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THE TREATMENT OF YELLOW FEVER.*

JAMES CARROLL, M.D.
CONTRACT SURGEON, U. S. ARMY.
WASHINGTON, D. C.

The treatment of yellow fever is a subject of very great importance and secondary only to the question of prophylaxis or prevention. We are now able, by promptly instituting the proper measures, to control the spread of this disease, and if the treatment of the persons already affected be successful, the excitement and panic that so frequently follow its invasion may be averted. It is important to bear in mind that the disease is one of short duration, and if the patient's strength and vitality can be maintained throughout the critical period his recovery is practically assured, provided, of course, that he was previously in good health and free from organic lesion.

Let us first review the treatment pursued by some of the older authorities and then, aided by the light of modern pathology, consider what modes of treatment will be simplest, safest and at the same time afford the best prospects for success to-day.

One of the earlier English writers on this subject, Richard Towne,¹ began his treatment by ordering the patient bled, to the extent of eight ounces, and that was to be repeated once in six or eight hours as long as the symptoms were not abated, lessening the quantity drawn each time. He then administered an emetic dose of squill, ipecac or tartar emetic. He directed that the patient be given liberal quantities of diluting, refrigerating and sub-acid drinks made with oranges, lemons, tamarinds; or the mineral acids in barley or spring water. He states that lemon juice diluted aids diaphoresis. He allowed slightly acid fruits, roasted plantains and bananas, guava jelly, etc., with barley water ad. lib. Toward evening he directed a clyster of cream of tartar and manna, and at night twenty-five drops of laudanum.

In the second stage he repeated the bleeding and applied wet cups and blisters. He insisted upon the necessity for absolute rest in the reclining position. Meats were forbidden and he only permitted panada or water gruel sweetened and slightly acidulated. Cooling and lenitive clysters once in eight hours and a good dose of laudanum at night sufficed for this period of the disease.

In the third or comatose stage he directed that blisters be applied freely to the neck, wrists, thighs and legs, but more especially a large one to the crown of the head, "to invigorate the circulation and give the spirits liberty to expand themselves." "To the soles of the feet," he says, "there may be applied lotions, plasters, pigeons

killed and cut open, lungs of sheep, goats, calves, etc." Cordials and volatile salts were administered to comfort and refresh the languishing patient. Camphor in six-grain doses gave him remarkable results in the later stages, when the condition was critical. Finally he resorted to the use of powerful purgative clysters.

He believed, with others of his day, that the poisonous element was largely an excess of bile in the circulation, and blisters were frequently used, because the serum withdrawn by them being tinged with bile, it was thought a certain amount of the poison had been extracted with the serum. Active purgation was used to remove and prevent reabsorption of the supposed poisonous material excreted into the stomach and intestine.

Dr. Henry Warren,² who treated the disease from 1734 to 1738, condemned the use of calomel, emetics, purgatives and blisters and advised the use of mild laxatives in repeated small doses for several days. By these means he observed that putrid feces were expelled, the secretion of urine increased, the intestinal glands were cleansed and much of the corrupt and infected serum carried off. He wisely said that great care should be had to keep up nature's strength and spirits by giving now and then a little warm Madeira wine, Canary or such cardiacs as were not too inflaming. In his experience the nitrous and sub-acid remedies disturbed the stomach.

When seeing the patient for the first time he ordered a moderate bleeding, and that he be then covered with a blanket and made to perspire freely for twenty-four hours, or as long as the fever lasted, by the use of posset drinks. After the first day he allowed chicken broth as often as the patient desired it. He always found this useful and necessary to support the strength and counteract the exhaustion that would follow the free sweating. In addition he allowed now and then a glass of Canary or Madeira wine a little diluted, besides gruels and panadas with wine added to them, or sack-whey made richer than usual, and similar forms of light nourishment. If there had been no stool for three or four days he ordered a clyster of fresh milk and brown sugar or small doses of rhubarb and manna.

If there were frequent stools at a later period he deemed it of the highest consequence to suppress them promptly by the use of clysters containing Venice turpentine, Venice treacle or burned wine or brandy. He attached the greatest importance to the use of sudorifics.

Dr. John Redman of Philadelphia, the first president of the College of Physicians of that city and a teacher of the celebrated Dr. Benjamin Rush, read a paper before that body in 1793, in which he described his treatment of yellow fever in 1762. He is said to have been one of the most advanced and successful practitioners of his time.

He began his treatment with one-dram doses of that much neglected drug, Glauber's salts, repeated every hour or two for four, five or six doses until there were free evacuations. He saw the advantage of this in 1741 or 1742, during a previous outbreak, while he was a pupil to Dr. Kearsley, who had saved most of his patients by the use of it, while others who began with an emetic lost many or most of their patients. At the same time he ordered wine, vinegar-whey, thin gruel or barley water, raisin drink with wine, etc. On the second and subsequent days he administered one or two doses of the salts to insure having two or three stools a day. Along with these he gave teaspoonful doses of a neutral mixture to keep the skin moist. In the beginning he applied over the stomach an anodyne plaster of theriac, etc., which was renewed at frequent intervals.

The above-mentioned drinks were alternated with pleasant herb teas, water acidulated with the mineral acids, lemonade, weak cold punch, fruit waters or weak wine and water. In hemorrhagic cases he used mineral acids in all drinks and in addition gave red wine and water with a decoction of Peruvian bark and Virginia snake-root. He avoided venesection and emetics and believed that most other practitioners did the same, because of the disastrous results they had seen follow these measures in the former epidemic.

