that the gonococcus is always present at first and that there may be a simultaneous or, more often, subsequent infection with pus organisms. In the cases in which no organisms are found, it is probable that the gonococci have early disappeared. In some such cases the arthritis may not be due to gonorrhœa at all. Some cases may be due to the toxins of the disease, without any bacteria, like the joint affection following the use of diphtheria antitoxin. But probably in most cases the gonococcus is at some time present in or about the joint.

As a result of severe and protracted cases fibrous adhesions are prone to result. There may be almost complete fibrous ankylosis. This is especially apt to occur as a result of repeated attacks of arthritis from repeated reinfections of the urethra, or when the joint has been long immobilized. Changes resembling those of chronic rheumatoid arthritis may result. Nearly every joint in the body may be permanently damaged.

ETIOLOGY.—Enough has already been said in speaking of pathology to indicate the etiological relationship of the disease to the gonococcus. It is always a sequel of local infection with this organism—usually urethritis. It has also resulted from vulvo-vaginitis in children and from gonorrhœal infection in which no urethritis existed, as in ophthalmia neonatorum.

No age or sex is exempt, but it occurs most commonly in adult males—in other words it is commonest where gonorrhœa is commonest. Exposure to cold and trauma act only, if at all, by increasing susceptibility. Individual susceptibility varies greatly. Some men have it with every new gonorrhœa. Others, the majority, never have it at all. Persons subject to ordinary rheumatism or having the rheumatic diathesis do not show any special susceptibility.

DISTRIBUTION.—Arthritis occurs in about ten per cent. of all cases of gonorrhœa (Taylor). The commonest site is the knee, and next the ankle, wrist, fingers and toes. While it is commonest in the larger joints any joint may be involved—even the jaw, chondrocostal, intervertebral, sacro-iliac, sterno-clavicular, and crico-arytenoid. In about forty per cent. of the cases but one joint is involved. But it may be polyarticular, and in fact a single attack may involve nearly every joint in the body.

SYMPTOMS.—The disease may begin in almost any stage of gonorrhœa, most commonly about the fourth week. According to Taylor it seldom begins in acute gonorrhœa earlier than the second or third week, when the posterior urethra is involved. It may be delayed for months, till the urethritis has run on into a chronic gleet.

The onset is rapid—beginning with slight pain and stiffness. Premonitory fever and malaise are rarely present. As a rule general symptoms are mild throughout. Fever is slight in most cases. Rarely there is delirium or profound sepsis. Sweating is not a prominent feature. As the case goes on anæmia and debility are marked, espe-

cially when there have been unusual pain and confinement.

When the inflammation is at its height the appearance of the joint is quite characteristic. There is much swelling, due to fluid in the joint cavity and to edema of the surrounding soft parts. Owing to the tendency of adjacent bursæ and tendon sheaths to share in the inflammation the swelling often extends up and down the limb for a considerable distance. There is not often great redness and the tenderness is usually less than in ordinary acute rheumatism. So, where the distribution is such that locomotion is not prevented, many cases are treated as hospital out-patients. Pain varies greatly: it may be almost lacking, so that the patient complains mainly of stiffness, or so severe as to prevent sleep and require morphine.

The course of the disease is slow and tedious. Once involved, the joint usually remains so till the case is over—there is no marked tendency to jump about from joint to joint. A large joint seldom recovers in less than from four to six weeks. The acute process may subside and leave a hydro-artrosis lasting for months in spite of all treatment. In some cases complete resolution may never occur, the joint remaining more or less ankylosed.

In the so-called arthralgic form of gonorrhœal arthritis there occur, in the course of a gonorrhœa, fugitive pains in the joints and muscles, without any active inflammatory process. The symptoms may be very persistent.

When the joint becomes infected with virulent pus bacteria the case becomes like any purulent arthritis. Fortunately this is not common. If prompt surgical relief is not afforded, and there is a general infection, such a case shows the symptoms of pyæmia—chills, irregular fever, progressive asthenia, and death.

Relapses do not occur unless there is a new urethral infection. One attack does not confer immunity. Indeed, some individuals seem to have it nearly every time they get the clap.

COMPLICATIONS.—Bursitis and teno-synovitis are not uncommon. Involvement of the muscles, and of the fasciæ, especially of the palm and sole, sometimes occurs. The eye may be involved by means of organisms or toxins brought by the blood, a condition to be distinguished from the gonorrhœal conjunctivitis due to infection from without. Endocarditis and general infection with the gonococcus or with pus organisms is a very serious complication.

DIAGNOSIS.—Gonorrhœa is common, and so are other forms of arthritis. Therefore even when joint inflammation occurs in the course of a urethritis it does not follow that the disease is gonorrhœal arthritis. The diagnosis can be made with absolute certainty only when the gonococcus is recognized in the fluid from the joint cavity. The distinguishing clinical features of the affection are the tendency to involve one or a small number of joints; its persistent character, long duration, and failure to jump from joint to joint; the usually slight general disturbance, the fusiform character of the swelling from the tendency to invasion of tendon sheaths, and the association with other manifestations of gonorrhœal infection.

Ordinary acute articular rheumatism usually involves many joints, shifting about from one to the other, the first ones recovering as others become involved. There are more elevation of temperature and greater redness, pain, and tenderness than in the gonorrhœal disease, and the bursæ and tendon sheaths are not apt to be invaded. These characters, together with the effects of treatment, explain why it is rarely mistaken long for gonorrhœal arthritis, even when coincident with gonorrhœa.

Long-continued cases may give rise to a suspicion of tuberculosis, especially when the joint in question is the hip. Gout and simple or traumatic synovitis should also be mentioned. In purulent cases it is of little moment whether the disease is the result of gonorrhœa or not, as the course and treatment are identical.

PROGNOSIS.—Complete recovery is the rule. But the disease is an obstinate one and the treatment is not satisfactory. There is often danger of ankylosis, especially

when the condition is recurrent. The patient should be warned that a new gonorrhœa is likely to mean a new arthritis, and that each new arthritis is likely to leave the joint in a less perfect condition than before. When the inflammation is purulent and associated with endocarditis from mixed infection with the streptococcus the prognosis is of course unfavorable.

TREATMENT.—It is of the first importance to remedy, by measures adapted to the individual case, the primary gonorrhœal focus. According to Taylor especial attention should be given to the posterior urethra.

Salicylates and alkalies are of no value in gonorrhœal arthritis. Yet on the chances of an error in diagnosis the writer is of the opinion that in many cases a vigorous trial should be given them—on the principles laid down for ordinary acute rheumatism. Potassium iodide has been much used, but is probably devoid of any specific action. The same may be said of quinine and methylene blue. Probably iron, arsenic and other tonics, together with fresh air and plenty of good food, are the best general measures.

During the acute stage the patient should be kept in bed and the part at rest. If pain is severe it may be relieved by an ice-bag. Immobilization by splints or plaster usually gives great relief. But immobilization should be as brief as possible, owing to the danger of ankylosis. Later on, "baking" the joint in hot, dry air or counter-irritation by means of tincture of iodine, vigorous blistering, or the cautery may hasten resolution. If ankylosis threatens massage and passive motion are indicated after the acute process has subsided.

