Chaulmoogra Oil and the Treatment of Leprosy

by John Parascandola*

Leprosy is perhaps the most feared, and the most misunderstood, disease in history. Although we have drugs today to control the disease, and we now know that it is one of the least contagious of the infectious diseases, the stigma attached to leprosy has still not been completely erased from the public mind. The connotations associated with the word leprosy have even led to an effort to rename the condition Hansen's disease, after the man who discovered the bacterial cause of the disease in the nineteenth century. Not surprisingly, many different substances were tried in an effort to treat this disease over the centuries, almost all of them worthless before the introduction of the sulfones in the 1940s. A 1964 monograph on the disease summarized past treatment efforts as follows:

> "A search of the literature during the past one hundred years or more reveals that almost every type of drug has been used in the attempt to bring about a cure of this disease. Very few remedies advocated during the past thirty or forty years are really new remedies. They have been tried by some workers at one time or another. These remedies include potassium iodide, arsenic, antimony, copper, sera, vaccines, and aniline dyes."[1]

A quick perusal of the section on treatment in a 1925 book on the disease allows one to add another batch of failed remedies to the above list, including thymol, strychnine, baths of various kinds, X-rays, radium, and electrical currents.[2] The two distinguished authors of this volume then go on to discuss in some detail what they call the "one remedy which has been very generally recognized for many years as of value in leprosy, namely, Chaulmoogra oil.[3]

Chaulmoogra Oil Enters Western Medicine

Chaulmoogra oil entered Western medicine only in the nineteenth century, but it had been used in the East against leprosy and various skin conditions for many hundreds of years. One traditional story concerning the discovery of the use of the oil against leprosy is believed to be based on Burmese folklore. According to this tale, a Burmese prince contracted leprosy and was advised by the gods to withdraw from the world and to go into the forest to meditate. In the woods he was directed by the gods to a tree with a large fruit with many seeds. He was told to eat the seeds, which he did, and was thereupon cured of leprosy.[4] Another version of the origins of the oil attributes the discovery to Rama, who was once king of the Indian city of Benares (now Varanasi) but abdicated his throne in favor of his son because he had contracted leprosy. Rama went into isolation in the jungle, where he lived off herbs and roots. He especially ate the fruit and leaves of the *Kalaw* tree, which cured him of leprosy. Next he met a young woman named Piya, who was living in a cave in the jungle. Piya, an Indian princess, has also been banished to the jungle because she had leprosy. Rama cured her of the disease with the *Kalaw*, and took her for his wife. The miraculous *Kalaw* tree, according to the legend, belonged to the genus *Hydnocarpus*, several species of which are the source of Chaulmoogra oil.[5]

Whatever we think of this mythical explanation of the origin of the drug, it appears clear that Chaulmoogra oil has a long history in Asia. The oil was long used in traditional Ayurvedic medicine in India for the treatment of leprosy and various skin conditions. It seems to also have been used for the treatment of leprosy in other Asian countries such as China and Burma.[6]

The oil was introduced into Western medicine by British physician Frederic John Mouat in 1854. Mouat, who came from a family of army surgeons, took his medical degree at

Edinburgh in 1839. The following year he entered the Indian Medical Service, where he served for 30 years. From 1841 to 1853, Mouat was professor at the Bengal Medical College, and it was during this period that he first became acquainted with chaulmoogra oil. He had an opportunity to try the remedy himself when he became first Physician to the Medical College Hospital in Calcutta in 1853.[7] In an 1854 paper in the *Indian Annals of Medical Science*, he wrote:

> "It is with considerable reluctance that I venture to submit for consideration of the profession in India, a few remarks upon the Chaulmoogra, as the opportunities which I have hitherto had of employing it are too few and restricted to enable me to recommend it with the confidence that I could wish. Its success was, however, so remarkable and indisputable in one well-marked case of the worst form of leprosy, that I venture to hope an external application of it to that most loathsome and intractable of diseases, may prove so successful, as to secure the general introduction of the remedy."[8]

Mouat notes that the oil comes from the seeds of the fruit of the tree known by the natives as Chaulmoogra. The seeds are beat up with a clarified butter into a soft mass which is used in the treatment of cutaneous diseases. The seeds also yield by expression an oil with a peculiar and slightly unpleasant smell and taste. He goes on to say:

