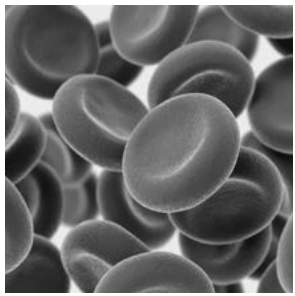

1 Bloodletting and Malariatherapy: Treatment Methods of the Past

Those interested in the history of medicine should read the details surrounding President George Washington's therapy by his physicians in December 1799.[1] Purging, bloodletting and other methods were employed, which hastened his death.

His treatment was discussed recently in the *New England Journal of Medicine*'s 200th Anniversary issue.[2] The authors used Washington's experience as a benchmark for measuring the remarkable progress medicine has made in the past two centuries.

Washington's Experience

Three physicians were responsible for Washington's medical care and each knew him well. The first doctor to arrive took the president's medical history. He found the president had mild hoarseness, difficulty breathing and was feverish and unable to swallow. A bloodletter was called to assist in treatment, and 12 to 14 ounces of blood were withdrawn.

Washington also was administered molasses, vinegar and butter, and near fatal choking ensued. The doctor then applied a blister of cantharides (Spanish flies) to the president's throat, followed by more (18 ounces) bloodletting in the morning. This was followed by the same blood removal less than two hours later.

Washington repeatedly gargled sage tea with vinegar. A fourth bleeding (32 ounces) was performed in the afternoon. Calomel (mercurous chloride) and tartar emetic (antimony potassium tartrate) were also given to the president. Both are extremely potent laxatives (purgatives).

After the fourth bloodletting, Washington's condition improved, and he was able to swallow. He returned to bed and was helped into an upright position, but he continued to struggle for air. His condition began to deteriorate.

Later that day, the physicians applied blisters of cantharides to his feet, arms and legs, and then applied wheat bran poultices to his throat. Despite all of the heroic treatment, George Washington died later that evening.[3]

According to some 19th century historians, Washington's physicians might have reasoned that because bloodletting (about 80 ounces) caused visible dermal vasoconstriction, it would also constrict the vessels associated with swelling in the windpipe.[4,5] In

addition, the dehydrating effects of purging with calomel, diaphoresis (sweating) with sage tea, subemetic doses of tartar emetic, and blistering with cantharides would potentiate the effect.

In retrospect, the doctors should have considered the fact the president previously had been subject to recurrent febrile respiratory infections and other acute fevers probably due to malaria and pneumonia. One of his several bouts of fever was life-threatening, and he required several weeks to recover.[6]

Treatment Methods

The scenario presented above was not unusual two centuries ago. Cathartics were major components of colonial American therapy. Physicians relied on these drugs, more than most others, to rid their patient's bodies of the noxious materials they thought produced some contagious diseases, to flush out the "unbalanced humors" thought to have produced their patient's symptoms by disturbing the normal tone of solid tissues.[7]

Blistering with an alcoholic cantharides solution applied to the skin raised large welts, which the physicians reasoned neutralized the naturally occurring inflammation responsible for the patient's symptoms. Emetics, drugs that induce vomiting, were thought to strengthen weak stomach muscle fibers. Diaphoretics were thought to make the patient sweat out the disease and remove excess fluids.[8]

Bloodletting

Bloodletting also was employed commonly, and the president received prompt and expert medical care that reflected the practices of that time.[9] Special instruments (scarificators, fleams, lancets) and cupping vessels were sold to facilitate the procedure.

Bloodletting, or phlebotomy, likely is the longest-running tradition in medicine, originating in the ancient civilizations of Egypt and Greece. The practice continued for 2,500 years until it was replaced by modern medical techniques. People did not begin to question its value until the 19th century.[10]

Bloodletting is one of many discredited forms of therapy. One even more strange was using one disease to treat another. The most glaring example was malariatherapy: infecting patients with malaria in an effort to cure neurosyphilis.

Malariatherapy

There are few examples of one living pathogen being used to treat a disease caused by another. However, malaria parasites were used for about 40 years to ameliorate or reverse the effects of neurosyphilis, a life-threatening advanced stage of syphilis.[11]

Syphilis progresses through a primary localized phase, a secondary phase, a latent period and, in some cases, a progressive tertiary phase involving almost any organ, but usually the ascending aorta and the central nervous system (neurosyphilis). About a third of neurosyphilitics remain asymptomatic.

Some eventually develop symptoms related to meningovascular or parenchymatous lesions, the latter reflecting destructive inflammatory and degenerative processes in the central nervous system. These are the imperative indications to induce fever to help avoid progressive mental retardation, blindness and death.

According to one researcher, "[p]atients who develop the progressive paralysis and dementia face one of mankind's most terrible diseases."[12]

These symptoms, often termed general paresis, result from a gradual loss of cortical function that may occur 10 to 20 years after an initial infection of syphilis in untreated patients. Patients suffering from these symptoms are deemed "paretics."

The Mechanisms for Fever

There is no clear answer as to why fever may benefit paretics' treatment. Some authors claim proteinaceous materials and vaccine-induced fevers are detrimental to the spirochetes that cause syphilis.