If the effusion persists the joint may be aspirated with or without the subsequent injection of corrosive sublimate solution 1 to 2,500, carbolic acid 1 to 50, or iodoform emulsion. This should of course be done under the most rigid antiseptic precautions. It may be repeated if necessary. It has given excellent results in competent hands. For suppurative cases prompt and vigorous surgical measures are demanded. *Ralph C. Larrabee.*

GORDON SPRINGS.—Lake County, California. These springs lie in Cobb's valley, about half-way between Calistoga and Lakeport. They are romantically situated in the heart of a mountain and forest region. The climate is very fine. The location is about 3,000 feet above the sea-level. The principal spring flows about 300 gallons of water hourly, having a temperature of 100° F. The waters are sparkling, alkaline, and have antacid and aperient properties. Following is Winslow Anderson's analysis:

| ONE UNITED STATES GALLON CONTAINS: | |
|------------------------------------|---------|
| Solids. | Grains. |
| Sodium chloride..... | 20.75 |
| Sodium carbonate..... | 3.19 |
| Sodium sulphate..... | 8.62 |
| Potassium carbonate..... | .73 |
| Magnesium carbonate..... | 6.14 |
| Magnesium sulphate..... | 10.93 |
| Calcium carbonate..... | 11.16 |
| Calcium sulphate..... | 23.46 |
| Alumina..... | 3.55 |
| Silica..... | 2.27 |
| Organic matter..... | Trace. |
| Total solids..... | 90.80 |
| Carbonic acid gas, large excess. | |

The waters have considerable reputation in chronic albuminuria and in cystitis; they are also valuable in acid dyspepsia. A pleasant resort has been established, and it is worthy of remark that persons suffering from chronic bronchitis, catarrh, asthma, and the early stages of consumption do well at this eyrie among the pines. *James K. Crook.*

GOSSYPIUM. See *Cotton*.

GOUDOU. See *Henpuye*.

GOUT.—The exact nature of gout is still unknown. One might with honesty begin a description of it as Sydenham did more than two hundred years ago: "Either

man will think that the nature of gout is wholly mysterious and incomprehensible or that a man like myself who has suffered from it thirty-four years must be of a slow and sluggish disposition not to have discovered something respecting the nature and treatment of a disease so peculiarly his own. Be this as it may, I will give a *bona fide* account of what I know. The difficulties and refinements relating to the disease itself and the methods of its cure, I will leave for time, the guide to truth, to clear up." Numerous hypotheses are described for the consideration of students of the subject, and our knowledge of the malady has greatly increased since Sydenham wrote, but its mystery has not yet been fathomed.

Gout has been recognized as a malady from the earliest times. It was well described by Hippocrates (350 B.C.). Five hundred years later Galen ascribed its origin to noxious substances as "black bile," "blood," or "phlegm" about the joints. He believed the tophi were produced by their consolidation.

In the middle ages, according to the prevailing theory, the disease was believed to originate from "tartar," which was supposed to come from wine that had been drunk and which formed incrustations about the joints, like those found in wine casks. This theory was disproved when Schule (1776) showed that tophi were composed of urates.

Gout has been thought contagious. This was the belief of Boerhaave. Cullen advocated a nervous origin for the malady. In 1848 Garrod's thesis on "The Blood and Urine in Gout, Rheumatism and Bright's Disease" established the existence of an excess of urate of sodium in the blood and ascribed to it a causative relationship to the malady. From that time to near the present a majority of pathologists and clinicians have regarded gout as due to an excess of uric acid in the blood, and they have described those prone to it in its typical or irregular forms as of the uric-acid diathesis.

As our clinical knowledge of gout is comparatively perfect, it seems best, therefore, to describe its symptoms first and to consider its nature, causation, prophylaxis, and treatment later. Cases of gout are clinically placed in three groups: (1) Acute gout; (2) chronic gout; (3) irregular gout.

ACUTE GOUT.—Premonitory symptoms are commonly observed. They are usually those of gastric indigestion, such as flatulence, sourness of the stomach, a feeling of fulness in the epigastrium and constipation, or irritability of temper, restlessness at night, dull headache, or melancholia. Twinges of pain in the small joints of the feet and toes are often felt for several days before the acute attack occurs.

Acute gout commonly makes its onset in the early morning hours, the patient awakening with intense pain in the metatarso-phalangeal joint of one big toe, oftenest the right. The pain is severe but becomes more intense during the next two or three nights. It is described as a sensation of squeezing. The feeling is as if the toe were in a vice. Throbbing, burning, and sometimes a lancinating pain, are also complained of. At first the veins about the affected part are unusually prominent. Soon, however, the joint swells uniformly and the skin becomes slightly red and glossy. It is exquisitely tender, so that even the weight of the bed-clothing is a source of increasing distress. The slightest motion of the joint also elicits a cry of anguish from the sufferer. Bodily temperature is increased, often only a little, sometimes to 102° or 103° F.

Often such attacks of podagra begin with a chill, or at least with chilly sensations and rise of temperature. After daybreak the pain subsides, fever lessens, and the patient may doze for a time. Although the intense pain is less, the swelling remains in the affected joint and it is kept immobile because of the pain which movements of it provoke. Toward night the symptoms again become more intense. So long as the attack lasts each night is made sleepless by an aggravation of the characteristic symptoms of the malady. Patients therefore become greatly wearied, even much debilitated by sleeplessness,

suffering, and inability to maintain good nutrition, for appetite is lacking and digestion is impaired. An attack such as this lasts for from one to several weeks. Gradually the symptoms grow less intense, the swelling of the joint subsides, mobility returns, and often after an attack a patient will feel unusually well. Sometimes during convalescence the skin over the joint which has been affected peels off.

Attacks are frequently prolonged by one great toe after the other being involved or by other joints than those of the toes being attacked. Although the large toes are commonly first involved, the fingers, and later the large joints, may be as well.

The urine is frequently concentrated and deposits urates. Traces of albumin or sugar are also sometimes found in it.

Acute gout is apt to occur in the late winter and early spring. It recurs at variable intervals; it may be annually or at longer or shorter periods. Usually after several attacks it begins to recur more and more frequently and the individual's health becomes permanently impaired. It is extremely rare that only one attack occurs in a lifetime.

CHRONIC GOUT.—Chronic gout results from several acute attacks. The joints which have been affected become permanently swollen or deformed by uratic deposits in the fibrous tissue about them, and are commonly stiffened and sometimes permanently immobile. Tophi, as these deposits of urate of sodium are called, are also found upon cartilages, on synovial membranes, and the sheaths of tendons. The cartilages of the ear are affected with especial frequency. Nodules are also formed along the course of tendons on the back of the hands and feet. Uratic deposits within joints where they first take place are invisible and do not always cause noticeable enlargement of them, but rarely last long before the neighboring ligaments are involved. Intracapsular deposits can sometimes be detected by a grating noise produced when the rough surfaces are moved upon one another. When joints are impaired in usefulness the muscles which control them atrophy. In severe cases the skin over the tophi becomes necrotic, sloughs, and exposes the "chalk stones," permitting them to crumble or to be easily removed. This, however, rarely happens until the lesions are so extensive that in spite of the partial removal of a source of stiffness and deformity a renewed usefulness of the joint is impossible. Patients, typifying the severest cases, are helpless invalids and constant sufferers. In mild cases there is some stiffness at all times but there is not complete helplessness. Frequent acute exacerbations increase the pain which these patients suffer. They are accompanied by the usual symptoms of acute gout, and frequently are complicated by uræmia, pleurisy, pericarditis, or other visceral lesions.

The digestive disorders which so often precede and accompany acute attacks are present more or less constantly in chronic cases. Flatulence, acid indigestion, constipation, and gastric discomfort are the commonest symptoms of them. They are associated with headache, neuralgia, lassitude, mental depression, and irritability. Eczema and urticaria are common skin complications. In chronic gout the kidneys are usually involved and gradually become contracted, producing the symptoms which are peculiar to interstitial nephritis. The arteries are also liable to atheromatous changes and the heart to hypertrophy and ultimate enfeeblement.

The digestive and nervous symptoms are aggravated by an inability to take exercise, due to the joint deformities. Pain causes sleeplessness and exhaustion. Indigestion contributes to malnutrition, and it is usual for those who have chronic gout slowly to lose flesh and strength.

In spite of this chronic state of disease, surprising as it may seem, life is often prolonged into the period of old age. Indeed, it is usual for the malady to last for many years. Patients commonly show remarkable mental vigor.

