

# Arthur E. Guedel Memorial Anesthesia Center

## “White Water and Black Magic”—70 Years Later

*By Merlin Larson, M.D.*

Over the 165 years since the discovery of anesthesia, new inventions and drugs related to the practice of anesthesia have grown to a sizable number. Forced-warm-air blankets, cerebral function monitors, pulse oximetry and laryngeal mask airways are recent examples. Private enterprise, legal patent protection and royalties have been good for the specialty of anesthesia and for individuals with new ideas.

However, for every success story there are probably 10 innovations that fail. Failure can be financial or scientific or both. Some ideas are doomed to failure because they are not founded upon sound physiology. Other ideas are completely valid and eventually successful, but the financial reward does not accrue to the individual with the original idea. Horace Wells and William T. G. Morton are examples. Both individuals came up with original ideas, but neither one profited from his innovation, even though their ideas had profound effects on the practice of medicine.

Richard C. Gill had original ideas that eventually developed into the widespread use of muscle relaxants during general anesthesia. It has been 70 years since the publication of Gill's book “White Water and Black Magic,” and it seems appropriate to look back on his original ideas and the rewards that came to him as a result of his ambitious project of exploration into the treacherous depths of the South American jungle.



**Figure 1:** Richard C. Gill and his wife Ruth Gill at their hacienda outside Baños, Ecuador, circa 1931. Gill arranged package tours from New York City for parties interesting in visiting Rio Negro—the “First Dude Ranch in South America.” Copyright material from the Guedel Library, printed by permission.

Gill was educated to be an instructor in English. Having a penchant for adventure, he worked briefly on a whaling station in the South Georgia Sea, then secured a position in Lima, Peru, working as a salesman for a rubber company. After the 1929 stock market crash, Gill lost his position and spent the next few years attempting to establish the first South American dude ranch in Ecuador, just east of Baños. As he was returning to the United States in 1934, he fell from his horse and suffered a severe neurological complication that resulted in a prolonged convalescence, accompanied by chronic painful muscle spasms.

His neurologist, Dr. Walter J. Freeman (eventually of ice-pick lobotomy fame—see *CSA Bulletin*, Spring 2008, pages 56–60), suggested that his spasms might be alleviated by small doses of the deadly arrow poison curare. However, in 1932, Ranyard West had published an article (*Proc Roy Soc Med* 25:1107, 1932) on the use of curare in spastic diseases, which concluded that it was of very little benefit and had undesirable side effects. Numerous investigators had also tried curare, without success, as therapy for tetanus, convulsive disorders and muscle spasms. So by 1936, when Gill was planning his proposed adventure, successful clinical use should have seemed very unlikely.

Nonetheless, Gill spent the next few years planning a costly and ambitious expedition into the tributaries of the Amazon River in order to extract a large quantity of curare and other jungle remedies that, he hoped, could be developed into commercial products. The expedition eventually started off in May 1938.

During his 1938 expedition, Gill and his wife faced risks from tropical diseases as well as from the Jivaro Indians. In the 1930s the Jivaro were known to murder strangers. Gill was suave, persuasive and confident. He understood the natives' culture and respected their beliefs. Even though he was still partially crippled from his spastic condition, the couple returned to the U.S. in December 1938 with 75 specimens of jungle remedies and 25 pounds of crude curare. However, Gill was unable to interest the medical profession in any of his "black magic" remedies. This is not surprising given the economic and political climate of the late 1930s. The threat of war with Germany and Italy was on the minds of the American populace, and the Great Depression still had a negative influence on economic activity. Capital was essentially nonexistent, and innovations such as Gill proposed would have seemed reckless to most investors.

Gill captured his adventure on 16 mm film, some in color. On his return he had it edited into a one-hour film, "White Water and Black Magic," which he used on his lecture tours. It is a fascinating account of this very first step on our 70-year-old journey into the wondrous realm of muscle relaxants. Upon Richard Gill's death, his widow donated the films to the Guedel Center. In 2002, the

## Guedel Center (cont'd)

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Health Sciences Library at California Pacific Medical Center, on behalf of the Arthur E. Guedel Memorial Center Archives, received a grant from the National Film Preservation Foundation to clean and preserve Gill's original 16 mm film. It can now be seen on DVD, by appointment, at the Guedel Center.