Others suggest even low-grade fevers will improve paresis without having a clear understanding of the cause and effect for inducing fever.[13] Another theory is a malaria-induced fever can cause alterations in the body's immunity or biochemistry.

Authors have argued induced fevers do not "cook" the organisms, because their thermal death point is about 41˚–42˚ C or higher for six hours. These temperatures are too high for patients to bear.[14]

Why Use Malaria?

Fever therapy was employed because drugs used to treat syphilis had been ineffective. Professor Wagner-Jauregg, in Vienna, may have been the first physician to treat syphilitic general paralysis of the insane (GPI) with malaria-induced fever. He was awarded the Nobel Prize in 1927 for his research.

Prior to this, GPI had been a killer. About 10% of all patients in mental hospitals in Britain were victims of the disease, and most would die a wretched, lingering death.[15]

Malaria initially was induced by administering venous blood from malaria-infected patients. Serious hazards were encountered due to a lack of awareness of certain human malaria parasites' lethal effects.

Colonel S. P. James, the first director of the Horton Laboratory in Britain, proposed a criterion to be met before a parasite strain could be considered safe for use in man. He was quite successful. His laboratory provided material for many thousands of GPI victims and some 16,000 patients in the Horton Hospital alone.[16]

All three species of human malaria (excluding the later accepted *Plasmodium ovale*) were available for therapeutic use in the 1920s: *P. malariae, P. falciparum* and *P. vivax*. The latter became the most widely used in malariatherapy, primarily because the infection was treated easily with quinine, and transmission by mosquito (used later) was relatively simple.[17]

There is no question about malariatherapy's efficacy. It spared thousands of paretics from horrible effects and premature death.[18]

However, with the advent of penicillin in the mid-1940s, it was obvious malariatherapy was being replaced slowly but inevitably. The final curtain, however, did not come down in Britain until the 1970s, and combined therapy with penicillin, once common in the US, ceased in the mid-1960s.[19,20]

When combination therapy was used, the two treatments were given concurrently or in succession. The basic course consisted of 3–10 million units of penicillin with a short course of fever therapy.[21]

A Few Surprises

In modern times, it would appear unlikely to find other instances where pathogenic organisms currently are used to treat a disease. Surprisingly, however, parasitic worms are being studied as Investigational New Drugs to ameliorate autoimmune diseases.

Eight studies now are listed on the US National Institutes of Health (NIH) website. Seven employ *Trichuris Suis ova* (pig whipworm) as treatment for multiple sclerosis, ulcerative colitis, autism, food allergy or Crohn's disease.[22] Fortunately, the porcine variety cannot survive inside the human body for very long.

Studies suggest helminths (parasitic worms) may ease the symptoms of autoimmune diseases by increasing mucus production.[23,24] The mucus production boost may help calm an excessively aggressive immune system. Production seems to correlate to a carbohydrate metabolism increase in the tissues where the helminths reside.

The other study on the NIH website, and even more strange, is one designed to inoculate celiac disease patients with human hookworm *Nector Americanus* to evaluate immunity and gluten sensitivity.

The second surprise relates to bloodletting. The procedure still is used to treat hemochromatosis and is the best method for removing excess iron from the body. One half-liter of blood is removed each week until the body's iron level is normal.[25] This may require many months or even years to accomplish.

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2

Pythons—A Model to Study Human Heart Disease?

Many of my previous articles for RAPS have featured a host of disparate animals that are or could be used in medicine or medical research, including leeches, maggots, rats, spiders, whipworms, Gila monsters and zebrafish. Now, there is new evidence Burmese pythons should be included on this distinguished list. This snake species may be used to develop drugs to treat human heart disease.[1] In anticipation of this event, it would be prudent to know more about Burmese pythons, their diet, their unusual digestive processes, why they were selected as a research tool and their possible therapeutic use.

Description

Burmese pythons (*Python molarus bivittatus)* are one of the six largest kinds of snakes in the world. They can weigh up to 200 pounds and can grow to great lengths. The largest pythons are always female; they can grow to be 13–18 feet long, while the smaller males typically grow to a maximum of 8–17 feet.[2]

According to one report, the record maximum length is 5.74 meters (18 feet, 10 inches).[3] Burmese pythons are dark colored with many brown blotches bordered in black down the back. The attractiveness of their skin contributes to their popularity with reptile keepers and the leather industry. They are native to a large number of tropical and subtropical areas of Southern and Southeast Asia.[4] Pythons are constrictors; therefore, they do not have fangs and are nonvenomous. Their back curving teeth are used to seize and hold their prey. Pythons have two lungs, one more than most snakes. This species lacks eyelids, but it does have a thin epidermal membrane covering the eyes to protect them. Pythons have small heat pits, or holes, in their upper lip that allow them to detect heat radiating from any animal nearby. They are able to smell with the aid of the "Jacobson's organ" in the roof the mouth. They dart their tongues in and out of their mouths to obtain gases in the air.[5] This gas detection method allows the python to catch its prey in light or dark conditions. Pythons do not have to eat very often and, for this reason, have proven invaluable in research.