Occasionally in the midst of acute articular gout or

acute exacerbations of chronic gout, the acute arthritis suddenly disappears or greatly lessens, but is replaced by visceral complications. Such cases are often described as cases of retrocedent or suppressed gout. The visceral complications may be inflammations or other lesions of the bronchi, lungs, pleura, nasopharynx or larynx, of the stomach, intestines, heart, kidneys, brain, or peripheral nerves.

Epilepsy, delirium, and insanity are rarely a part of the disease. But neuralgias are common. Of these sciatica is the form most frequently observed. Gastralgia is also of frequent occurrence. It is associated with the usual indigestion of the affection. Of all the visceral complications of gout those of the circulatory system and kidneys are the most dangerous. Myocarditis is common. Endocarditis and pericarditis are of less frequent occurrence, but angina pectoris is often seen. Aortitis and aneurisms are other common circulatory affections. Functional irregularity of the heart and tachycardia are disturbances of frequent occurrence. Hypertrophy of the heart muscle is the rule in all chronic cases.

Interstitial nephritis develops sooner or later in those who suffer from chronic gout. It or uræmia growing out of it is a common cause of death. Indeed, fatalities rarely result from uncomplicated gout.

IRREGULAR GOUT.—Irregular gout is difficult to describe and often to recognize with certainty. Some of the viscera or the skin may develop lesions which the gouty are known to be prone to, and their sequence may make a diagnosis possible or their nature may be recognized by reasoning by exclusion. Irregular gout is very much commoner than classical gout. It frequently occurs in the women in families in which acute and chronic gout attacks the men.

In early life urticaria is common in those having a gouty diathesis, or the lithæmic state, and in late life chronic eczema is. Asthma, bronchitis, renal calculus, and diabetes mellitus are other maladies to which these same individuals are liable. Flatulent, acid indigestion and constipation associated with myalgias and neuralgias, with hemicrania or with mental depression or irritability are particularly significant of a tendency to the disease. Hot and itching feet at night and hot and itching eyeballs by day are common symptoms in women. Any of the various visceral lesions already mentioned may develop in those inclined to gout, although podagra or other articular evidence of the ailment may be wanting. Sooner or later the cardio-vascular and renal disorders incident to chronic gout develop in a majority of those who suffer long with irregular gout. Iritis, glaucoma, and hemorrhagic retinitis are common complications of the malady.

Urine.—Between attacks of acute gout the urine may be normal. During an acute attack it is concentrated and diminished in amount. On standing a pink or "brick-dust" sediment is thrown down. Although concentrated a diminished amount of uric acid is usually voided. When convalescence is established a moderate excess of this ingredient may be eliminated. In chronic gout the urine is commonly copious, of low specific gravity, and contains a diminished quantity of uric acid. However, not infrequently gouty men are found who habitually void normal quantities of uric acid. When interstitial nephritis exists the urine, besides being copious and of low specific gravity, contains small amounts of albumin and hyaline and fine granular casts.

Blood.—During acute attacks and while the disease is chronic an excess of urates can be demonstrated in the blood. But in the early stages of the disease, during the intervals between attacks, the blood is quite normal. Uric acid can be demonstrated in the serum of those who have gout by adding ten or twelve drops of acetic acid to a few cubic centimetres of blood or of serum obtained from a blister produced upon the skin. A thread must be immersed in this mixture of serum and acid for twenty-four or forty-eight hours, when it will be found to be covered with crystals of uric acid.

DIAGNOSIS.—A diagnosis of acute gout can usually be

made with ease, so distinct and characteristic are the symptoms. However, I have known a first attack to be mistaken for a trauma. But the development of symptoms characteristic of the course of the malady will correct such an error. It is rarely confused with acute articular rheumatism. In this last disease the large joints or numerous joints are involved from the beginning, the temperature is usually higher, and the skin is bathed with perspiration.

The presence of tophi makes it possible to distinguish chronic gout from chronic rheumatism and other forms of chronic arthritis. The history of numerous acute attacks is also a help to a diagnosis.

Irregular gout is more difficult to recognize, but attention to the symptoms described above and to their interchangeability in different attacks in the same person and connection, commonly with characteristic digestive disturbances, makes a diagnosis possible.

ANATOMICAL CHANGES.—The evidences of inflammation in the tissues involved are not different from those of other forms of inflammation, except that deposits of urates are observed with them. At first these deposits occur in the articular cartilages. They are seen as white dots or lines beneath the surface. Later they increase in size, coalesce, and produce destruction of the surface. The cartilages and capsules of joints, the fibrous tissue in bursæ, tendons, the periosteum, and the auricles are the structures in which tophi are oftenest found. The aorta is frequently thickened in spots by uratic deposits, as are sometimes the coronary arteries. An increase of fibrous tissue in the myocardium is also occasionally observable. The kidneys are commonly contracted and exhibit the conditions peculiar to interstitial nephritis. Lines of urates can be seen in many cases, both in the cortex and medullary portions of these organs. These deposits occur in parallel lines, partly in the uriniferous tubules, but mainly in the interstitial tissue between them. The liver is sometimes found in a condition of slight interstitial hyperplasia.

Theories as to Nature.—Although a clinical knowledge of gout has been possessed by physicians since the earliest times, its exact nature and cause are to-day unknown. A variety of hypothetical explanations have been offered, but none of them has as yet been established as correct. Garrod's theory has for many years been accepted by the majority of the profession. According to him, gout is due to an excess of urates in the blood and fluids of the body, from which they are deposited in certain tissues because of a diminished alkalinity of them. The excess of urates, it has been supposed, is due in part to excessive production because of disturbed metabolism, and in part to imperfect elimination. That the renal epithelium has a power of selecting certain substances for elimination is a demonstrated fact, and it has been supposed by some that in gout it refuses to excrete uric acid in the normal or necessary amounts. Ebstein modified the theory of Garrod by advocating that an excess of uric acid was produced in muscles and bones because of a peculiar local metabolic anomaly which is usually inherited. The deposit of urates in cartilage and fibrous tissue he accounted for because of the naturally slow circulation of blood through them, which, when it contains an excess of uric acid, causes a cellular necrosis in those tissues. The necrosis always produces a local acidity, and the alkaline urates of the blood are then precipitated as comparatively insoluble acid urates.

The uric-acid theory has also been modified by the hypothetical explanation that uric acid is an intermediate product in the transformation of waste nitrogenous matter into urea, a transformation made in the liver, and that an excess of uric acid in the blood results from such a derangement of hepatic functions as causes the formation of a lessened amount of urea and a proportionately larger amount of uric acid. The observed coincidence of gout and digestive disturbances has given color to this theory. Of late, however, physiologists have become convinced that uric acid is not an intermediate step in the formation of urea from proteid. Indeed very recent researches

(Kossel, Horbaczewski) have led physiological chemists to believe that uric acid is derived from nucleins and not from other parts of cells.

Unfortunately for all these uric-acid theories gout cannot be produced experimentally by injecting uric acid into the blood or by preventing its elimination through the kidneys. Nor do the phenomena of the disease arise in other ailments, notably leukaemia, in which uric acid often exists in the blood in quite as large quantities as in gout. Experiment affords us no evidence that toxic properties are possessed by uric acid even when it is introduced into the blood in much larger amounts than have ever been found in gout itself.

Another theory which has not in the last fifty years had so many supporters as the uric-acid hypothesis or so many as at the end of the eighteenth century, but which nevertheless at all times has had influential advocates, is the theory of its nervous origin. According to it, gout is due to a disturbed metabolism, a fault of the system in which the chemical balance is deranged. The metabolic processes are presumed to be under the control of the nervous system, therefore such a perversion of them as occurs in gout primarily must be due to a disturbance of nerve centres. Just what change takes place in the central nervous system is not conjectured. Those who believe in a nervous origin of gout base their faith chiefly upon the following points: (1) Its frequent inheritance. (2) The effect of psychic disturbances, such as anger or mental depression, in provoking its attacks. (3) A tendency to neuralgia and myalgia in such patients. (4) Influence of barometric changes. (5) Joint involvement, which is common to many nervous diseases. (6) Many neurotic manifestations observed in other members of the family in which gout appears.