After the third day wine was given more freely and beef tea or chicken broth was added to the diet which was regulated by the taste and desire of the patient. Tea, coffee and weak chocolate were permitted under the same condition of their being agreeable to the patient. He laid stress upon the necessity for discharging the morbid matter as fast as possible, first by the *primæ viæ* and then by the pores of the skin and urinary passages, at the same time stimulating the body by means of strengthening nutriment. He attached great importance to the use of mineral acids and sulphate of soda. His general line of treatment was rational and based upon sound principles.

Hillary,³ who treated the disease in the West Indies from 1752 to 1756, declared that the objects to be obtained by treatment were the following: First, "to moderate the too great heat and rapid motion of the fluids, and abate the too great heat and violence of the fever, in the two first days of the disease, as safely and as much as we can. In other words, to diminish the fever." To attain this end he withdrew blood to the extent of from twelve to twenty ounces on the first and second days of the fever only. He strongly advised against bleeding after the second day, and when it was to be performed the quantity of blood to be withdrawn was determined by the general condition of the patient. The second indication was "to evacuate and carry out of the body as much of that putrid bile and those putrid humors as expeditiously and as safely as we possibly can."

He regarded the administration of emetics, so frequently practiced then, as dangerous and likely to prove disastrous. He ordered large draughts of warm water. After the vomiting excited by these had subsided he gave a grain or a grain and a half of extract of opium and nothing more was to be taken into the stomach for two hours. If the patient had had no stool a purgative clyster was given as soon as the vomiting had subsided and before the opiate had exerted any effect, and six or eight hours later a gentle purge. The treatment then followed was the administration of an infusion of Virginia snake-root with elixir of vitriol and Madeira wine. For nourishment barley water and wine-whey were given often and in small quantities during the first two days of

the fever, and after the third day the quantity of wine was increased.

Dr. Brown of Boston⁴ began his discussion of the treatment by citing from a letter written in September, 1798, by Dr. Mitchell, professor of chemistry and natural history in Columbia College, New York. Dr. Mitchell stated that in cases with symptoms of gastritis, anorexia, vomiting, etc., he had obtained happy results with watery solutions of lime, potash or soda, aided by a cathartic, such as castor oil, Rochelle salts, etc.

He wrote that the alkaline remedies were much used by the physicians of New York during the epidemic of that summer. They allayed anorexia, nausea and black vomiting. In some cases with high fever, dry skin, a full pulse, delirium, etc., he pronounced blood-letting a grand remedy and in many instances indispensable.

He exercised an admirable discrimination in the practice of venesection, in which regard, he differed from Rush and others of his contemporaries, who advocated bleeding in nearly all cases.

He summarized the treatment as follows: At the onset a thorough evacuation by mercurial cathartics, by diaphoretics and by blood-letting; poultices, fomentations, pediluvia, cold and warm bathing, blisters, enemas, etc., according to the indications.

After one or two evacuations he gave mercurial pills in doses of one, two or three grains, frequently repeated, to insure an evacuation every day or every other day. The drinks were to be subacid, diluent or emollient and were continued until after the subsidence of the fever, when he advised wine, bark and other restoratives. The food was to be light and easily digested, generous and gently stimulating; to be given often and in small quantities.

For primary catharsis he preferred ten or fifteen grains of calomel with twenty or twenty-five grains of jalap; calomel was given subsequently in doses of one, two or three grains, as before stated. He cites Warren,⁵ who asserted that it was the universal opinion of physicians in Boston that the most efficacious remedy, and the only one to be relied upon, was mercury. That in his observation more patients recovered under this treatment than under any other. It seems that he gave one-grain doses hourly until the patient was salivated, and he claimed by this means he effected a cure in all but two of his patients. Opium was frequently administered with the calomel to retain the latter in the intestine and insure its absorption. He was a strong advocate of the use of mercury in the form of calomel.

Brown tells us that "when there is a full, hard pulse, dry skin, great heat and violent pains in the head, stomach and bowels, bleeding is certainly an excellent remedy, if not a *sine qua non* of a cure." He applied blisters to the back of the neck, under the occiput or over the stomach to relieve pain, nausea, retchings or vomiting. Laudanum was used to quiet the stomach. Blisters were also applied to the temples, neck, back, thighs and arms, "to arouse the system from the torpor, low delirium and extreme debility of the second stage of the disease." Pediluvia with poultices were frequently used to moderate the violent determination of the blood to the head and to bring on perspiration, but for these purposes he preferred the warm bath.

He says that Drs. Rush and Griffiths advised bringing on a profuse perspiration by wrapping the patient in blankets and applying several hot bricks wet with vinegar to different parts of the body, giving at the same time repeated draughts of hot, teas, lemonade or weak

punch, to be repeated once a day for four or five hours, as long as the fever continued.

Brown used cold bathing during the fever, either by sponging or by dashing the water upon the patient. When the stomach was extremely irritable he advocated the use of cathartic and nutritive enemata at frequent intervals. For this purpose he used chicken or veal broth or water gruel, and if a cathartic effect were desired a tablespoonful each of Glauber's salt, sweet oil and molasses were added.

In the early period large quantities of diluent and sub-acid drinks, such as toast-water, lemonade, tamarind water, apple or barley water, etc., were given, and later these were changed for porter and water, claret or milk and water. No food was given until after the crisis. Then feeding was begun with light, easily-digested foods, such as weak tea or coffee, thin porridge, roasted or baked fruits, chocolate, sago, weak chicken or veal broth.