> "It appears to have been long known to, and prized by the Natives in the treatment of leprosy, and few of the faquirs traveling about the country are unacquainted with its properties. I was first informed of its properties by Mr. Jones, the Headmaster of the Hindoo College, a gentleman of eminent acquirements, who brought it to the notice of other practitioners in this city, and at whose recommendation it was tried at the Leper

Asylum, with a favorable result."[9]

Mouat decided to try the oil on two cases of leprosy in his ward. He dressed the external ulcers of the patients with the oil, and also gave it to them internally in the form of a pill, made by beating the seeds into a pulp. He reported that the ulcers healed and the patients improved. He believed that the results were sufficiently encouraging to justify further trials.[10] He admitted that the remedy required "much more extended employment before any sound judgement can be framed of its *modus operandi*, and probable value." He added that his main objective in publishing these "crude notes" was to call the remedy to the attention of the profession. The oil was cheap and readily procurable, and might turn out to be efficient in the treatment of a large "and not unimportant class of cases met with in all Indian hospitals." In this connection, he mentioned that he had sent a quantity of the oil to a hospital in China and to a hospital in the Mauritius to be tried against leprosy.[11]

Mouat indicates that the remedy and its use in cutaneous diseases was apparently first described by William Roxburgh under the name of *Chaulmoogra odorata*. In 1815, Roxburgh, a surgeon and naturalist, published a catalog of the plants in the East India Company's botanical garden in Calcutta. In this work, he mistakenly identified the seeds of the *Kalaw* tree, which according to the legend discussed above was a cure for leprosy, as those of the tree *Chaulmoogra odorata* under a different name.[12] The tree, indigenous to East India, was also known under the name of *Gynocardia odorata.* Throughout the 19th century, *Gynocardia* was believed to be the source of the seeds used to produce chaulmoogra oil. Then in 1901, Sir David Prain identified the true chaulmoogra seeds of the Calcutta bazaar and of the Paris and London drugs sellers as coming from the tree *Taraktogenos kurzii*, which grows in Burma and Northeast

India.[13] It appears that the chaulmoogra oil mentioned in early Ayurvedic texts, and available in South India, was from yet another tree. This tree, known as *Tuvakara* in Sanskrit, is *Hydnocarpus wightiana*, and is called "chaulmugra" in Hindu and Persian. It is a close relative of the *Taraktogenos* tree.[14]

Chaulmoogra oil was reintroduced as a treatment for leprosy in the Madras Leper Hospital in India in 1874. It had apparently been used there in the first half of the nineteenth century, but then abandoned for some reason. Although the oil continued to find some use, especially in India, it was not until the turn of the twentieth century that the remedy began to receive more attention from the medical profession in Europe and the United States.[15]

F. B. Power and the Chemistry of Chaulmoogra

Although there had been some work in the nineteenth century on the chemical constituents of chaulmoogra, the first comprehensive chemical analysis of the remedy was carried out by Frederick B. Power and his colleagues at the Wellcome Chemical Research Laboratories in London in the first decade of the twentieth century. Power had begun his career as a pharmacist, obtaining his pharmacy degree from the Philadelphia College of Pharmacy in 1874. After working for two years in the Philadelphia pharmacy of Edward Parrish, he went to Germany to undertake graduate studies. In 1880, he received his Ph.D. from the University of Strassburg for a thesis in plant chemistry under the direction of the eminent pharmacognosist Freidrich Flückiger. Upon returning to the United States he served for a year as professor of analytical chemistry at the Philadelphia College of Pharmacy before being called to the University of Wisconsin in 1883 to establish a school of pharmacy there.