In 1884 Gaucher discovered that the injection of xanthin and hypoxanthin into healthy animals caused changes in the structure of the kidneys, similar to those of interstitial nephritis. More recently others have confirmed these observations and found that the xanthin bases will produce various nervous phenomena as well as high arterial tension and ultimately arteriosclerosis.

Horbaczewski, who in 1891 showed that uric acid is probably derived from nuclein, has also gathered evidence to show that xanthin and hypoxanthin or the alloxuric bases are to blame for the phenomena of irregular gout or lithæmia rather than the urates. It is true that uric acid in the form of biurate of sodium constitutes the tophi of gout and produces local deformities and sometimes inflammation, but in the form of a soluble, alkaline, quadriurate in which it exists in the blood it is not toxic.

Although gout has been supposed by some to be an infectious disease, there is no adequate evidence that such is the case.

Causative Conditions.—It is quite evident from this brief review of the leading hypotheses advanced to explain the causation of gout that we are to-day about as ignorant as our predecessors a century or two ago were. What knowledge we possess to-day is negative, that is, disproves theories that have been widely held. Nevertheless, much is known of the conditions under which gout is likely to arise. Heredity plays a large part in its production. According to Garrod seventy-five per cent. of all cases inherit the disease. Oftentimes the habits of families which their inherited environment produces also predispose them to it. But gout may be acquired as well as inherited. Acute and chronic gout are rarely seen in this country, but irregular gout is common and is increasing. Gout occurs oftenest in England, next in frequency in France and Holland, less in Germany and rarely elsewhere in Europe. Symptoms of it have been observed at all periods of life, but its onset occurs in much the largest proportion of cases between the thirtieth and fortieth years. Initial symptoms are extremely rare in infancy, childhood, and old age. Women are attacked less frequently than men, at least with the symptoms of podagra and chronic gout. Insufficient exercise, and what amounts to the same thing, a deficient supply of oxygen, are important factors in creating a

disposition to the ailment. A sedentary life causes the inhalation of relatively a small amount of oxygen. Shallow breathing, which is cultivated under the circumstances, lessens the vigor of the lymphatic and venous currents which carry off waste matters from the viscera, and causes a torpidity of liver and digestive organs. Lack of exercise also causes the same interference with vigorous metabolism in the voluntary muscles. When people live or work in overcrowded rooms they are sure to feel the need of oxygen. Virchow has laid stress upon the frequent production of tophi in the joints of the poor who live under these conditions. Since the earliest times it has been admitted that eating unduly large quantities of food will produce the ailment in many persons. Especially is this true of the use of large quantities of meats rich in extractives, or cooked with rich gravies and sauces. Although oftenest too much food, that which is too rich, and too little exercise together cause gout, rare cases have been observed in which an acute attack was provoked in those disposed to it by too little food and too much exercise. In these latter patients a lowering of vitality by underfeeding and overworking excited the ailment. The habitual use of fermented liquors is a most common and universally recognized cause of gout. It is difficult to explain the mode of action of these liquors. It is not merely the alcohol which they contain, for the users of distilled liquors are much less prone to the disease than are the users of fermented beverages. Nor is it an acid, nor sugar, nor, as far as we know, any one ingredient in beers and wines which makes the drinkers of them so liable to develop gout. Often a few glasses of wine will awaken symptoms of the malady in those who are susceptible to it. It may be that the disturbances of digestion which overeating and the use of fermented liquors cause are more to blame than individual articles of food or beverages. Mental depression such as grief and anxiety or prolonged mental exertion are also frequent predisposing causes. They may help to produce their ill effects by making digestion slow and disturbing the functional power of the organs which play a part in it. It is well known that lead workers are especially liable to symptoms of gout as well as to arteriosclerosis and interstitial nephritis.

Many of these conditions which predispose to the disease act together, that is, simultaneously upon individuals. Many of them are also the exciting causes of acute outbreaks of the ailment. Exposure to cold, great fatigue, anything which lowers the vitality for the moment may be an exciting cause for those who are susceptible.

PROPHYLAXIS.—A knowledge of the conditions which dispose the gouty to attacks affords us a key to its prophylactic treatment. Good hygienic surroundings, daily sufficient exercise (often large amounts are required), moderate eating, and freedom from undue anxiety, worry or mental labor, are the best prophylactic measures.

TREATMENT.—Little can be done to shorten acute attacks of gout, but the pain attending them may be lessened by suitable treatment, and a great deal can be done to prevent a recurrence of acute attacks by instituting a proper regimen.

It is impossible to remove the inherited fault of nutrition, but it is possible to retard the development of symptoms. Temperance must be taught as the cardinal rule of life, abstemiousness in eating, drinking, the enjoyments of the pleasures of life, or the inclination for mental work. Overeating, even the most moderate kind, must be avoided. A varied diet may be permitted, provided it includes foods which are simply prepared and easily digested, and provided they are eaten in moderate quantities.

When gout is fairly established, not only must temperance be insisted upon, but certain articles of diet must be forbidden. These are sweets, confections of all kinds, fats, articles cooked with much fat, game, and the richer meats, especially when dressed with rich sauces. Vegetables, rich in oxalates, ought also to be avoided by the gouty.

These patients should eat fairly varied foods and the diet should be well balanced, containing a normal proportion of albumin, carbohydrates, and fats; and the individual articles of food should be so prepared as to be most easily digested. Meat may be eaten moderately, but green vegetables, certain fats, and cereals, may be taken generously. The diet for those who are gouty must not be so restricted as to lessen their vitality. A milk diet has been urged as the best for the prevention of outbreaks of gout in those disposed to them; but milk, unless used in excessively large quantities, is not sufficiently nutritious; and while it may well be used as an important element of food it should not be the only article taken by the gouty.

Soups should be forbidden when the symptoms of goutiness are clearly manifested, but they may be taken in small amounts by those inclined to this ailment. Whenever they are used, they should be entirely free from fats, and preferably should not be made with a meat stock. Eggs, oysters, and clams may also be eaten, but lobsters, crabs, and shrimps are not to be recommended. Most fish can be eaten without harm, especially such as bluefish, whitefish, perch, shad, bass, and trout; but fish richer in fats and those that are smoked and salted, such as salmon, mackerel, halibut, and cod, are not so wholesome. Rich sauces should always be avoided. Meat should be eaten not oftener than once daily, and generally roasted or broiled. Those which are most to be avoided are pork, veal, game, and salted or smoked meats. Fat should be used in very moderate amounts except butter which can be used with a reasonable degree of freedom, and cream in moderation. Such carbohydrate foods as bread, rice, sago, tapioca, oatmeal, and cracked wheat may be eaten generously, but pastries, hot breads, pancakes, and other articles of a similar kind, which are liable to form doughy masses in the stomach during the period of gastric digestion, should be avoided.

Sugar is not wholesome for the gouty. Such vegetables as rhubarb, tomatoes, radishes, spinach, cabbage, and, if they cause flatulence, baked beans, should be avoided.

The following green vegetables may be used freely: peas, stringbeans, corn, potatoes, turnips, carrots, parsnips, celery and celery plant, cauliflower, artichokes, broccoli, salads, cucumbers, and egg plant. Of the fruits, the following are best adapted for the use of these patients: pears, apples, raspberries, blueberries, blackberries, and oranges; but grapes, bananas, prunes, strawberries, and melons are not so wholesome. Pickles and condiments are to be avoided at all times.

Eating between meals should not be permitted. Gouty patients should be taught to eat slowly and to masticate their food carefully.

Especially should those inclined to gout avoid eating a large variety of food at one meal. Simplicity in diet as well as temperance in eating must be taught them. The variety which we all crave should be furnished by changes in food from meal to meal and from day to day.