Lind⁶ relied mostly upon tartar emetic and blisters together with the administration of Peruvian bark. He attributed great virtues to fresh air, because he noted that sailors often recovered without treatment or care, while patients removed to hospitals died in spite of his best treatment, which was hardly to be wondered at.

Rush, who was a follower of Sydenham, carried the practice of venesection to excess. In a published table⁷ he enumerates twenty-three patients, each of whom was bled from three to thirteen times, and from each of whom he drew, in all, quantities of blood varying from fifty to one hundred and fifty ounces. He carried the administration of mercury to the same extreme, for he states⁸ that he gave to one patient one hundred and fifty grains of calomel in six days. He thought this a large quantity until he read that Dr. Chisholm gave four hundred grains to one patient in the course of his fever, and to another fifty grains at a single dose three times a day.

His general treatment was bleeding, purging, blistering, the use of cold water internally, externally and by means of clysters. He condemned the use of stimulants and found niter and antimonials to be ineffectual. He ascribed great value to blisters and aimed to induce salivation with calomel. He declares that in 1794 he was delighted with the effect of salivation in every case in which it occurred. As compared with some other physicians, however, Rush used calomel in moderation, for La Roche cites instances in which patients were given from one to several thousand grains of calomel during the course of an attack.

Currie⁹ objected to the use of mercury on the ground that it protracted the fever and retarded the cure. He asserted that in all malignant cases in which he saw it used, whether in large or small doses, it hastened the end. He made exception in cases where there was coma with dilated pupils. In these he stated that it had saved many lives when given in large and repeated doses. The treatment by sweating accompanied by cordial and stimulating remedies he regarded as not only unsuccessful but pernicious. Bleeding and catharsis he considered to be of the greatest benefit during the three first days in inflammatory cases. In adynamic cases he asserted these measures did manifest and irreparable injury. The cold bath and the use of wine, bark and opium were all condemned by him. The juices of lemons, oranges, grapes and currants he found to be grateful and beneficial.

Clark,¹⁰ who treated yellow fever in the West Indies in the time of Rush and Currie, was opposed to bleeding in most cases. Mercury was his "sheet anchor." He generally ordered a pediluvium and a purging clyster

at first, then a large dose of calomel and jalap, and repeated small doses until a free movement had been obtained. Saline draughts, given while effervescing, checked the vomiting and were serviceable during the first stage of the disease. He encouraged perspiration by giving warm drinks when the vomiting was not too violent. He found that excessive vomiting and purging were generally restrained by opium; he gave as much wine and opium as the stomach could bear; if the purging was free he gave chicken broth with sago or panada, Madeira wine or old hock, and he laid great stress upon giving nourishment and wine frequently. He attached great importance to careful nursing and the necessity for early treatment, and said that in the worst cases or those neglected at the beginning, no remedy seemed to retard or arrest the disease.

La Roche,¹¹ whose treatise on yellow fever is without doubt the most exhaustive one in the English language, divides the cases according to their severity into three classes.

First, those in which the patient appears to be stricken with death from the beginning. In these no treatment avails and recovery, where it occurs, is due, not to treatment, but to the vital resisting power of the patient.

Second, those cases which are so mild as to recover spontaneously without any treatment, or under the influence of any rational or even irrational management.

Third, those in whom the disease assumes an intermediate grade, whose chances of life or death are equally or nearly balanced, and in whom, consequently, it becomes an object of the utmost importance to apply means calculated to produce a favorable impression, and thereby arrest the dangerous tendencies.

He says we must, while watching carefully the course of the disease, prevent undue mischief being done, especially to organs essential to life. We must keep these organs in as healthy a condition as possible—restore, if possible, equilibrium in the play of the functions—reduce undue and dangerous excitement, and sustain the powers of life when these threaten to become impaired or are greatly reduced beyond the point of safety. Beyond this art is of little avail.

He quotes Harrison¹² as follows: "Accidents or acts of imprudence which, in other diseases, are mere trifles, are of tremendous importance in this. The mere getting out of bed has cost many a man his life. A man in this disease, however safe the physician may think him, is hovering between life and death—a trifle may decide his fate." (This fearful truth is too often only sufficiently impressed upon the physician after he has seen a number of deaths occur in patients whose condition would ordinarily excite no apprehension.)

La Roche insists upon the necessity for absolute rest in bed and cleanliness. In cases of the so-called inflammatory type he concludes that the experience of innumerable observers shows that sanguine evacuations—bleeding—and purgation are indispensable parts of the treatment. He says it is everywhere conceded, even among physicians who are opposed to sanguine evacuations, that in the first stage, antiphlogistic, sedative and evacuant measures must be resorted to, due care being exercised not to reduce the strength of the patient beyond the power of recuperation. He advises, in the congestive forms, external stimulation by means of rubefacients; hot baths, sinapisms, vesicants, etc., must be resorted to, with the internal use of stimulants, tonics, etc., by the stomach or bowels, and in milder cases stimulating and mercurial cathartics with general and topical bleeding to relieve congestion, when it can be done. He disap-

proves the use of emetics and finds the use of purgatives universally advocated.