Power served for ten years as head of the pharmacy program at Wisconsin, placing the new school on a sound scientific footing and establishing a tradition of research. He left Madison in 1892 to become scientific director of the newly-established laboratories of Fritzsche Brothers of New Jersey, a firm devoted to the production of essential oils and fine organic chemicals. Over the next few years he published a series of important chemical studies on essential oils such as those of peppermint, cloves, bay, and wintergreen. Tragedy struck in late 1894 when Power's wife died after the birth of their third child, a son who himself lived for only a few days.[16]

Soon thereafter, Power's old friend and pharmacy school classmate, Henry Wellcome , contacted Power and offered him a job. Wellcome had left the United States in 1880 to partner with fellow American Silas Burroughs in founding the pharmaceutical firm Burroughs Wellcome and Company in London. After the death of Burroughs in 1895, Wellcome became the sole proprietor of the firm. Wellcome had always been more interested in scientific and medical research then his partner, and already in 1894 he had established the Wellcome Physiological Laboratories. Anxious to expand into chemical studies, Wellcome convinced Power to join the firm in 1896 to direct the newly-established Wellcome Chemical Research Laboratories.[17]

In London, Power continued his researches in plant chemistry. In 1904, Power obtained a large quantity of fresh Chaulmoogra seeds from a London market and decided to make a complete investigation of the seeds. He identified the seeds as coming from the *Taraktogenos Kurzii*. The shells were separated from the seeds, and the kernels were then subjected to hydraulic pressure yielding an oil. A residual "press-cake" was left behind. Each of the three components into which the seeds had been separated, the shells, the oil, and the "press-cake"

made up about a third of the overall weight of the seeds.

Power and his colleagues subjected the oil and the press-cake to further chemical procedures, and isolated a number of compounds from these products. One of these was a new unsaturated fatty acid, isolated from the oil, which they named Chaulmoogric acid. The acid was shown to have the formula $C_{18}H_{32}O_2$.[18]

The Wellcome investigators next turned their attention to two species of the *Hydnocarpus* tree which belonged to the same natural order as *Taraktogenos*, and which had also been long used in Western India and China for the same purposes as which chaulmoogra oil was employed. These species were *Hydnocarpus Wightiana*, mentioned above, and *Hydnocarpus anthelmintica*.

From the seeds of these trees, Power and his colleagues isolated fatty oils which were very similar in physical characteristics and chemical composition to Chaulmoogra oil. When they subjected the oils from these two trees to further chemical analysis, they obtained Chaulmoogric acid and a lower homologue of the same series. The new acid had the formula $C_{16}H_{28}O_2$ and was named Hydnocarpus acid.[19] Power's laboratory also went on to investigate the seeds of *Gynocardia odorata*, which (as mentioned above) had long been erroneously believed to be the source of the Chaulmoogra oil of commerce. The Wellcome group was able to clearly demonstrate that the oil from this tree was not Chaulmoogric oil and contained neither Chaulmoogric nor Hydnocarpus acids.[20]

Power's group had thus established that two species of *Hydnocarpus* are sources of Chaulmoogra oil, in addition to the *Taraktogenos* (later called *Hydnocarpus kurzii*) tree. They found that the oil from all three of these species yields two significant acids, which they named

Chaulmoogric acid and Hydnocarpus acid, and they determined the chemical composition of these acids. They also confirmed that *Gynocardia odorata* was not a source of the oil. The two fatty acids and their derivatives were to come to play a significant role in the treatment of leprosy over the next few decades, and so their isolation and the determination of their chemical formulae were important contributions.

The Administration of Chaulmoogra

The question of the best form in which to administer Chaulmoogra oil and its derivatives was one that troubled physicians who treated leprosy for some time. Originally the oil was either applied topically to leprous areas on the body or taken internally. External application had only limited value in treating the disease. Although oral administration of the remedy was more effective, this procedure was complicated by the fact that effective does of the oil tended to have a very nauseating effect on the patient. The effectiveness of the drug was limited by the digestive tolerance of the patient.[21] As one U. S. Public Health Service doctor reported in his autobiography, many patients would tell him, "Doctor, I'd rather have leprosy than take another dose."[22]

At the Louisiana Leper Home in Carville, Louisiana, the use of orally-administered Chaulmoogra oil, in the form of drops, was begun in 1901 by Isadore Dyer.[23] In 1916, the attending physician at the Home, Ralph Hopkins, reported on the results of 170 patients treated with Chaulmoogra oil. He divided these patients into two categories, incipient cases and advanced cases. With the 82 incipient cases, Hopkins reported results as follows: 17% discharged cured; 4% lesions disappeared; 24% improved and remaining at the Home; 24%

absconded in improved condition; 8% worse; and 4% died. His results were less favorable with the advanced cases, where there were no cures and only about a quarter of the patients showed improvement or arrest.[24]