Although by clinicians generally red meats are forbidden those who have chronic gout, cases have been successfully treated upon an almost exclusive meat diet. Salisbury steak, a little lettuce or spinach, and stale bread, varied occasionally by chicken, squab, eggs and fish, have constituted the entire list of foods of these patients. The uniformity of the food and the ease of its digestion have prevented abnormal fermentations in the gastro-intestinal tract just as an exclusive milk diet will do. This is the secret of success in such cases.

In the midst of acute attacks it is best to administer little of any kind of food. Milk is the best staple article and may be the only one. Gruels and eggs may also be eaten, and oranges and lemons may usually be permitted.

Tea and coffee in small amounts and with no, or very little, sugar, may be used by those who are predisposed to gout, provided they have no acute symptoms of the disease or of indigestion; but if digestion is slow, or there are other symptoms of gout or goutiness, these beverages should be forbidden.

It is universally admitted that alcoholic beverages of all kinds are harmful. Even in very small amounts they will, not infrequently, provoke attacks of gout. The degree of tolerance of alcoholic beverages by those who are gouty is, of course, very variable. It is not necessary, in order to provoke gout, that these beverages should be taken to the point of intoxication. Indeed the habitual drunkard rarely develops symptoms of the disease, but it occurs most frequently in those who are habitual users of alcoholic beverages in moderate amounts. Ale, beer, and the sweet and the heavy wines are the beverages which are most apt to provoke the trouble. Of wines, the dry white wines and old Bordeaux have been found the least harmful. Although individuals vary in their susceptibility to the ill effects of alcoholic beverages, and although the different beverages vary in their potency to do harm, they should all be forbidden the gouty.

Patients who are gouty should drink water copiously in order that the kidneys may be made to act freely and that the waste matter may thus be washed out of the system. From five to eight glasses of good pure water should be drunk daily.

Many spring waters have been recommended as preventives of gout. It is probable that large quantities of water do more good by the physical presence of fluid in the blood-vessels and tissues than the various mineral ingredients which spring water may from time to time contain. There are three varieties of spring waters especially recommended for gout: First, those which are particularly pure and contain a minimum amount of mineral matter. Without doubt, their effect is a physical one. Second, the alkaline waters of which Vichy is a type. Alkalies well diluted, introduced into the blood, do seem to stimulate normal nutritive changes in the tissues of the body. The alkaline waters also have a beneficial effect upon the contents of the stomach, which are usually acid because of abnormal fermentation. Third, spring waters which contain iron, arsenic, and lithium. They are useful, especially the arsenical waters, for those gouty persons who have affections of the skin and bronchial mucous membranes. Many of the cases of gouty dyspepsia are helped by these waters. Royat, in France, may be regarded as a type of this group of mineral waters.

Spring waters rich in sodium salts are not beneficial for the gouty, as these salts in unusual quantities in the blood hasten the precipitation of insoluble urates in joints or other tissues.

Hot mineral springs are resorted to by many who have chronic gout, for the purpose of bathing. Acute attacks are not benefited, but partially immobile joints with muscular atrophy are benefited. If patients have high arterial tension or hypertrophied hearts hot baths must be avoided.

Exercise is essential in order to prevent gout and to avert repeated attacks in those who are prone to it. The amount of exercise required must be determined by each person. As a rule it must insure several hours of outdoor life each day and for at least a few minutes daily must be violent enough to provoke sweating. When repeated attacks have stiffened the joints and enfeebled patients, it must be more gentle. Walking, bicycling, horseback-riding are the best. These more gentle means of exercise can often be supplemented with benefit by daily or frequent massage. Of sports golf, which insures mild exercise for several hours out-of-doors, is the best. The more violent games are rarely adapted to the gouty who are in middle life or have passed it.

Sufficient exercise should be taken daily, for the results thus obtained cannot be stored up at one time for future use.

In acute attacks physicians still resort, as Cullen recommended them to do, "to patience and flannels." Abortive treatment cannot be recommended. It has been attempted by strapping tightly the affected joint, applying ice to it, administering large doses of colchicum and sometimes morphine. Attacks have undoubtedly been

stopped short in this way, but very dangerous symptoms have also followed the treatment, such as fainting and disorders of the heart. Most frequently soothing applications are made to the diseased joint, such as chloroform liniment or menthol (8 gm.) in camphorated soap liniment (120 c.c.), or in an oil composed of Guaiacol 25 c.c., Ol. gautheriae, 25 c.c., and Ol. olivæ, 50 c.c. Pomades with cacao butter and olive oil as bases are often used. To them may be added morphine, cocaine, belladonna, menthol, guaiacol, and other local anæsthetics and analgesics.

After each local application has been made the affected foot or joint is wrapped thickly in flannel to protect it from cold and to promote local sweating. Rendu ("Traité de Therapeutique Appliquée," 1895, Paris) advises wet bandages which are gradually made colder until the diseased part is accustomed to ice-cold applications. The cold benumbs the sensibility, lessens pains and swelling, and shortens the duration of the malady. Like the so-called abortive treatment it must be used with care.

Blood-letting and blisters are no longer used in gout, but purgatives are. Calomel and jalap constitute a favorite prescription of English physicians. Certainly at the onset of an attack it is important to empty the gastro-intestinal tract. A full dose of calomel followed in a few hours by a saline (the liquid citrate of magnesia is particularly eligible) does much good. At the same time the patient should abstain from food for from twenty-four to forty-eight hours but should drink water freely. When food is administered, and this should not be until copious bowel movements have insured the emptiness of the intestines, milk should be given.

Of medicine colchicum is chiefly relied upon to relieve the acute symptoms. Twenty to twenty-five minims of the wine of colchicum root may be given three or four times daily. Instead of this preparation the tincture of the seeds of colchicum may be used. As soon as the sedative effects of the drug are obtained it should be given in smaller quantities and often can be discontinued. If used too long it will provoke nausea and excessive diarrhoea. Indeed, a peculiar susceptibility to these effects of the drug makes its employment impossible in certain cases. Colchicum probably produces its good results by its sedative action upon the nervous and cardio-vascular systems and by helping elimination by its purgative properties.

Next to colchicum the salicylates are found useful. The salicylate of sodium is most used, but by some physicians the salicylate of lithium is preferred. A combination of the salicylate of sodium and bromide of lithium has proved useful to my patients. The salicylates are less certain in their effect than colchicum, but especially useful after colchicum is discontinued and in prolonged subacute attacks.

Alkalies are also used commonly. The best are the potassium and lithium salts. They are usually combined with colchicum or the salicylates. Originally they were given to hasten the elimination of uric acid by making soluble salts of it. Numerous other drugs in recent years have been tried for the same purpose, such as piperazin, lycetol, and lysidin. The doubt which prevails to-day in the minds of pathologists in regard to the pathogenic properties of uric acid makes their employment theoretically less urgent. Lithium has been shown to be useless so far as increasing the solubility of urates in the blood is concerned, for when administered by the mouth it forms insoluble compounds in the stomach and does not unite with the uric acid. However, I am convinced that lithium salts are beneficial in the indigestion of the gouty, probably because they unite with constituents of the contents of the stomach, lessen their acidity and toxicity.

Guaiac is another remedy which is often employed in gout with benefit. Its mode of action cannot be satisfactorily explained. It proves most useful in subacute or mild acute cases.

Chronic gout must be treated hygienically for the most part and acute exacerbations must be treated as acute gout is. The salicylates and alkalies are especially use-

ful in these cases. Piperazin and similar drugs have been much used of late years to dissolve tophi. The clinical results of their employment as they are described in periodical literature are conflicting. It and lysidin are also credited with the relief of pain. Massage can be employed in chronic gout, and often after acute attacks, with benefit. It must, however, be applied with gentleness. It helps to reduce swelling, to make the joints more supple, and to strengthen the unused muscles. When joints are permanently deformed it is necessary by massage, electricity, and hydrotherapy to keep the atrophying muscles strong, in order that as much usefulness as possible may be preserved to the diseased part.