Dr. Andrew Davidson¹³ states that in the milder form little more will be necessary than a hot mustard foot-bath and a purgative. When the temperature is moderate, the skin moist and irritability of the stomach absent or trifling, a meddlesome line of treatment is to be avoided. As a purgative he mentions castor oil in capsules or emulsion, or ten grains of calomel with or without jalap. He insists upon the necessity for obtaining and keeping up a free action of the bowels. As an antipyretic he suggests antipyrin if the condition of the heart will permit its use. The common saline mixture containing acetate of ammonium, nitrate of potassium and spirit of nitrous ether will promote the action of the skin and kidneys and five to ten drops of the tincture of veratrum viride can be added if the arterial excitement be great. He favors the sponging of the body with cold or tepid water and the application of ice-cold cloths to the head. A few drops of chloroform or one-drop doses of creasote to relieve gastric irritability. He refers to the use by Dr. Physick and Dr. Rush of ten-drop doses of oil of turpentine in syrup; the latter used it with success even in the later stages of the disease. The use of opium he regards as dangerous, even though it allays gastric irritability. He advocates the use of milk and lime water and the swallowing of small morsels of ice. A large sinapism should always be applied over the epigastrium.

In the third stage, when vomiting is urgent and prostration extreme, moderate doses of iced champagne should be given frequently. Perchlorid of iron has been given with apparently good results in arresting the hemorrhages.

He refers to the success obtained by Sternberg's method of treatment in which the mortality was only 7.3-10 per cent. in 374 cases in the United States, Cuba and Brazil. I shall refer to this again later.

Touatre¹⁴ of New Orleans gives the therapeutic treatment of yellow fever as "rest, aëration of the sick room, the administration of warm drinks in abundance and of liquid food, such as milk and thin broth." He states the two principal indications of treatment as follows:

1. To strengthen and sustain the organism by fortifying the nervous system, by arresting congestion and by increasing blood pressure and diuresis. To meet this he uses cold sponging and cold bathing.

2. To consume, destroy and eliminate the toxin. This is met by aëration of the sick room and by the administration of two, three or four quarts of Celestin's Vichy water in twenty-four hours.

Our interpretation of the result of this admirable line of treatment would be that the cold sponging reduced temperature, promoted the action of the skin and perhaps toned the nervous system. It certainly induces a feeling of comfort. The Vichy water, by promoting active diuresis, ameliorates all the symptoms by rapidly eliminating the toxin that produces them. This eminent observer, who passed through nine epidemics in thirty-three years' study of the disease,¹⁵ makes the following statements which are true and worthy of the greatest attention: "At the outset of the infection the patient can be succored, but what can be done when the organism is poisoned, when the toxin has already affected the hepatic cells and the renal parenchyma, and when the mucous membranes are bleeding? The physician is practically disarmed, for such lesions are nearly always fatal. It is during the three first days of the disease that the physician must act. When black vomit has

come to darken the situation, we can yet save some patients, but we are much better prepared to prevent the occurrence of black vomit than to cure it. The first and most indispensable thing for success in the treatment of yellow fever is that it be begun as soon as the disease has declared itself."

At the onset he always ordered a hot mustard foot-bath to relieve congestion and produce diaphoresis; a small dose of calomel, more as an intestinal antiseptic than as a purgative, and an enema consisting of a tablespoonful of sulphate of soda or magnesia in a pint of warm water every morning and night throughout the course of the disease.

He allowed no nourishment whatever during the first seventy-two hours of the fever unless the temperature fell below 102 F., in which case he ordered milk and Vichy every four hours. With the temperature above 102 F. he gave only Vichy during the three first days. This usually allays nausea and vomiting, and if it is not retained he injects it slowly into the bowel at frequent intervals. For black vomit he advises the application of an ice bag over the epigastrium.

Izett Anderson,¹⁶ after thirty-four years' experience with yellow fever in the West Indies, commenced the treatment by giving from six to ten grains of calomel combined with the compound rhubarb pill or colocynth and hyosciamus. This was followed three or four hours later by a purgative of magnesium sulphate, two drams, magnesium carbonate and potassium carbonate of each one scruple, with a tablespoonful of fresh lime juice, to be taken ice cold and while effervescing. This was repeated every third hour until the bowels had acted freely. This ingenious combination shows a wise determination to act upon the kidneys as well as the bowel. The systematic treatment after this was still diuretic and consisted of a neutral mixture composed of thirty grains of potassium bicarbonate and a dessertspoonful of freshly expressed and strained lime juice with three grains of carbolic acid. This was given every second or third hour, ice cold and while effervescing, unless the gas appeared to disturb the stomach, in which case it would be given after effervescence had subsided. High temperature in the early stage was treated by the wet pack. He states that since the adoption of this method of treatment he has never met with any cases of hyperpyrexia requiring other special treatment, nor has he encountered the profuse and uncontrollable black vomit that he had previously met with. For partial suppression of urine he used dry cups, warm turpentine stupes, acetate and citrate of potash, but he had most faith in dram doses of spirit of nitrous ether given every hour. If there were signs of heart failure he used strychnin and alcoholic stimulants. The only food allowed throughout the attack was ice-cold milk with lime water, and in some instances albumin water. No gruels, paps or broths were permitted until the beginning of convalescence. Stimulants were never used until the second stage, and he preferred a sound, iced, Rhenish wine, which proved of the highest value.

Loomis¹⁷ favored the diaphoretic and expectant plan with the use of cracked ice, milk and lime water or hypodermic injections of morphia for nausea and vomiting, cold compresses for hematemeses and the judicious use of stimulants to counteract exhaustion.

Osler¹⁸ states that careful nursing and a symptomatic plan of treatment probably give the best results. He advises hydrotherapy for the fever, morphia hypodermically and ice in small quantities for the vomiting, and the hot bath for uremic symptoms. Stimulants are to be used

freely during the second stage and the patient is to be carefully fed, using nutrient enemata if the stomach be irritable.

