Hepatic gout and its treatment / by J. Leffingwell Hatch.

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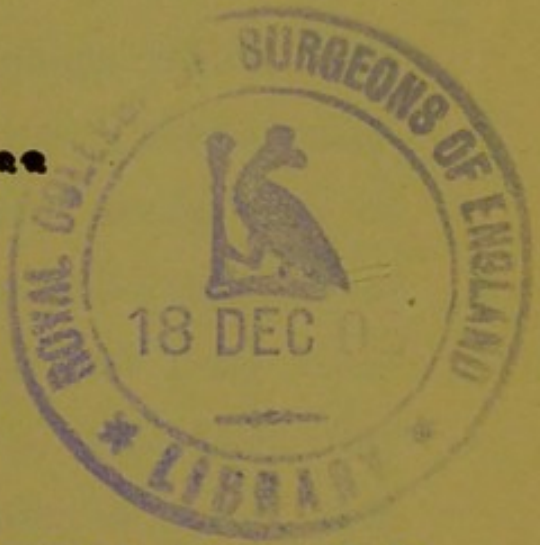

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Hepatic Gout,

and its Treatment.

A certain train of symptoms which have hitherto obstinately refused to yield to treatment, led me to make a careful study, both at the bedside, and post-mortem, in several cases of acute and chronic hepatitis, and from these studies I have come to the conclusion (for reasons which I shall endeavor to show), that there exists a form of hepatitis which can be traced to the uric acid diathesis.

The history of rheumatism and of gout its congener, goes back far into the shadowy vista of the past, at least as far back as Hippocrates, where we find they are considered to have both originated from a common ancestor, first observed in the feet, hence the term "podagra."

Passing through different stages of development with symptomatic manifestations, it has progressed in definition through the hands of such men as Arétée of Cappadocia (138 A. D.), Coelius, Aurelius, of the 2nd century, Radulfe of the 13th, Baillon of the 16th, Sydenham of the 17th, Tennant and Pearson of the 18th, and Bouillard, Garrod, Charcot, Luff, Lecorche, etc., etc., up to the present day, so that while the cause of the disease is still obscure, we have the observations of twenty centuries to throw light on its etiology.

Ever since Garrod discovered the true connection between gout and an excess of uric acid in the blood, we have been trying to find out how it is formed and how it accumulates there.

It is understood generally that uric acid is due to defective metabolism, the disassimilation of albuminoids, giving rise to uric acid, through the intermediate stages of nuclein and xanthine (Kossel), which if the emunctories are in perfect condition, are readily eliminated from the body without deleterious effects: if however the liver and kidneys do not act normally, it is easy to

understand how the blood becomes surcharged with these effete substances.

Dr. A. L. Benedict in the Medical Fortnightly says: "There are found in muscles and glands, especially after active function, many products of oxidation of nitrogenous tissues which are not found in the urine, bile, perspiration or other excretions. Most of these are converted by the liver into urea, a small quantity into uric acid and other nitrogenous waste, traces of which are found in the urine and bile. Leucin and tyrosin are also changed into urea. Most of these products of nitrogenous synthesis are excreted by the kidneys, so that the liver acts in this respect, as a ductless gland. Small amounts escape in the bile. A failure of the liver to perform fully the function results in gout and rheumatism, known in its milder forms, as lithæmia. Nuclear activity or the ingestion of foods especially rich in nuclein, such as thymus gland, cheese, etc., increases the amount of uric acid in the system, and tends to overcome the power of the liver in changing nitrogenous waste into urea."

Pathology of the kidney lesion.

In post-mortem examination of gouty and rheumatic subjects, the kidneys are always found diseased; Critzman (Paris 1899) claims that he has always been able to find lesions of the epithelial cells of the contorted tubules.

These changes in structure are due to a previous derangement of the blood supply, either a hyper-aemia or anaemia, which in turn is caused either by a germ, *in situ* or reflexly, by nervous stimulation or inhibition.

Pathology of the liver lesion.

In cases that I have examined (post-mortem), the process in most instances had become chronic, so that the primitive lesion was masked by an excessive amount of connective tissue, there was a distinct fatty degeneration of the hepatic cells, even where the parenchyma had not been obliterated by connective tissue overgrowth.

Another important feature, was the invariably affected kidneys, while in some instances it extended to the heart. The majority of

cases showed hypertrophy of the liver, but few of atrophy.

Their history usually gave evidence of the excessive use of alcohol, which probably was the cause of the first physiological change by bringing about hyperaemia, and in turn gave rise to a cloudy swelling, followed later by a slight increase of connective tissue, which, shutting off the blood supply through pressure and density of structure, gave rise to fatty degeneration and the degenerate cells were no longer able to perform their proper functions and complete normal metabolism. Of course the pathological alterations in the parenchyma of the organ, formed a favorable nidus to germs present, and although bacteriologists have so far been unable to isolate a rheumatic germ *sui generis*, there is some probability of one being discovered: and Gros, of Paris says: * "All our clinical testimony points to the fact that acute rheumatism is an infective disease, due to a special micro-organism."

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*"A Modern Study of Gouty and Rheumatic Manifestations," by Edmond Gros, 1896.

Symptomatology.

The symptoms are in the beginning vague, wandering, muscular and neuralgic pains, great susceptibility to change of temperature, headaches in the morning accompanied by dizziness: there are frequently hemorrhages from the nose, and also from the rectum, where hemorrhoids exist. Hemorrhages usually relieve the headaches and dizziness. Fits of nervous sweating, which are localized in different parts of the body occur and sometimes peculiar eruptions resembling eczema appear on the chest, abdomen and extremities.