Little can be done to remove uratic deposits. Most attempts by local treatment are found to be more harmful than useful. Surgical interference is not to be recommended unless suppuration occurs near them (and it is a rare complication, not a part of the disease) or sloughing of the skin over them takes place; then the pus should be evacuated and any exposed urates scraped out and the wound treated as any other sluggish and infected wound would be.

A residence in a mild genial climate where an outdoor life can be had continuously is of great advantage in checking the progress of this ailment.

Often diet must be still further modified because of arteriosclerosis or contracted kidney and albuminuria. It must then be made even simpler. Red meats should not be used or, if at all, rarely. Indigestion and constipation must be carefully corrected or guarded against. Great pains must be taken to prevent fermentation in the gastrointestinal tract.

The iodides are frequently needed to lessen arterial tension. They may have to be given for weeks at a time. Potassium iodide is chiefly used, but Bouchard and Dyce Duckworth recommend the iodide of lithium. Nitroglycerin is sometimes needed for its temporary but more pronounced effects upon the arteries.

In irregular gout chief reliance must be placed upon hygienic treatment. Various symptoms of the malady may for a time need medical treatment addressed to meet them. For instance, in the eczema of the gouty local applications are of benefit; but an abstemious, carefully regulated diet, the copious drinking of water, the maintenance of good elimination by the bowels, kidneys, and skin, and suitable exercise, are essential to success.

For the headaches and neuralgias much can be done with the compounds of salicylic acid, phenacetin, anti-febrin, and similar drugs, but the relief is imperfect or transitory unless a suitable regimen is prescribed and maintained. Hemiplegia can frequently be averted, when the temporal arteries begin to be tense and twinges of pain give warning of an attack, by a full dose of citrate of magnesia.

Often such patients must change their business in order to obtain permanent relief, thereby avoiding the anxiety and confinement which a commercial or professional life necessitates. *N. S. Davis, Jr.*

GOWERS' TOXIC PARAPLEGIA. See *Spinal Cord Diseases: Combined Scleroses.*

GRAMINEÆ.—(The Grass Family.) This is doubtless, all things considered, the most important family of plants. The bamboos contribute most important building and structural material in the tropics, as well as considerable fibre material, which latter is also contributed by many other grasses. The uses of straw in this connection are too well known to require description. The grasses contribute by far the most important stock fodders, while the cereals constitute the most important part of human food and the principal source of alcoholic beverages and of alcohol itself. The sugar-cane, as well as sorghum, is a grass. An important fixed oil is obtained from Indian corn, which is also the chief source of glucose, and the importance of the starch yielded by it, as well as of those obtained from wheat, rye, rice, and barley, is apparent. Several important volatile oils are yielded by species

of *Andropogon*. With one or two unimportant exceptions, poisonous properties are unknown in the family. Very few of the species are of distinct medicinal use, though *Triticum* is official, and ergot proceeds indirectly from rye. *Henry H. Rusby.*

GRANATUM. See *Pomegranate.*

GRAND HAVEN MINERAL SPRING.—Ottawa County, Michigan.

POST-OFFICE.—Grand Haven. This is the terminal station, on Lake Michigan, of the Detroit, Grand Haven and Milwaukee Railroad. It can also be reached from Chicago by lake steamer. The location is a cool and pleasant place in summer, and excellent opportunities are afforded for surf bathing in the lake. According to an analysis by C. G. Wheeler, the water is composed as follows:

ONE UNITED STATES GALLON CONTAINS:

| Solids. | Grains. |
|--------------------------|---------|
| Sodium carbonate..... | 2.69 |
| Potassium carbonate..... | 2.74 |
| Calcium carbonate..... | 2.01 |
| Magnesium carbonate..... | 1.52 |
| Iron carbonate..... | .08 |
| Sodium sulphate..... | 71.29 |
| Sodium chloride..... | 306.03 |
| Potassium chloride..... | 1.93 |
| Calcium chloride..... | 148.05 |
| Magnesium chloride..... | 71.53 |
| Magnesium iodide..... | .05 |
| Magnesium bromide..... | .17 |
| Calcium fluoride..... | .45 |
| Alumina..... | .30 |
| Silica..... | 1.05 |
| Total..... | 608.89 |

This water contains sufficient sulphate of sodium to give it great efficacy in cases of engorgement of the liver, abdominal plethora, and dyspepsia associated with these conditions. *James K. Crook.*

GRANULATION TISSUE.—**DEFINITION.**—In crushing injuries, wounds involving the loss of considerable tissue, neglected wounds or those infected with pathogenic bacteria, or in wounds in which close coaptation by sutures is impossible, the healing process takes place by secondary intention, or, it is said, healing occurs by granulation. The origin of the latter expression is traceable to the appearance in such injured parts of minute pink or rosy elevations, the granulations; such surfaces are said to be granulating and the tissue forming the tiny nodules, as well as that below and about them, is granulation tissue. Granulations are peculiarly limited to exposed situations; similar processes of healing upon other surfaces, such as the intestinal canal and serous membranes, are very rarely if ever marked by elevations comparable to the granulations of healing wounds. This term consequently had its birth in the outward objective features of healing injuries of various sorts as well as locations. Granulations are described, in the older works of surgery and pathology, as arising from the sectioned ends of bones, in abscesses undergoing "self-purification," chronic ulcers, fistulous openings, etc. The essential requisite seems to have been that they should occur either where they would be plainly visible or easily demonstrable or in such hidden locations where previous experience had proven their development. Necessarily this conception of granulation tissue was from the clinical viewpoint almost exclusively.

With the fuller knowledge of the process of inflammation, and especially of the regenerative changes connected with resolution, the designation granulation tissue has invaded topics of a more general character than those connected simply with surgical pathology. This tendency is, without doubt, due to the selection, by writers, of wound healing by secondary intention, as the type of regeneration or resolution in the inflammatory process; and because the cellular changes in resolution have more or less in common, no matter what the location is. The

term granulation tissue has, therefore, by degrees acquired the significance of embryonal tissue. From this pathological conception, the chronic processes of inflammation, tuberculosis, syphilis, actinomycosis, leprosy, etc., in which proliferative changes predominate, acquired the group-name granulomata. There may be no granulations in the surgical sense in a gumma or actinomycotic growth, yet they are commonly described as made up of granulation tissue. The analogy between the granulation tissue of a healing wound and a deeply seated chronic inflammation such as a gumma of the liver or testicle, is a histologic one; the former possesses perceptible granulations, the latter a structure similar to such delicate and sometimes barely visible excrescences. Granulations do not, as a rule, develop in the granulomata, but they are obvious characteristics of all sorts of wounds.

That consideration of granulation tissue which maintains its parity to embryonal tissue and its inflammatory origin belongs to the general subject of inflammation (see *Inflammation*), whereas the following description deals solely with granulation tissue as it is met with clinically, with the structures that gained the name primarily.

HEALTHY GRANULATIONS.—The surface of open wounds after a few hours becomes covered over with a delicate pellucid, gray or whitish layer which slowly becomes thicker and finally resembles the buffy coat. Its formation takes place after the cessation of hemorrhage, although some clear or slightly blood-tinged fluid may ooze from spots on its surface or from the edges for some time. Exposure to the drying influences of the air causes this exudate to change into a compact, rather brittle crust that effectually protects the underlying tissue; it is often some shade of brown from the admixture of blood. The protection of wounds by dressings may lessen the formation of a crust and the fibrinous coating may remain thin and translucent. For a number of days there may be no change in the appearance of such defensive vestures. After a variable length of time, depending upon the anatomical location, the variety of tissue, the individual's age, and other factors, granulations arise. It is usually a number of days, from four to ten, before they attain macroscopic proportions.