In the last decade of the nineteenth century, some clinicians began experimenting with the administration of the oil by intramuscular or subcutaneous injections. This method eliminated the nausea caused by oral administration of the drug, but could be very painful. The injections often produced severe local reactions and fever. In the early years of the twentieth century, a physician of the United States Public Health Service, Victor Heiser, found a way to diminish the pain and irritation caused by injection, as well as to secure greater absorption of the oil.[25]

Heiser was a career Public Health Service Officer who was serving as the Chief Quarantine Officer and Director of Health for the Philppine Island at the time of this work. Chaulmoogra oil had been used at the San Lazaro Hospital for lepers in Manila since the early years of the American occupation of the Philippines, but with limited success. In 1908, Heiser visited the Louisiana Leper Home and gained a favorable impression of the treatment of leprosy with Chaulmoogra oil that was being carried out there. From Ralph Hopkins and Isador Dyer, Heiser learned better techniques for the oral administration of the oil. Upon his return to the Philippines, he arranged for the Louisiana method to be given a thorough trial at the San Lazaro Hospital in Manila under the immediate charge of the house physician, Elidoro Mercado.

The new method, which was initiated at San Lazaro in 1909, was much more successful than the former one, but still oral administration of the oil resulted in nausea and patient resistantance to taking the drug. The physicians tried various methods to solve this problem, such

as coating the Chaulmoogra capsules with various substances and giving the oil by enema, but the results were unsuccessful. A review of the literature revealed that some physicians had tried hypodermic injection. So the hypodermic method was tried at San Lazaro, but it did not work well because the oil was not satisfactorily absorbed. Heiser then wrote to Merck and Company in Germany to ask if they could suggest a substance that might increase the absorption of the oil when injected. The company replied that it had no definite knowledge on the subject, but that theoretically the addition of camphor or ether might have the desired result.[26]

Heiser and Mercado decided to add camphor to a prescription of Chaulmoogra and resorcin which was typically given orally. To their great joy they found that the camphor-resorcin solution of Chaulmoogra was readily absorbed.[27] Heiser wrote in his autobiography years later about the excitement of the first case treated:

> "Few can imagine with what a thrill we watched the first case to which chaulmoogra was administered in hypodermic form, how we watched for the first faint suspicion of eyebrows beginning to grow in again and sensation returning to paralyzed areas. We took photographs at frequent and regular intervals to compare progress and to check on our observations, fearing our imagination might be playing tricks upon us..."[28]

Heiser published an account of the first two cases in *Public Health Reports* in 1913. These two patients had apparently been cured of the disease, i.e., leprosy bacilli were no longer found on clinical and microscopical examination, and were both released on probation. Because these patients were treated with a vaccine as well as the Chaulmoogra oil, the results were compromised.[29] The following year, Heiser published an account of two more cases who had been successfully treated with Chaulmoogra oil by hypodermic injection and released, and this

time there was no other treatment given so that the results were clear.[30] In a supplement to the 1914 volume of *Public Health Reports*, Heiser reported on 12 more cases. The results were encouraging, but not definitive. Three of the patients stopped the treatment before any improvement could be seen. Of the remaining nine patients, one was considered microscopically negative and cured, four had progressed to the point where clinical evidence of the disease had practically disappeared, three showed marked improvement, and one showed only slight evidence of improvement.[31] Heiser concluded:

> "The present stage of development of the treatment herein described does not warrant a claim that anything like a specific for leprosy has been found, but experience does show that it gives more consistently favorable results than any other that has come to our attention, and it holds out the hope that further improvement may be brought about. It produces apparent cures in some cases, causes great improvement in many others, and arrests the progress of the disease in almost every instance."[32]

However, Heiser later stated that he was not completely satisfied with the continuing results. He thought that the treatment was too slow, and he admitted that "after the first flush of excitement, the interest of doctors, nurses, and patients all began to wane." The Public Health Service doctor recognized the need for a more effective cure.[33]