For 10 months after his return, Gill must have thought his entire adventure was a total waste of energy, time and money. Luckily for him, Abram E. Bennett (a psychiatrist who was a friend of Walter Freeman) wrote a short note to Squibb and Co. in October 1939: "I think we are onto something with curare." He had found a use for the drug in the prevention of bone fractures during Metrazol-induced convulsive therapy for schizophrenia. Thus by the time Gill's book "White Water and Black Magic" was printed in 1940, many of Gill's apprehensions had been assuaged, and he was highly confident that his plant therapies would succeed.

However, even though Harold Griffith in 1942 demonstrated the use of curare in anesthesia, Gill was unable to gain any significant economic return from a more widespread demand for the drug. Squibb and Co. had Gill's supply of the plant product, but within a few years other drug companies had procured the drug from alternative sources in South America. A major development came through the effort of the French chemist Daniel Bovet, who studied the molecular structure of curare and devised the synthetic drugs decamethonium and gallamine (Flaxedil). These agents were introduced in 1949, and thus the demand for the plant product slowly abated.

Gill was essentially a businessman motivated by a potential for profit that never materialized. He might have thought himself an anthropologist, but subsequent studies on the Jivaro Indians of Peru and Ecuador revealed the naïveté of his opinions. Michael Harner, considered the authority on the culture of the Jivaro in the mid-20th century, did not even mention Gill's experiences in the extensive bibliography of his 1957 book entitled "The Jivaro: People of the Sacred Waterfalls." Gill was also an amateur ethnobiologist/ethnobotanist, but his enthusiasm for the remedies of the native population was apparently overly optimistic. "White Water and Black Magic" contains an extensive discussion of jungle therapies for several diseases, but none of these has found acceptance in the 70 years since.

By 1946, Burroughs Welcome had produced the pure alkaloid, Interostrin (their trade name for curare), and Gill and Squibb lost the lead in commercialization of the agent. However, a closer look at material in the Guedel archives reveals Gill's unremitting search for a more lucrative breakthrough. From our perspective as anesthesiologists, it seems that he did achieve an important clinical breakthrough, but alas, he was not a clinician and his letters reveal that

he considered the applications of curare in the field of anesthesia as having limited potential. His more abiding interest was in using curare and other jungle drugs as medication for other diverse ailments that would have a wider use in the general population. Gill was convinced that there was an important use for curare, perhaps particularly in treating anxiety states associated with muscle tension.



**Figure 2:** The staff at Cugill Laboratories July 27, 1949. The project to develop a slow-release form of curare failed without ever developing a commercial product. Gill is in the back row on the left and his wife Ruth is sitting in the front row on the right. Copyright material from the Guedel Library, printed by permission.

Together with the chemist George I. Dundee, Gill formed a new company called Cugill Laboratories with headquarters at 3839 El Camino Real in Palo Alto (Figures 2 and 3). (The building is still there, but it has been redesigned into an in-and-out oil change business.) Cugill's product, called Tubalex, was made with curare, peanut oil, beeswax and cholesterol. The Guedel archival papers contain Gill's correspondence with the FDA to obtain approval for the distribution of Tubalex, but in 1956 Richard Gill died, and the product expired with him. Thus, as with Wells and Morton before him, Richard Gill's struggle to succeed did not lead to financial success, but the end result was an enormous benefit to our profession. Most historians of our specialty agree that without Gill's persistence in promoting the use of curare paste, our use of paralytic agents would have been delayed by several years, perhaps decades.



**Figure 3:** George Dundee working in the Cugill Laboratory at 3839 El Camino Real in Palo Alto. Gill invested his own capital in the project. The ingredients of the slow-release product are extensively documented in the Guedel Archives. Copyright material from the Guedel Library, printed by permission.

Gill's foresight and intelligence are evident in the following passages from the preface to "White Water and Black Magic":

*The part played by doctors and research men in the development of curare therapy is, of course, incalculably important. The story probably will be told more than once in the years to come, as curare comes to occupy the vital place in the medicine of the future which I am sure it is going to take. . . .*

*"Functional" exploring is a valuable thing. The particular corner of the wilderness world of the tropics which I happen to know fairly well still has a number of major contributions to make to civilized society. The jungle pharmaceuticals which I have been lucky enough to study off and on for a good many years is not, as a lot of people assume, purely a matter of superstition and primitive quackery. Savages are apt to know a good many things we do not, and their "magic"—which I have tried to explain as a part of their life-pattern—is usually founded upon substantial verity. The function of exploration, it seems to me, is to discover those verities and whenever possible contribute their values to civilization.*