When it was regarded as good surgical treatment to approximate the edges of the flaps with strips of adhesive, after amputation of an extremity, it was observed that granulations appeared earliest on the vascular soft parts and sooner on the sectioned cancellous than compact bone. If, after a certain period of repose, the dried blood clot of the exposed wound or the dressing of the more carefully protected wound be removed, minute pink points will be visible upon the paler tissue around. They mark the site of future granulations, whose development is easily followed by examination at intervals. The pink spots deepen in hue and others appear; they enlarge to blotches that have a bright ruddy aspect, and become elevated as small globular tuberosities. In *sensu strictu*, this is granulation tissue.

These small eminences vary in size and give the surface a decided granular appearance; they level the smaller irregularities of rough and lacerated injuries. The tissue that forms them is common to all chronic inflammations; it is embryonal tissue in process of cicatrix production. The elevations containing loops of newly proliferated blood-vessels have been explained by Hamilton upon the basis of lessened pressure; in this manner he would account for their absence in deeply seated morbid conditions. It is doubtful if altered conditions of pressure are the only agencies influencing their development.

Perfectly healthy granulations may vary in height and form, they may possess flat or rounded tops and a uniformity or irregularity in size may be observed. Double or compound granulations are described. Their consistency varies within narrow limits; possessed of broad bases these warty growths give the impression of firmly interwoven tissue with soft but not fluid contents. On removal of the covering exudate by gentle washing, a clean, moist or glazed surface, translucent and devoid of

visible vessels is exposed. Although there is no distinctive color to healthy granulations, the more livid hues bespeak poor circulatory conditions. A faint pellicle with bluish zones that merge into the white of the adjacent skin marks the healing margins from which epithelization has already begun. Healthy granulations are extremely sensitive if they arise in tissues well supplied with nerves; others from such structures as compact bone and tendons have no sensibility. When situated on a flat surface they seldom rise much above the level of the adjacent skin. The cells composing granulation tissue are those peculiar to chronic inflammation; how-



Fig. 2347.—Injected Blood-Vessels in the Granulation Tissue from an Experimental Injury of the Tongue of a Dog. The arteries have a greater tortuosity. Six days after injury. (Modified from Thoma.)

ever, in the average granulating wound there are probably a greater variety than in the usual deeply seated chronic inflammation. Our knowledge of the histology and histogenesis of the healing process is in the main derived from experimental work upon animals, nevertheless it is generally accepted that healthy human granulations may contain all varieties of leucocytes and all forms of fibre-producing cells; also red blood corpuscles, phagocytes, giant cells, budding blood-vessels, fibrin, bacteria, and an intercellular substance of altered fluid from the blood and lymph vessels.

PATHOLOGICAL GRANULATIONS.—The extent to which, in a specific example, the exudative and retrogressive or degenerative changes exceed those of proliferation, depends upon many factors; chief among these are the stage of healing and the initial cause. It has long been recognized by surgeons that variations may occur in the general mode of healing, deviations from the normal that permit the use of such a pleonastic expression as pathological granulations. The luxuriant or exuberant granulations have been known by the laity immemorably as "proud flesh" and as altogether undesirable in a healing wound. The torpid or languid granulations and the spongy or fungous forms may so delay healing that there is an easy transition from granulation tissue to ulcers. Ulcers consist of granulation tissue when the macroscopic evidences of proliferation attain the degree of distinct granulations; other ulcers, the seat of extensive necrosis and exudation, may not possess any proliferating tissue; such ulcers are not granulating. Over forty years ago Paget made the statement that "all the varieties in the aspect of granulating wounds and sores, which the practised eye can recognize as signs of deflection from the right way to healing, are so many instances of different diseases of the granulation substance, diseases not enough investigated, though of much interest in the study of both the healing process and the organization of new products in inflammation."

This complaint finds an echo in the claim made by Reinbach, who, in an article recently published, states

that he was unable to find in the literature at his command a single instance of researches of this character, and he adds that Ziegler also knew of none. Reinbach prefers to abandon the older nomenclature comprising such terms as fungous, spongy, erythemic, croupous, etc., for the general term pathological granulations.

Of these he recognizes two forms with several subordinate types: (1) The luxuriant superficial granulation,



Fig. 2348.—Organizing Granulation Tissue. The left edge represents the deeper part. The round cells are both mono- and polymorphonuclear leucocytes. There are many spindle-shaped fibroblasts. (Modified from Ribbert.)

that is usually "self-purifying" and characteristic of acute processes, and (2) the superficial chronic granulation. The strictly torpid granulations he classifies with ulcers on account of the absence of formative tissue. As for the first form they are marked by the histologic features that belong to the process of suppuration (see *Inflammation*). Quantities of bacteria occur—generally cocci that show no special arrangement—and at different levels the changes indicative of miliary or microscopic abscesses. Leucocytes swarm within such granulations, and among them eosinophiles and mononuclear leucocytes are numerous. The capillary loops of the outer zones suffer some necrosis. In spite of the exudative and destructive changes karyokinetic figures are numerous in the deeper portions in fibroblasts and endothelial cells, and the fibroblasts produce fibres and become connected in the usual way.

As examples of superficial chronic granulations, Reinbach mentions both the torpid granulations, which, however, show some signs of growth, and those covered with mottled and white patches caused by necrosis of the outermost parts. The first of these subdivisions, although very slow to heal, nevertheless contain vertical bands of fibre-forming cells. They often follow burns and constitute virtually lesions intermediate between granulation tissue and real ulcers. The second variety, covered by a fibrinous exudate in spots and by necrotic tissue, was described by Billroth as "croup of the granulations." Surgeons on meeting with these hindrances to the normal course of healing are inclined to suspect wound diphtheria, *i.e.*, a true infection with the bacillus of diphtheria. However, such areas of necrosis superficially located upon otherwise healthy granulations may be caused by other non-pyogenic bacteria, for example, the *Bacillus coli*.

The fibrin upon these diseased granulations, commonly limited to the periphery, may extend to considerable depths; when the spots clinically are dark yellow and brown, the necrosis may be accompanied by practically no inflammatory changes.

A careful review of the work of Reinbach demonstrates quite clearly that the interferences with the process of cicatrization in granulation tissue are due to the precipitation of fibrin either as a covering or among the cells, to simple necrosis, or to that form of necrosis which with serous exudation or liquefaction is generally known as suppuration. His work is based upon the careful histologic examination of tissue removed from many conditions that were associated with granulating surfaces.

There is urgent need of equally thorough bacteriologic examination of such diseased human granulation tissue, especially researches that would include the use of animals.

There is yet another fact that prevents normal cicatrization, and that is obstruction to the blood supply of the growing tissue. The obstruction is only partial, and without doubt in many instances is attributable to an arterial supply that is inadequate in the number of vessels or their total calibre. In other cases the action of morbid conditions more centrally located or dependency of the part leads to inefficient supply of blood. That an oedema of granulation tissue may occur is well known; doubtless a deficiency in quality or quantity of nourishment is responsible for the occasional total failure of resolution. Briefly, granulation tissue may be the seat of extensive necrosis, oedema, and suppurative or fibrinous inflammations as well as combinations of these processes. Other pathological conditions, such as hemorrhage and the various cellular degenerations, may arise, but generally only as minor and incidental changes. The causes of pathological granulations often are to be sought in the character of the primary lesion, rather than in secondary infection or the injury of healthy granulations. Infection at the time of injury is frequently responsible for subsequent difficulties in healing.

THE PROTECTIVE QUALITIES OF GRANULATION TISSUE.—It is well known that granulations bleed readily; slight trauma of any sort disturbs the unorganized tissue and lacerates the embryonal and sprouting capillaries. As for infection, many experiments have proven that in this respect granulation tissue constitutes a serviceable barrier. One of these was the now classical experiment of Billroth. He ascertained that no ill effects followed daily dressing of healthy and experimentally produced granulations of a dog's back with lint saturated with pus, whereas inoculating such animals with the same material caused death. This simple test was many years later followed by the extensive experimental study of Afanassieff, who in a more scientific manner and by exact bacteriologic technique verified the results of Billroth.