In 1915 Heiser visited Calcutta, India and met Sir Leonard Rogers of the Indian Medical Service. Heiser told Rogers about his results with Chaulmoogra oil, and learned that one of Rogers' patients had nearly recovered from leprosy when treated with large does of gynocardic acid (a mixture of fatty acids from Chaulmoogra oil). The acid seemed to be better tolerated by patients and more efficient than the oil itself. Rogers was apparently contemplating retiring and

returning to England, but Heiser convinced him to remain in India and continue his work with Chaulmoogra.[34] Rogers later recalled the next steps:

> "With the help of the Medical College Professor of Chemistry, Dr. Chuni Lal Bose, the soluble sodium salt or soap of gynocardic acid was made, which was easily soluble in water. From July 31, 1915 onwards, it was injected subcutaneously in a 3 per cent soultion in leprosy patients with only slight local induration and pain...By the end of the year I had satisfied myself that a definite advance had been made..."
>
> "Progress was still slow and rather painful, so I next ascertained by means of a few painless animal experiments that sodium gynocardate could safely be injected intravenously (1916). It soon became apparent that by this route the drug was also more effective, so that a further advance had been made."[35]

Heiser claimed that on a visit to Hawaii, he alerted the authorities at the leper colony on Molakai to the work done in India, and suggested that they follow up on this research in the laboratory.[36] Whether or not it was actually Heiser who stimulated the effort, research on the treatment of leprosy with Chaulmoogra derivatives was undertaken in Hawaii at about this time. The sequence of events leading to the next development in the Chaulmoogra story, namely the introduction of ethyl esters derived from the oil, is not entirely clear. It appears, however, that the work was begun by a young African-American woman named Alice Ball at the suggestion of Dr. Harry Hollmann, who was an Acting Assistant Surgeon at the Leprosy Investigation Station of the U. S. Public Health Service in Hawaii. It is possible that Hollmann learned of the work done in India through his Public Health Service colleague Victor Heiser, whether on his visit to Hawaii (the date of which is not known) or via some other contact.

Alice Ball was the first woman to earn a masters degree in science from the College of Hawaii in 1915, for a thesis dealing with the chemical constituents of *Piper methysticum*. She was then appointed to teach chemistry at the College of Hawaii. Either during her graduate work or shortly thereafter, she took up Hollmann's suggestion to experiment with the chemistry of Chaulmoogra oil. Ball unfortunately became ill and died at the very young age of 24 on December 31, 1916. Her work on Chaulmoogra was then taken up by her supervisor, Arthur Dean, head of the College of Hawaii's chemistry department (and later the College's President).[37] Since Ball did not have an opportunity to publish any of her research, it is not certain exactly how far she got on the problem. Dean and his coauthors do not credit Ball for any of the work that they reported in a series of publications on Chaulmoogra between 1920 and 1922, but in an article in a medical journal in 1922, Hollmann clearly gives her credit for the discovery.

> "About the time that Rogers and Ghosh were starting their investigations in India, in Hawaii I interested Miss Alice Ball, M.S., an instructress in chemistry at the College of Hawaii in the chemical problem of obtaining for me the active agents in the oil of chaulmoogra."
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> After a great amount of experimental work, Miss Ball solved the problem for me by making the ethyl esters of the fatty acids found in chaulmoogra oil, employing the technic herewith described."[38]

Hollmann then goes on to described the preparation of the esters by "Ball's Method." Stan Ali has led an effort in Hawaii to gain recognition for Ball for this work, and a plaque in her honor was placed on the campus of the University of Hawaii-Manoa in 2000 commemorating her

work on Chaulmoogra. [39] Nevertheless it was Dean and his coworkers who published on the subject and received credit for the work They reported that they had investigated the fatty acids of Chaulmoogra oil with the intent of trying to find a suitable form of the material for injection which would allow rapid absorption into the circulation. They stated that they found that the ethyl esters of the acids were thin fluid oils that lent themselves readily to intramuscular injections and were readily absorbed. They also described their methods for preparing the esters.[40] The ethyl esters came to be referred to as Dean's derivatives. [41]