The urine has a high specific gravity and is surcharged with urates, phosphates and uric acid: very frequently bile will be present and in the advanced stage, glycosuria is manifest. The appetite is poor and pica takes its place, the patient craving peculiar dishes, especially such as are acid. After eating there is a sense of heaviness followed later by pain in the gastric region, and when so called acute "bilious" attacks occur, there is great nausea, perhaps vomiting, the matter ejected containing bile.

At such times there is great prostration,

trembling, chills, alternating fever, depression of the heart, often cramps in the muscles of the calves of the leg, inability for physical exertion and laxity of all the muscles. This is followed by profuse sweating, and intense throbbing pains in the head, with distended veins of the temples, sometimes relieved temporarily by the vomiting.

There may or may not be jaundice: and it is more apt to be present in obese subjects. It is at such times that the patient begins to realize that he has a liver, and a sense of uneasiness in that region.

The chief feature for differential diagnosis between these "bilious attacks" (for want of a better term we prefer this popular expression) and those due simply to hepatic torpor, is the excess of uric acid in the urine, and the heavy deposit of urates following an attack, with the subsequent relief; (which is noticeable for some days afterwards) so too the history of previous attacks of acute articular rheumatism is a differential point.

Etiology.

These symptoms are due to excess of uric

acid, which is not eliminated owing to the hepatic inhibition and the crippled condition of the kidneys, which are unable to aid the liver vicariously: the results are a form of uremic intoxication and an hepatic explosion with the concomitant symptoms I have attempted to describe.

Treatment.

The cases which led to my making a study of the subject, were first treated as in ordinary bilious fever due to liver torpidity, with calomel, bicarbonate of soda, nitro-muriatic acid, podophyllin, etc., associated with cathartics, but with little or no benefit.

As soon as I recognised its true origin, the usual remedies, from potassium salts to piperazine, were tried with varying results. Colchicum and salicylate of soda seemed to give the best results, more especially when given during the crisis, as experience with these agents showed that the profuse diuresis and moderate watery evacuations they produce unload the system of pernicious toxines.

The salicylates are analgesic, diuretic, diaphoretic, antiseptic, antipyretic: they liquify and increase the flow of bile from the duct, reduce hyperaemia by facilitating the resolution of the products of inflammation, and above all, cause the elimination of urea, uric acid and its salts, as well as other solid constituents of the urine in excess. The best results, however, were obtained when the natural salicylate of methyl (derived from betula lenta) was used in preference to salicylate of soda which is synthetically produced.

Colchicum is the historical specific for rheumatism and gout, and this has been so much insisted on by such eminent therapists as Wood, Bartholow, Garrod, Dyce Duckworth, Lecorche, et al, that it is useless to recapitulate here. It is however, a most uncertain drug, not without some danger on account of its violently irritating effects on the mucous membranes and epithelial tissues: the stomach and kidneys suffer from large doses of the wine or tincture, which is never twice of equal strength. The active principle, colchicine, however,

is uniform in action and therefore free from all danger, as it can be given in mathematically precise doses.

Its physiological action depends upon its ability to quiet pain, diminish the production of uric acid and increase its elimination: to promote tissue oxidation and increase the flow of bile, all of which are assisted by its diuretic and purgative properties. Taking all the features of the two drugs, pure natural salicylate of methyl and colchicine together, their administration conjointly would seem logically correct, and in the combination known as colchi-sal, we have the remedy par excellence for gouty and rheumatic manifestations. Actual experience with colchi-sal surpasses the results we might expect: much smaller doses being really required than theory would dictate. I have no longer any trouble in arresting the violent bilious explosions I have described and by its judicious administration when premonitory symptoms point to an approaching attack, the evil can certainly be averted.

Colchi-Sal is dispensed in capsules of 20 cen-

tigrammes (4 minims) and is a peculiar compound of ¼ of a milligramme ($\frac{1}{250}$th of a grain) of crystalized colchicine, dissolved in an excess of natural methyl salicylate distilled from betula lenta. Numerous substitutes, made from the artificial salicylate and colored green to imitate the true colchi-sal, often lead to disappointing physiological results and should be avoided. As many as fifteen to twenty capsules can be administered daily without any deleterious results: all unpleasant symptoms, such as ringing in the ears, vertigo, delirium, congestion of the kidneys, and digestive troubles which are observed when the cheaper artificial substitutes are used, are absent in the true colchi-sal capsules. They are best given in small and repeated doses, distributed over a certain length of time.

Laborde of the French Academy has laid down rules for the administration of colchicine and these may be well applied in the case of colchi-sal. As soon then as the first symptoms appear, colchi-sal capsules should be given in the following doses:—

1st Day.—Four capsules, four times a day, at a quarter of an hour's interval each (16 capsules per diem).

2nd Day.—Three capsules four times a day (12 capsules per diem).

In most gouty and rheumatic cases it may be necessary to continue small doses for a day or two longer, but in this hepatic variety I have not found it required: there is not, however, any danger in continuing its use. In fact the supposed danger of accumulation has been much exaggerated in connection with all colchicine preparations.

Conclusions.

From the above exposition, therefore, we may draw the following conclusions:—that there is a certain form of hepatitis due to excess of uric acid in the blood, that this is the result of defective metabolism and that when a certain limit is reached, a toxaemia results and a consequent nervous explosion with symptoms of

headaches, vertigo, vomiting, wandering pains, cramps, trembling of the limbs, fever, etc., which fully justifies us in classifying it as an arthritic manifestation which is amenable to treatment, like others of this class, by administration of colchi-sal capsules, and that complete removal of the symptoms may be effected, if persistently carried out.

(Signed) J. LEFFINGWELL HATCH, B.Sc.M.D.