CLINICAL PATHOLOGY IN GENERAL PRACTICE

EVIDENCE OF GOUT

BY

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Gout has been a recognized disease since the beginning of the civilized world. It was described as podagra by Hippocrates in the fifth century B.C., long before chemical pathology had been envisaged. It has been an accepted fact up to the present day that the history and signs of gout are far more important in the diagnosis than any pathological estimation.

Gout occurs predominantly in males after puberty and much more rarely in females at or after the menopause. The typical story is of an acute onset first in a big toe and later in other joints, often at night, with excruciating pain developing in a few hours. Intense pain is the hallmark of gout and has led to many colourful descriptions, such as "tearing the joint asunder," and the well-known quotation of Sir Thomas Watson: "Place your joint in a vice and screw the vice up until you can endure it no longer—that represents rheumatism; then give the instrument another twist and you will obtain a notion of gout." The site of the attack gives a classical appearance, with the skin for some distance around the affected joint rapidly becoming shiny, bright red or mauve in colour, but remaining dry, and with distension of the neighbouring veins. Early attacks occur commonly in spring and autumn and are usually confined to the metatarso-phalangeal joints of the big toe but may later spread to almost any joint in the body.

A description of such an attack, which may be brought on for the first time by local injury or an operation, will lead to a diagnosis of gout without supporting pathological evidence. When the attacks are atypical, or when treatment has been applied without relief, further evidence of the disease may be sought with the aid of the pathologist.

Plasma Uric Acid

The pathological evidence most frequently required by the doctor to support a diagnosis of gout is an estimation of the uric acid in the blood or serum. Garrod in 1848 showed that the blood of gouty subjects contains abnormal amounts of uric acid, and to demonstrate this he devised the "thread experiment": when a thread is placed in the blood of such a patient the sodium urate crystallizes and adheres to it. In 1913 Folin introduced a reliable method for determining the uric acid content of the blood, and modifications of it are used to-day by most laboratories, though the uric acid content of the serum is now more often estimated. This is preferred by pathologists because anticoagulants tend to produce errors in the test. The estimation can be carried out by most laboratories. For serum estimations the pathologist requires 10 ml. of venous blood collected in a plain bottle. Your local laboratory may prefer the blood in oxalate bottles and it would be as well to inquire about this point.

Difficulties of Interpretation

There are certain points about the significance of the plasma uric acid estimation which should be understood by any doctor using this test as an aid to diagnosis in gout. The figures given for a normal level of uric acid in the blood vary from textbook to textbook and from laboratory to laboratory, and unless the normal figures are indicated in

the result the practitioner should ask the pathologist for them. Most textbooks in this country give a figure of 5 mg. per 100 ml. of blood as the highest normal, and the American normal figures of below 5 mg. per 100 ml. for women and 6 mg. per 100 ml. for men for the serum uric acid are regarded as too high by most British pathologists.

Another difficulty is that the level varies from day to day, and even in cases of gout a normal figure may result from an isolated estimation. It is suspected that a normal figure is more likely to occur in this disease during or immediately after an attack, though this is by no means proved. One reason may be that during an attack the patient is often given salicylates, which cause an increased urinary output of uric acid and so a lowered blood level. The reason for changes in blood uric acid levels is not properly understood because the mechanism of urate metabolism is still not clear. Recent work with isotopically labelled uric acid which has been injected intravenously into normal and gouty subjects has shown that there is a pool of uric acid spread throughout the body. The size of the pool in the normal subject is about 1,200 mg. and in gouty patients may be fifteen times as high as this. In the normal man 50 to 75% of the uric acid in this pool is replaced each day. Such studies may in time explain the variation in blood uric acid which occurs from day to day.

Although isolated estimations in gout may give a normal figure, in most cases the blood level will be raised enough to support the diagnosis. Hench has stated that an abnormally raised figure is found at some time in 75% of cases.

Other Causes of Hyperuricaemia

One of the curious anomalies of this disease is the fact that the high level of uric acid in the blood has apparently no connexion with the attacks of gout. If in fact uric acid is injected either into a vein or into a joint it will not produce an attack. Other causes of hyperuricaemia are leukaemia, polycythaemia, lead-poisoning, and chronic nephritis. In none of these are attacks of gout common, though they have been reported in both leukaemia and polycythaemia. It has also been shown that hyperuricaemia is a familial condition and that in such families the level of uric acid in the blood rises at puberty in the males and at the menopause in the females. Stecher, of Cleveland, has made a careful study of the hereditary aspects of gout and has shown that hyperuricaemia is a common finding in the families of patients with gout, though in fact many members may never suffer an attack in the whole course of their lives.

Tophi

One of the clinical findings in long-standing cases of this disease is the appearance of deposits of urates in articular, peri-articular and subcutaneous tissues and in bursae. They occur most often upon the helix or antihelix of the ear and less commonly in the olecranon and prepatellar bursae and in the tendons

Gouty tophi.

of the fingers, wrists, toes, ankles, and heels. They may break down and ulcerate, discharging a white chalky material which can be identified by the recognition of the typical needle-like crystals of monosodium biurate under the microscope.