Strümpell¹⁹ says that the earlier proper treatment can be instituted the better. He advocates absolute rest; evacuation of the bowel; a hot mustard foot-bath early in the attack; opium or morphia for lumbar pains; sinapisms, ice and hydrocyanic acid or chloroform for gastric irritability; cold spongings, the wet pack and cold bath for high fever.

Sternberg's treatment, referred to by Davidson²⁰ has given phenomenal results. In 374 cases treated in the United States, Cuba and Brazil, the mortality was only 7.3-10 per cent. It is not to be believed that such brilliant results can ever be exceeded by any other single line of treatment. A greater percentage of lives has been saved by it than by the use of the Brand method in typhoid fever. The Brand method reduced the mortality in typhoid fever from about 14 to 7.5 per cent.;²¹ the Sternberg treatment reduced the mortality of yellow fever from at least 20 or 25 per cent. to the same figure.

In addition to the administration of bichlorid of mercury and sodium bicarbonate, the special treatment he advises is as follows:²² A hot mustard foot-bath during the first twenty-four hours; cold sponging; cold applications to the head; protection of the patient from currents of air; sinapisms over the stomach and lumbar region when called for; the promotion of perspiration, and the withholding of food during the first three days; stimulants in the form of iced champagne or good brandy after the fourth day. If the stomach be irritable he advises milk and lime water, and if this do not agree, nutrient enemata. Later on he allows milk punch, ale, porter, etc.

Having reviewed the older as well as the more modern methods of treatment we are in a position to profit by the experiences of the numerous observers who have placed their methods and results on record.

In yellow fever we are dealing with a disease of short duration and one that tests severely the vital powers of the patient. I believe, however, that in previously healthy, non-debilitated subjects, free from organic lesions, the mortality can be reduced practically to zero by careful and judicious treatment instituted in the incipency of the attack. On the other hand, if there be present debility from any cause, anemia, organic lesions of the heart, liver or kidneys, the outlook is always serious and recovery doubtful. The treatment must be essentially eliminative and supporting, with the incidental use of measures tending to reduce hyperpyrexia, relieve pain and nausea and remove internal congestions.

Before taking up the treatment in detail it will be better to consider briefly the conspicuous pathological lesions that are present and the deductions to be drawn from them. In the first place, the lesions and symptoms are produced by a powerful toxin circulating in the blood and tissue fluids. This poison appears to act with greatest intensity upon the liver and next upon the kidneys. The changes in the liver are at first a congestion, which is followed by cloudy swelling, granular and fatty degeneration with more or less extensive cell necrosis. In cloudy swelling the organ is enlarged and firm, and a great deal of the blood is displaced by the pressure of the swollen cells upon the capillaries. With granular and early fatty degeneration the swelling and pressure are slightly increased so that there is considerable obstruction to the flow of blood through the organ. Practically all of the blood supplied to the liver comes through the portal vein, in which the pressure is very

low, and any serious obstruction to the flow of blood through that viscus will necessarily result in a damming up of blood primarily in the portal vein, secondarily in the vessels from which it receives its supply.

Of these the duodenal and pyloric veins are the shortest and have the least communication with other vessels. On the other hand, the mesenteric veins are of greater length and are distributed over large areas. Hence the passive congestion and hemorrhages which result from obstruction to the portal circulation, when of rapid onset, are more intense and manifested earlier in the pylorus and duodenum than in other portions of the small intestine. This explains the pain and tenderness on deep pressure in the epigastric region, which is so early and constant a symptom in yellow fever and which is the result, not of a specific action of the toxin upon the mucous membrane itself, but of obstruction to the portal circulation, causing a backward pressure along these short vessels—the pyloric and duodenal veins—that promptly affects the rich capillary plexus in which each of them originates. The hemorrhages which occur later result from capillary stasis, aided, possibly, by a condition of toxemia.

That this is probably the correct explanation appears from the fact that we find the same condition of the gastro-intestinal mucous membrane with hemorrhages, black vomit or bloody discharges, in other conditions than yellow fever, where the liver is seriously damaged. I refer to advanced cirrhosis, acute yellow atrophy, acute phosphorus poisoning and excessive fatty degeneration with cell necrosis, occurring with or without infection. And more than this, in these latter conditions the patient dies with the same cerebral, eclamptic or so-called uremic symptoms that we see so very frequently in this disease. And further, the autopsies and subsequent microscopic examinations develop the fact that in numerous instances the liver and not the kidney is the organ most seriously affected. This statement applies also to yellow fever, and I believe that the supposed uremic condition in this disease is often more probably one of poisoning from the accumulation in the circulation of the organic ammonia compounds which the liver normally converts into urea, with other waste or end products, the constitution of which is not well known, though some of them are thought to be of an acid nature. These are developed as the products of proteid digestion and as the nitrogenous end products of cell metabolism throughout the body largely in the form of carbonate, lactate and perhaps carbonate of ammonium.²³ Where the liver loses its functioning power, therefore, there must be a deficiency in urea,²⁴ and the kidneys cease to secrete urine because urea, the normal stimulus to that function, is absent. Osler²⁵ states that there are cases in which anuria is prerenal, and among the conditions in which this occurs, he mentions fevers and inflammations, acute poisoning by phosphorus, etc.; in the collapse after severe injuries or operations, and "in the collapse stage of cholera and yellow fever."