Clinical trials were then carried out by Dean with the collaboration of J. T. McDonald, Director of the Public Health Service Leprosy Investigation Station and Superintending Physician to Kalihi Hospital in Honolulu. The esters were given in conjunction with other means of treatment, such as iodine, but eventually were given by themselves.[42] The results were encouraging, with 94 patients being "paroled" from the hospital in fiscal year 1921, although it was recognized that follow-up of these patients would be necessary to insure that the improvement was permanent rather than temporary. In the 1921 annual report of the Public Health Service, the report on the leprosy work in Hawaii stated that:

> "A few paroled patients going to their homes and describing the therapeutic and administrative methods of the station, has had a greater effect in inducing sufferers from leprosy to seek treatment than all the legal requirements or scientific discussions that can be invoked."
>
> "The morale of the patients in the hospital is excellent and in striking contrast to that of former days, when a leprous person was doomed to a long term of isolation, in most cases to be terminated only by death. All patients are zealously cooperating with the

authorities of the hospital, intent upon becoming free of their afflictions and returning to their homes as useful members of society."[43]

The report went on to indicate that chaulmoogra oil derivatives (presumably the esters of the fatty acids) were being furnished by the Public Health Service to medical authorities in a variety of counties, from Bombay to China to Ecuador.

Hunting the Chaulmoogra Tree

As the use of Chaulmoogra oil and its derivatives became more widespread, the demand for the oil increased. Concern about having an adequate supply of the oil led David Fairchild, head of the Division of Foreign Seed and Plant Introduction, Bureau of Plant Industry, U. S. Department of Agriculture to take action to prevent a shortage. For assistance, Fairchild turned to Joseph Rock, Professor of Systematic Botany at the College of Hawaii. Rock described his mission and the reasons for it as follows:

"Owing to the high price of the oil on the United States and the probable scarcity of it in the near future, due to is successful application in the treatment of leprosy in Hawaii, I was authorized by the U. S. Department of Agriculture to obtain seeds of this species, to be introduced into Hawaii and our tropical possessions, with a view to establishing Chaulmoogra plantations."[44]

Rock was born in Vienna, Austria in 1884. From early on he showed an interest in foreign lands and languages, and learned Arabic and Chinese while still a boy. After he graduated from the University of Vienna, he wandered around Europe for a time. In 1905, he traveled to the United States, settling briefly in New York. His health then forced him to seek a

warmer and drier climate, so he soon moved to Texas, where he undertook further university studies to improve his English. In 1913, he became an American citizen.

Meanwhile, Rock had moved to Hawaii in 1907, where he taught school for a time. The following year he joined the Division of Forestry of the Board of Commissioners of Agriculture and Forestry for the Territory of Hawaii. Rock joined the faculty of the College of Hawaii and was placed in charge of its herbarium in 1911. Over the next few years he traveled to various parts of the world, collecting seeds and plants.[45]

Rock had always had a desire to travel in the Orient, and he got his opportunity when the Department of Agriculture asked him to go to Indo-China, Siam, Burma, and India to find seeds of the Chaulmoogra tree. He first came across a genuine Chaulmoogra tree in Burma, but is was not in fruit, so he could not collect any seeds. With the help of local villagers, he was finally led to a nearby forest with many Chaulmoogra trees bearing fruit, and he was able to collect a large number of seeds. The seeds were then shipped to the United States, and eventually used to establish a plantation of 2,980 trees on the island of Oahu, Hawaii in 1921-1922.[46]

The Fall Of Chaulmoogra

Chaulmoogra oil probably reached its height of popularity as a treatment of leprosy in the 1920s and 1930s. The oil, or perhaps more commonly the esters of its acids, had become the treatment of choice at facilities such as the Public Health Service leprosy hospital at Carville, LA, which had taken over the Louisiana Leper Home in 1921. Stanley Stein, who had entered the Carville hospital as a patient in 1931, recalled taking the oil for years without being cured of the disease, although he believed that it had once cleared up a cluster of nodules on his temple.