Granulations were produced upon many animals of different species, and upon them virulent cultures of such bacteria as the bacillus of anthrax and the vibrio Metchnikovi were carefully smeared with a thick platinum needle. The serum exuding from granulations so treated was examined from time to time, stained preparations and media inoculations being made also; the virulence

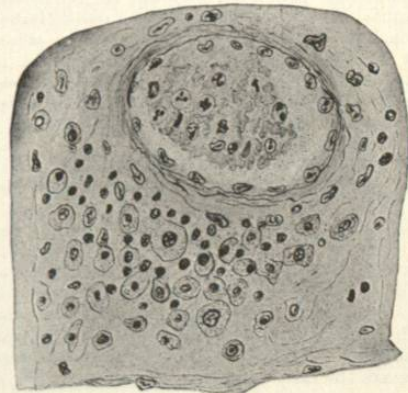


Fig. 2349.—Perivascular Collection of Round Cells or So-called Lymphoid Tissue. They contain various forms of leucocytes, and as the inflammation becomes chronic, plasma cells occur in such cell accumulations. (Modified from Ribbert.)

of the resulting growths was examined; histologic examination of the granulation tissue for bacteria and the inflammatory changes was carried out, and animals were killed in order to ascertain if general infection had occurred. Ample control experiments were employed.

He found that bacteria placed upon healthy granulations of animals did not penetrate, nor did general infection result. Inoculations made with recovered growths of the bacteria denoted an attenuation in virulence by the sojourn upon granulation tissue. Afanassieff was strongly inclined to look upon the protection afforded by the granulation tissue in the light of a vaccination. Such an explanation, however, is controverted by two facts. One of these is that local reactions in the granulation tissue were not observed with sufficient regularity in all animals to be in accord with the production of a bacterial immunity. Another fact is that Noetzel has repeated many of the experiments of Afanassieff and found that after bacteria were kept in contact with granulating wounds for many days the animals did not acquire any immunity.

It must be remembered that in granulation tissue mechanical obstacles exist to infection, such as the outward current of fluid from the vessels and the exceedingly slow circulation. Phagocytosis undoubtedly plays some part, although it may be that the ingested bacteria are no longer viable at the time of their incorporation. The extracellular destruction of the bacteria by the fluids present in granulation tissue (Afanassieff) or by enzymes, belongs to fundamental problems of immunity (see *Immunity*).

One cannot overlook the fact that when granulation tissue has formed, a defensive mechanism has been produced and its production is in response to external injury. But granulation tissue usually contains bacteria; especially frequent are the ordinary pyogenic forms.

Although resistant to bacterial infection, granulating wounds allow of the ready absorption of many soluble substances. Roux, Bonnet, Demarquay, Gorny, Maas, and Hack, and many others, have made experiments regarding this. Not all substances are absorbed with equal facility. The concentration of the solution, its chemical composition, the size of the granulating surface, and the character of the injury producing it, as well as the time contact is allowed, all influence the absorption. Granulating surfaces following burns and caustics are not so permeable as some others; absorption is more rapid from some healing wounds than from freshly cut surfaces. Apomorphine and curare are not readily absorbed, but carbolic acid diffuses with great facility. Various alkaloids such as strychnine, morphine, pilocarpine, cocaine, etc., have been used, and carmine, sodium sulpho-indigotate, iodoform, potassium iodide, sodium salicylate, as well as many other substances. Hack recovered ferrocyanide of potassium from the urine ten minutes after its application to a granulating surface, and Maas was able by spraying abscess cavities with a camphor solution, in a patient with vertebral caries and pyemia, to sustain the heart action sufficiently to allow operation. These and many other interesting and curious facts have been discovered about this phase of granulation tissue.

CICATRIZATION.—With healing of wounds by granulation a scar is formed that becomes paler as contraction takes place. Resolution in this form of inflammation is not marked by any peculiarities that distinguish it from cicatrization elsewhere. It is, however, customary to refer in this connection to the very deforming contractions that sometimes follow burns, but it is the location of the cicatrix rather than any special properties it possesses that marks it as singular. The loose subcutaneous adipose and areolar tissues allow scars to produce disfigurements that excite special interest on account of their exteriority. Similar malformations may occur in less exposed locations that are fully as interesting and as remarkable—for instance, the acquired dextrocardia and lesser dislocations of the heart that follow indurative processes of the neighboring viscera. They constitute excellent examples of the partial failure of inflammation as an adaptive process. The development of keloids in scars might be cited as another instance in which abnormal resolution builds a growth, which, to the surgeon at

least, must ever serve as a striking illustration of the failure of inflammation as an adaptive process. In contrast to these irregularities in resolution and fully as interesting is the failure of granulation tissue to organize about certain fistulous passages and their openings that lead to foreign bodies, necrotic tissue, etc. These are the so-called "sequester granulations." The failure of cicatrization in these cases seems to indicate a better adaptation of the process of inflammation, as it occurs in granulation tissue, to meet the requirements.

E. R. Le Count.

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GRAPE.—(Including *Raisin*, or *Uva Passa*.) The genus *Vitis* Tourn. (fam. *Vitaceae*) comprises about thirty species of Vine, a number of which, either in their improved forms, or as hybrids, contribute our grapes. The young leaves, tendrils, and green fruit of the vine are sour and astringent, containing tartaric, malic, and other fruit acids or their salts; tannic acid, quercetin, quercitrin, etc., sugar, gum, and several earthy and alkaline bases. They are more or less employed in Europe in the form of "teas" or syrups as domestic remedies. The juice of one particularly sour variety expressed from the green fruit, and known as *verjus*, is used to make a flavoring and refreshing syrup. The sap of the stems has also been employed. Ripe grapes, and especially raisins, are much sweeter, containing from ten to forty per cent. of sugars (*dextrose*, *levulose*, *inosite*) besides the acids, salts, etc., above mentioned. Still these are more or less employed for the same purposes as the herbage. Their medicinal virtues are very unimportant.

From the ripe fruit of the European Vine, *Vitis vinifera* L., raisins, and from one of its varieties the Greek, *Zante* or English "currants" are made merely by careful drying. Raisins are slightly laxative, like figs and other dried sweet fruits, and they have a peculiar power in imparting flavor.

Henry H. Rusby.

GRASSE, FRANCE, a town of 15,000 inhabitants, is eleven miles north of Cannes, from which it is reached by railway in forty minutes, and also by direct railway from Nice. This resort of the Riviera was brought especially to public notice by the visit of the Queen of England in the spring of 1891. It is very picturesquely situated, high above the hillsides, and is well sheltered from the cold winds on the north. It has an elevation of 1,070 feet, and possesses a very mild and salubrious climate, essentially the same as that of Cannes, with the exception that it is less stimulating than a resort directly upon the seashore.

The temperature is a little lower in winter than that at Cannes, on account of the elevation; the mean temperature of the year being 60.2° and for the winter 46.4°, while that at Cannes is 60° and 47.75° F. respectively. "Grasse," say Weber and Foster (Albutt's "System of Medicine," 1896), "forms a useful intermediate station during April and May for patients who find the heat in those months already too oppressive at Cannes."

For the climatic detail one is referred to the articles upon Cannes and Nice. In brief, Grasse affords a favorable winter resort for invalids unable to remain near the sea. Grasse possesses a luxuriant vegetation and is celebrated for the cultivation of flowers and the manufacture of perfume, which is the most extensive in France, if not in the world. The air is heavy with the scent of flowers, which with some invalids is said to produce an exaggerated form of hay fever. Great fields of orange blossoms, heliotrope, hyacinth, roses, violets, jonquils, geranium, and other flowers are cultivated about Cannes and Grasse; 60,000 acres being devoted to this industry, yielding an-