About two years ago I performed an autopsy on a woman who died with uremic symptoms on the third day following a laparotomy. The wound was found to be perfectly healed and there were no signs of inflammation. The kidney changes found on macroscopical and microscopical examination were comparatively insignificant while the liver showed excessive fatty degeneration with some cell necrosis and a beginning hypertrophic cirrhosis. Cultures from the abdominal cavity, blood, liver, kidney and spleen were all negative. I believe now that death was due to the inability of the previously

fatty and cirrhotic liver to dispose of the products of greatly increased cell metabolism, the result of the operation. As there appeared to be a deficiency of bile, the case was supposed to be one of acholia.²⁶

It is quite plain from our text-books that retention of urea in the blood is not always the cause of "uremic symptoms." In some cases, no doubt, where the liver and kidney are both seriously at fault, the condition may be one of combined uremia and ammonemia or other intoxication. Urea seems to exert a toxic effect only when it is present in large amount, and patients frequently recover from pronounced attacks of uremia even in scarlet fever.²⁷

Urea may be present in the blood in large quantity without producing symptoms,²⁸ and in uremic conditions ten to fifteen times the normal amount of urea is sometimes found in the blood. Loomis²⁹ states that after withdrawal the blood of yellow-fever patients undergoes ammoniacal decomposition, and some affirm that the blood contains free ammonia. According to Joseph Jones³⁰ of New Orleans, yellow fever blood contains abnormal amounts of urea, extractive matter and ammonia. But carbonate of ammonia is scarcely ever found in the blood of uremic patients, and the theory of the decomposition of urea into ammonia in the blood is untenable.³¹ La Roche found the blood in yellow fever to be acid or neutral to litmus.³²

The primary indication in the treatment of yellow fever is to remove the immediate cause of the condition present, viz., the toxin. This is best and most expeditiously effected through the normal channel with the urinary secretion, aided by a moderately free action of the skin and moderate depletion of the digestive tract by the use of mild saline cathartics. With the evacuation of these fluids and the toxin they contain the symptoms abate—speaking of the early stage—and the stomach will retain an increased amount of fluid to replace that which has been removed. Care should be taken to maintain one or more of these functions throughout the attack, sustaining the patient's strength by the judicious use of the appropriate stimulants. It is much to be regretted that we have no means of acting directly upon the liver.

In the earliest stage a hot mustard foot-bath is of great service and should be used as a matter of general routine when the case is seen sufficiently early. It relieves internal congestions, lessens the headache and promotes diaphoresis. From personal experience I think more stress should be laid on the necessity for confining the hot mustard foot-baths to the earliest stage as laid down by Sternberg and nearly all writers. In my own case it was used for the first time on the third day, and I shall never forget the effect of it. Within about half an hour after the removal of the bath and while I was oppressed by the weight of a heavy load of gray blankets, I felt a sudden pain and embarrassment at the heart. The pain was very acute and accompanied by a feeling of distension, as if the organ was much distended and was being arrested in diastole. Happily, it lasted but a few moments. This was the only time I felt myself to be in imminent danger. The bath was not repeated and there was no recurrence of the paroxysm.

If nausea be present a sinapism should be applied over the region of the stomach and the same application should be used for pain in the lumbar region. Cold applications afford most relief for the pain in the head. The muscular pains usually become ameliorated after a few hours, and it is best not to administer remedies for them unless they are unusually severe, in which case it

would be permissible to use very small doses of anti-pyrin or phenacetin. It is advisable and probably necessary to give a mild cathartic at the beginning; say several one-sixth grain doses of calomel or three or four grains each of calomel, rhubarb and soda in capsules. These should be followed by several dram doses of sulphate of soda at hourly intervals until there is a free evacuation. In small doses this salt is diuretic as well as laxative, and, in my opinion, it is the least disagreeable of the saline cathartics. The nauseating effect of castor oil should forbid its use unless the patient expresses a preference for it. The routine administration of a tablespoonful of sulphate of soda in a pint of warm water as an enema, night and morning, as practiced by Touatré, seems to me an excellent plan. The patient should be encouraged to take plenty of fluid in small quantities at frequent intervals or cracked ice if there be nausea or irritability of the stomach. In this case it would be well to try also small quantities of milk and lime water, carbonated Vichy or an effervescing neutral mixture given ice cold. My preference is for carbonated Vichy *ad libitum*, and if it be not obtainable, the neutral mixture prepared with fresh lime juice as used by Anderson, but omitting the carbolic acid. This mixture should be neither acid nor alkaline, but neutral.

If sufficient fluid cannot be taken by the stomach, give very slowly high rectal injections of warm or tepid water to which may be added bicarbonate of sodium, sulphate of sodium, chlorid of sodium, citrate of potassium or any of the simple alkaline diuretics. Bicarbonate of sodium is probably the best because it is said to exert a soothing effect upon the mucous membranes in general, and should be easily retained. As the purpose of this injection would be chiefly to secure absorption of the fluid and its effect upon the kidneys, it should not be too cold. I have seen patients complain bitterly after the use of ice-water enemas. If the temperature be high and the skin dry, cold or tepid sponge baths will give comfort and aid the action of the skin; at the same time half-dram doses of spirit of nitrous ether could be given every half hour until the skin became moist or the temperature began to decline.* The quantity of urine passed must be carefully noted; it is often necessary to use the catheter. If the pain in the lumbar region be severe and the bladder remain empty, the patient should be placed into a warm bath to which a little mustard has been added and kept there until the skin becomes reddened. This should be used only in the first stage, to relieve congestion and determine the blood to the skin. If the temperature be moderate, the skin moist and the bowels and kidneys active, the patient should be given absolute rest in bed in a well-ventilated, slightly darkened room. He must be lightly covered and protected from draughts. The use of mosquito nets and wire screens is an important adjunct to the treatment.