He wrote of his experiences with the drug at Carville at follows:

> "Whether I was to take the oil externally, internally, or - as someone once said - eternally, was up to me. The oral doses were nauseously given out in the cafeteria at mealtime. The injections were administered in what to me was a distressingly public manner...the after effects were sometimes frightful - painful suppurating abscesses which would generate in the patient's backside...I was hospitalized several times with chaulmoogra-induced, rear end ulceration."[47]

Even given the advances that had been made with Chaulmoogra, it was obviously not an ideal treatment for leprosy. Side effects still created problems, treatment was extended, and there was disagreement about how effective it really was. Although there were numerous reports in the literature about the drug's efficacy and many physicians swore by it, others were skeptical about the therapeutic claims made for the drug. Then Director of the National Institute (later Institutes) of Health George McCoy, who had once headed the Leprosy Investigation Station in Hawaii and supported the use of Chaulmoogra, had by 1942 come to doubt its therapeutic value. He published an attack on the drug in that year, noting that many experienced students of the disease expressed serious doubts about the value of the oil in treating leprosy, especially when discussing the subject in private. He quoted (anonymously) the views of four experts in leprosy whom he had consulted, all of them critical about the effectiveness of the drug.[48]

The downfall of Chaulmoogra came about through the introduction of the sulfones to treat leprosy in the 1940s. Public Health Service Officer Guy Faget, Medical Director of the Carville hospital, was able to demonstrate through clinical trials the effectiveness of sulfone drugs against the disease. In 1947, Chaulmoogra oil therapy was officially abandoned at

Carville, and the sulfones became the treatment of choice. The sulfones also eventually led to a change of policy from one of isolation of leprosy victims to one of outpatient treatment with drugs. As early as 1948, the Carville hospital began to allow, under certain conditions, the medical discharge of patients who were still in the so-called "communicable state" (i.e., who were not bacteriologically negative).[49] As for Chaulmoogra oil, by the 1950s it had essentially become just a colorful relic of pharmacy's past.

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24. Ralph Hopkins, "Observations on the Treatment of Leprosy with Special Reference to Chaulmoogra Oil," *New Orleans Med. Surg. J.* 69 (1916-1917): 223-232.

25. Rogers and Muir, *Leprosy*, p. 255.

26. Heiser, *American*, pp. 250-251; Victor Heiser, "Leprosy. Its Treatment in the Philippine Islands By the Hypodermic Use of a Chaulmoogra Oil Mixture," Supplement No. 20 to *Pub. Health Rep.*, volume 29, 1914, p. 23. Excerpt of this supplement were also published in *Pub. Health Rep.* 29 (1914): 2763-2767 because of the "general interest" of the conclusions.

27. Heiser, *American*, p. 250.

28. *Ibid*., p. 251.

29. Victor Heiser, "Leprosy. A Note Regarding the Apparent Cure of Two Lepers in Manila," *Pub. Health Rep.* 28 (1913): 1855-1856.

30. Victor Heiser, "Leprosy. Treatment of Two Cases with Apparent Cure," *Pub. Health Rep.* 29 (1914): 21-22.

31. Heiser, "Leprosy. Its Treatment in the Philippines." There appears to be an error in the statistical summary on p. 22, but the net results shown in percentage terms and a review of the 12 individual cases confirms the figures I have given.

32. *Ibid.*, p. 25.

33. Heiser, *American*, p. 251.

34. *Ibid*., p. 251; Leonard Rogers, *Happy Toil: Fifty-Five Years of Tropical Medicine* (London: Frederick Muller, 1950), pp. 189-193; lecture by Leonard Rogers as quoted in Frank Oldrieve, *India's Lepers: How to Rid India of Leprosy* (London: Marshall Brothers, 1924), pp. 77-78.

35. Rogers, *Happy Toil*, pp. 190-191.

36. Heiser, *American*, pp. 251-252.

37. Charles J. Dutton, *The Samaritans of Molokai: The Lives of Father Damien and Brother Dutton Among the Lepers* (New York: Dodd, Mead, 1932), p. 231; Susan Kreifels, "Alice Ball Made a Stunning Find in Her Early 20s," *Honolulu Star-Bulletin*, February 18,2000; Susan Kreifels, "Ground Breaking African-American UH Chemist Finally Recognized," *Honolulu Star-Bulletin*, March 1, 2000. The *Star-Bulletin* is online at starbulletin.com. See also n. 36.