Tophi can also be identified chemically by the murexide test, which is carried out as follows. Heat the removed contents of the tophus with five drops of dilute nitric acid until evaporation is complete; a reddish residue remains (alloxan); add a few drops of ammonia solution to the residue when cool; the result is a purplish red colour owing to the formation of ammonium murexide.

Other Tests

The sedimentation rate is raised during an attack of gout, but as this rate is raised in so many conditions it is of no particular help in diagnosis. There is a moderate leucocytosis during an attack, and unless this is recognized it may raise difficulties when a septic condition of the joint is suspected. Liver-function tests in gout have not shown any constant impairment and are of no value in diagnosis.

In conclusion, the history and clinical findings form the basis for a diagnosis of gout and are more important than any laboratory investigations. A raised level of uric acid in the blood or serum will support a diagnosis, but a normal result does not necessarily exclude it. The severity of an attack can be better judged by the physical appearance and the degree of pain than by chemical data.

Next article on Clinical Pathology.—"Blood Grouping," by Dr. A. E. Mourant.

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PHYSIOLOGICAL CHANGES IN BLOOD IN THE ANTARCTIC A PRELIMINARY REPORT

BY

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During the Norwegian-British-Swedish Expedition to the Antarctic in 1949-52 I spent two years in Queen Maud Land as medical officer of the wintering party. While there I made continuous physiological investigations on the expedition members, who numbered 15 men the first year and 14 the second. My investigations included basal metabolic rates and blood tests, the intention being to register the changes that occurred during acclimatization to the Antarctic climate and then back to temperate conditions. The blood tests were begun at home, and, with minor interruptions, were conducted monthly throughout the two-year stay, even on long sledge trips into the interior during several months of field work, and during the sea voyage south and back again.

Difficulties

I soon realized that the planning of physiological research on a polar expedition to an unknown country with an adverse climate is one thing, and the carrying out of it under extreme and unexpected conditions is quite another.

Cramped quarters, limited resources, primitive working conditions, the small restricted number of test subjects, and, above all, the human factor in these persons made large-scale investigations impossible, especially as all the other scientific programmes had priority when time and assistance mattered. Because of the extreme and primitive experimental environments even normally simple tests became time-consuming. During tests solutions and pipettes had to be kept at temperatures quite different from that of the surrounding air, which was often near freezing-point.

Owing to the fact that all scientists on the expedition had to do their part as handymen during the building of the base and afterwards, the tests planned could be done only when time permitted. Those that were thought most important were started first. This procedure was also of psychological importance, as the impact of all the blood tests begun at once would certainly have been to dismay some of the members and make them hesitate in giving "such quantities" of blood. In the way it happened they were coaxed into one series of tests after another with suitable intervals, and in the end they were all willing, though grumbling, guinea-pigs.

During sledging trips, to carry out only red-cell and white-cell counts, blood smears, and blood-sugar estimations on four persons usually took 10 to 12 hours. Consequently such tests had to be made when weather prevented sledging and outdoor work, which of course increased difficulties still more. The morning air temperatures in the tent varied from -5° to -30° C. (20° to -20° F.) before heating with the primus stove; this necessitated the thawing of frozen solutions, and in addition there was constant condensation in glass tubes and pipettes. The struggle to get from one tent to the other in drifting snow and subfreezing temperatures with half-full test-tubes to take blood samples in the early morning from shivering comrades who had just got out of their sleeping-bags in a cramped and poorly lighted tent is fun to tell about—afterwards!

Scope of the Tests

The blood investigations included: red-cell count, haemoglobin content, adrenaline in blood, blood sugar (fasting), white-cell count (morning and afternoon values), and white-cell differential count. The tests were made monthly, sometimes oftener, with three interruptions: (1) during landing operations and the month during which the base was established no tests could be done; (2) during the first summer's field work all tests at base were discontinued, as I went sledging inland for four months; however, while sledging I continued making regular blood tests on a small field group; and (3) during the second summer's field work tests were similarly discontinued for one month.

To avoid the influence of the prevailing extreme working conditions much trouble was taken to standardize the tests in every detail. As the same person did the tests all the time, the personal bias in colorimetric readings and laboratory operations can be disregarded. The morning tests were taken between 7.30 and 10 o'clock, and the afternoon tests between 4 and 6 o'clock. To avoid the influence of the daily variations in blood cells the tests on each particular individual were taken approximately the same hour every time, the procedure being made easier by the divergent times of getting up in the morning owing to the different personal jobs.

Samples were always taken from the ear-lobes, alternating between left and right, because wounds in finger-tips healed slowly and became painful. It was also more difficult to get blood from the finger-tips, which more often were cold and ischaemic because of the climate. For psychological reasons I did not take the blood samples on myself, but let them be done by any of my comrades who liked to try their skill. In this way some of them took a "cruel revenge" on their torturer, often inspired by the spectators' delighted remarks. Most of my comrades attained considerable skill in blood-letting during those two years.