All food should be withheld during the first three days with the possible exception of milk and lime water or milk and Vichy if it be well retained. Should the patient desire it, I would not hesitate to give an occasional small dose, say two or three drams, of champagne, ice-cold and diluted. Besides being a grateful stimulant, it quiets the stomach and retards tissue waste. The necessity for buoying up the heart is apparent when we consider that the passive congestion of the stomach and intestine is best relieved by strengthening the circulation until the cause can be removed by elimination.

* There seems to be a hesitancy to use diuretics in this disease probably for fear of damaging the kidneys. No simple drug will do so much damage as the toxin. If this poison be freely eliminated, the subsequent course of the disease will be modified.

In the selection of an agent for this purpose there is room for choice. The sodium salt appears to possess several advantages. It is the normal alkaline base of the blood plasma; it is bland, non-irritating, acceptable to the stomach, and mildly diuretic; and, according to high authority,³³ "it is reported to be singularly efficient in the suppression of urine from renal disease." We must not lose sight of the reported diminished alkalinity of the blood in this disease and the possibility that this may be due to the presence of an acid poison which is neutralized by the sodium salt. In the Sternberg treatment, about two and one-half drams of the bicarbonate of sodium are administered in twenty-four hours. The Vichy water treatment is practically treatment by bicarbonate of sodium.

Sulphate of sodium, the value of which was first shown by Dr. Kearsley of Philadelphia in 1741, is endorsed by Dr. Touatre of New Orleans, and Surgeon R. D. Murray of the Marine-Hospital Service gives it the preference over other salines.³⁴ A good dry champagne is the best stimulant to begin with; when the patient tires of it a sound Rhenish wine should be substituted; Dr. Murray has had good results with dry catawba.³⁵

If there are signs of heart failure, strychnin should be used freely. If the patient is not seen until the second stage the treatment must be symptomatic. For vomiting, ice bags to the epigastrium are probably the best remedy; they can be supplemented by small doses of cocain and hypodermics of morphin according to indications, but carbonated Vichy, lime water or champagne will probably prove sufficient unless black vomit has set in or is impending. In this case turpentine has been recommended and is worth considering on account of its properties as a local and general stimulant, hemostatic and diuretic. Tincture of capsicum is also said to be a valuable local and general stimulant in this condition. The patient's strength must be sustained as far as possible, the action of the kidneys encouraged through absorption of fluid from the bowel and the blood determined to the surface by friction of the skin with mustard water. The value of the hot-air bath in cases of anuria is too well known and appreciated to require more than a mention of it. Whether the poisonous agent be urea or any other soluble substance it is equally important to secure its elimination by this or any other method.

The nutrition of the patient is a subject well worthy of consideration. Food is frequently withheld for varying periods from three to five days or a week; in my own case I think for at least eight days nothing was allowed but water, Apollinaris, ice and champagne. Now, during all this time certain cells of the body are functioning and using up their own protoplasm, for in conditions of anemia, debility or malnutrition and in the infectious diseases we know that the cells of the vital organs undergo degeneration and often necrosis from lack of nutritive material. In specific fevers the functions of some of these cells are greatly stimulated. The proteid constituents of the cells are consumed in the performance of these functions,³⁶ and converted into waste material and end-products which add to the general intoxication. Physiologists teach us that there are certain foods that will prevent this degeneration of the cells to a considerable extent by saving their proteid constituents.³⁷ Among these are gelatin and fat, non-proteid foods, the latter of which, in the form of olive oil, has been used with marked success by Spanish physicians in the treatment of yellow fever. According to La Roche, of thirty-six patients admitted to the hospital

at Vera Cruz with black vomit, no less than thirty recovered after treatment by inunction with the heated oil,³⁸ and other equally remarkable results are mentioned. In another place we find that Father Constans acquired a great reputation in Spain in the early part of the nineteenth century, in the treatment of yellow fever, and his chief reliance was olive oil which he gave in large doses. The rationale of this treatment seems to be that the oil is highly nutritious, a proteid saver, and is readily absorbed by the epithelial and endothelial cells of the capillaries. In this way the integrity of the latter is preserved and hemorrhage prevented. Pathology teaches us that where there is capillary blood stasis, hemorrhage soon takes place from deprivation of nutriment, the endothelial cells of the capillaries being nourished by the blood that circulates within the vessels. This suggests the early administration of olive oil in emulsion with lime water.

Animal foods have long been condemned, but the use of toast-water or thin barley, rice, sago or hominy water, after prolonged boiling and salting, are probably advantageous. Some of these are strongly advocated by Surgeon Murray³⁹ and the older observers, and one can readily believe that the starches they contain would be of service in restoring the functioning power of the hepatic cells. Murray also records eighty cases that were fed on ice cream, *ad libitum*, with only four deaths. And ice cream is rich in fat. So that if the stomach is reasonably quiet, we can safely satisfy the gnawings of hunger by the use of barley, rice or toast-water, milk and Vichy or lime water, ice cream, lemon jelly and fruit juices in addition to mild stimulation and the use of olive oil internally or externally. To withhold all nourishment throughout the course of the fever seems injudicious and unsafe. With the temperature below 102 degrees F., and the stomach quiet I believe the patient will be greatly benefited by small quantities of such of the foods mentioned above as his taste may call for.