38. Harry T. Hollmann, "The Fatty Acids of Chaulmoogra Oil in the Treatment of Leprosy and Other Diseases," *Arch. Dermatol. Syph.* 5 (1922): 94-101, p. 95. I am grateful to Margaret Brynes and Karen Sinkule of the National Library of Medicine for assistance in locating the journal volume and obtaining a copy of this article for me when the volume had been removed from the shelves for microfilming.

39. Kreifels, "Ground Breaking."

40. See, for example, Arthur L Dean and Richard Wrenshall, "Fractionation of

Chaulmoogra Oil," *J. Amer. Chem. Soc.* 42 (1920): 2626-2645; Arthur L. Dean and Richard Wrenshall, "Fractionation of Chaulmoogra Oil," *Pub. Health Rep.* 36 (1921): 641-660; Arthur L. Dean and Richard Wrenshall, "Preparation of Chaulmoogra Oil Derivatives for the Treatment of Leprosy," *Pub. Health Rep.* 37 (1922): 1395-1399.

41. See, for example, G. L. Hagman, "On the Treatment of Leprosy with Dean's Derivatives of Chaulmoogra Oil," *China Med. J.* 37 (1923): 568-571; J. T. McDonald, "Treatment of Leprosy with the Dean Derivatives of Chaulmoogra Oil," *J. Amer. Med. Assoc.* 75 (1920): 1483-1487.

42. J. T. McDonald and A. L. Dean, "The Treatment of Leprosy. With Especial Reference to Some New Chaulmoogra Oil Derivatives," *Pub. Health Rep.* 35 (1920): 1959-1974; J. T. McDonald and A. L. Dean, "The Constituents of Chaulmoogra Oil Effective in Leprosy," *J. Amer. Med. Assoc.* 76 (1921): 1470-1474.

43. *Annual Report of the Surgeon General of the Public Health Service of the United States*, 1921, p. 79. For further information on the Public Health Service leprosy investigations in Hawaii, see O. A. Bushnell, "The United States Leprosy Investigation Station as Kalawao," *Hawaiian J. Hist.* 2 (1968): 76-94; Jerrold M. Michael, "The Public Health Service Leprosy Investigation Station on Molokai, Hawaii, 1909-13 - An Opportunity Lost," *Pub. Health Rep.* 95 (1980): 203-209.

44. J. F. Rock, "Hunting the Chaulmoogra Tree," *Nat. Geog.* 41 (1922): 242-276, p. 242.

45. For biographical information on Rock, see Alvin K. Chock, "Joseph F. Rock, 1884-

1962," *Amer. Horticul. Mag.* 42 (1963): 158-167; Mike Edwards, "Our Man in China: Joseph Rock," *Nat. Geog.* 191 (1997): 65-81.

46. Rock, "Hunting;" Chock, "Rock," p. 162. See also Norman Taylor, *Plant Drugs that Changed the World* (Dodd, Mead: 1965), pp. 219-227.

47. Stanley Stein (with Lawrence G. Blochman), *Alone No Longer: The Story of a Man who Refused to Be One of the Living Dead* (New York: Funk and Wagnalls, 1963), pp. 38-39.

48. G. W. McCoy, "Chaulmoogra Oil in the Treatment of Leprosy," *Pub. Health Rep.* 57 (1942): 1727-1733.

49. For the story of the discovery of the sulfones, see John Parascandola, "Miracle at Carville: The Introduction of the Sulfones for the Treatment of Leprosy," *Pharm. Hist.* 40 (1998): 59-66.

[captions for photos - Chaulmoogra oil paper]

A man holds the fruit of the Chaulmoogra tree (courtesy of The Leprosy Mission International).

Preparing Chaulmoogra oil, 1928 (courtesy of The Leprosy Mission International).

Administering Chaulmoogra oil by injection (courtesy of The Leprosy Mission

International).

A bottle of Chaulmoogra oil manufactured by Parke, Davis (from the G. W. Aimar Collection of the National Museum of American History, Smithsonian Institution).