The early involvement of the liver as indicated by the early lesion in the duodenum naturally suggests an equally early defect in the functioning power of the liver in the elaboration of urea. This deficiency which must sooner or later become marked, is manifested in the failure of the kidneys to secrete the normal amount of urine. As the rate of elimination by these organs increases normally with an increase in the urea in the blood,⁴⁰ it would seem justifiable to supply the defect by the medicinal administration of urea either through the stomach or by hypodermic injection, as soon as the ordinary remedies cease to have the desired effect. The injection of urea into the blood soon evokes a very copious secretion of urine, "even if, previously to the injection, the secretion had been at a standstill."⁴¹ We can hardly do better than follow Nature's method of stimulating these organs to perform their normal functions. And the danger of an excessive accumulation of urea in the blood must be very slight in a condition where that substance is manifestly deficient. The longer the kidneys are permitted to act imperfectly, the greater will be the retention of toxins which will react by increasing the damage already done to both liver and kidneys. This is not by any means a new suggestion, for urea was proposed as a diuretic by the older French physicians and it was used by Prof. Mauthner⁴² of Vienna. Fifty years ago Dr. T. H. Tanner⁴³ of London reported success with it in cases of dropsy. In one case he used ten grains every six hours for nine days with the effect of increasing the flow of urine from 14 to 44 ounces in twenty-four hours; during the nine days the quantity

passed varied from 35 to 49 ounces. It was then discontinued because the dropsy had been removed. After three weeks it was again resorted to with the same satisfactory results.

In my opinion the services of trained female nurses are indispensable to secure the very best results. They should be under strict discipline, and the tour of duty with patients who are seriously ill should be eight hours in twenty-four.

The physician should not treat his patients by proxy, but should assure himself that his line of treatment is being faithfully carried out. All meddling medication should be prohibited.

It is well to bear in mind the possibility of the occurrence of complications through secondary infection by the streptococcus, staphylococcus, colon bacillus or bacilli of the hog cholera group, known also under the name of *B. icteroides*, *B. enteritidis*, paracolon, paratyphoid, etc.⁴⁴ The chances for the occurrence of such infection will probably be greatly diminished by the early institution of such treatment as will best maintain the integrity of the intestinal mucosa and conserve the patient's strength.

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ULCER OF THE BLADDER.

LOUIS E. SCHMIDT, M.Sc., M.D.

Associate Professor of Genito-Urinary Diseases, Chicago Policlinic;
Attending Genito-Urinary Surgeon and Dermatologist,
Alexian Brothers' Hospital.
CHICAGO.

Under the general title of "Ulcer of the Bladder," it will be best to avoid complicating considerations by stating definitely what is intended to be understood. I mean to speak only of ulcers in the usual pathologic sense: that is to say, the loss of substance which does not show any intention of healing, which produces abnormal secretion and whose base is covered with regular granulations; and furthermore, a loss of tissue not due to any cause which comes from the exterior of the bladder or which destroys the continuity of the bladder wall, as abscesses, foreign bodies, ligatures, etc.

PROGRESS IN KNOWLEDGE.

Ever since the more exact diagnosis of diseases of the interior of the bladder, including ulcerations, has been considered, constant advances have been made and we find that the interest of genito-urinary surgeons has also correspondingly increased. Still greater attention was given to this particular subject, as soon as it was no longer a matter of conjecture, that these ulcers were the cause of a series of distinct symptoms, the nature of which had not been clear up to this time. As clinical experience has shown, the diagnosis of ulcer of the bladder has become of greater significance, because we can treat them in a rational and successful manner.

THE VARIETIES OF ULCER.

It is possible to classify the ulcers occurring in the bladder in a general way as follows: gonorrheal, traumatic, ulcerations which occur in a non-gonorrheal cystitis, tubercular ulcerations which follow necrosis of malignant tumors, solitary, perforating and syphilitic.

THE GONORRHEAL TYPE.

There can scarcely be a question of doubt that the most common ulcers are those that occur on a gonorrheal base. The course, as a rule, is somewhat as follows: A severe infiltration commences to form about a single or around numerous centers of infection characteristic of gonorrheal cystitis and in the course of time the summits of these areas of infiltrations become necrotic; this loss of tissue leads to the formation of ulcers. The individual points of necrosis may become larger and larger and numerous ulcers may be present or, again, they may become confluent and form a single ulcer. This has been, up to the present time, the more usual in my findings, probably because the cases do not present themselves in the initial stage. From their etiology the peculiar configuration of these ulcerations and the appearance of the ulcers themselves can easily be accounted for. These ulcers are apparently sunken in on a plateau; this is entirely due to the summit of an infiltrated area becoming necrotic, while the remaining infiltration is still above the normal level of the surrounding mucosa. The surface of such an ulceration is covered with a membrane which is almost white in color, slightly reflecting in character and which is adherent to the base. If this covering is forcibly removed, an uneven surface composed of easily-bleeding granulations is seen. These ulcers have a tendency to occur in the same bladder in different stages, if not, at least in the immediate neighborhood other rounded infiltrations are to be seen in different periods of development. If the apices are not necrosed, they may be at the point of becoming so. The condition of the remaining mucosa

Heart Suture Again.—In choosing the subject of his oration before the annual meeting of the American Medical Association Harry M. Sherman made a happy choice in selecting "The Suture of Heart Wounds." This is a subject which has lately been brought prominently before us by three cases operated on by American surgeons, and we have editorially invited the attention of our readers to this interesting advance in surgery. . . . We believe with the orator that the surgery of the heart will be still more perfected and its field greatly extended.—*Philadelphia Medical Journal*.