

History of Hoxsey Treatment

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Explanatory note: In 1988, the Office of Technology Assessment (OTA) of the United States Congress commissioned the following "contract report" as a background paper to aid in its consideration of the Hoxsey Therapy. The OTA, at the request of Congress, was the first Federal agency to review the Hoxsey Therapy and other major unconventional or alternative cancer treatments during a five year long process that resulted in the OTA's 1990 publication Unconventional Cancer Treatments.

For its review of Hoxsey, the OTA staff turned to the late Patricia Spain Ward, PhD, a widely published academic medical historian who, at the time, held the position of Historian of the University of Illinois at Chicago.

In the midst of the highly charged, politicized environment that enveloped the OTA's cancer study, Ward brought her considerable skills, and a refreshingly open and fair mind, to the challenging task that faced her. The May 1988 report that follows is a landmark piece of work -- nothing less than a truly revolutionary document -- in the history of both the Hoxsey Therapy and the field of unconventional or alternative medicine in general.

The cancer treatment practiced by Harry M. Hoxsey (1901-1974) is one of the longest-lived unconventional therapies of this century. It has retained great popular appeal, despite unrelenting opposition by the medical profession; despite 40 years of biting journalistic ridicule by such skilled AMA journalists as Arthur Cramp and Morris Fishbein; despite an unceasing stream of court actions; even despite an unprecedented "Public Warning Against Hoxsey Cancer Treatment" which the Commissioner of the FDA ordered mounted in 46,000 US post offices and substations in 1956 (Young, 1967, 387; Larrick, 1956). Since Hoxsey's death, his treatment has continued under his longtime nurse assistant, Mildred Nelson, [RN,] who currently oversees the thriving Bio-Medical Center at Tijuana, within sight of the border between Mexico and the United States. (Hoxsey himself chose this site in 1963, when his heart had begun to fail and the combined pressures of organized medicine and the FDA had finally closed down his last operation in the US [Chowka, 1984; New York Times, 1955].)

An Illinois coal miner before he began to promote himself as a healer in the 20s, the colorful, dynamic Hoxsey mixed his medicine with flamboyant public statements that

skillfully contrasted his populist heritage with the growing elitism and *hauteur* of the American medical profession at mid-twentieth century (Young, 1967). In common with many advocates of unconventional therapies, Hoxsey considered cancer a systemic disease, however localized its manifestations might appear to be. Hence his therapy aims to restore "physiological normalcy" to a disturbed metabolism throughout the body, with emphasis on purgation, to help carry away wastes from the tumors he believed his herbal mixtures caused to necrotize (Hoxsey, 1956, 44-48, 60).

Hoxsey treated external cancers apparently with considerable success, even in the judgment of his critics, with local applications: sometimes by a red paste containing antimony sulfide, bloodroot (*Sanguinaria canadensis*) and zinc chloride; sometimes by a yellow powder containing arsenic and antimony sulfides, various plant substances, talc, and what Hoxsey called yellow precipitate (JAMA, 1951, 253; Hoxsey, 1956, 47). In 1941 Frederick Mohs, a respected surgeon in Madison, Wisconsin, with the help of the Dean of the University of Wisconsin Medical School and several of its faculty, devised a method of surgically removing accessible cancers under complete microscopic control (Mohs, 1941). The substance which Dr. Mohs and his co-workers created for fixing the suspected tissue *in situ*, to enable him to excise it layer by microscopic layer, contained the same ingredients as Hoxsey's red paste. Dr. Mohs published his new method in 1941 in the ultra-respectable *Archives of Surgery* and in 1948 in JAMA (for later refinements, see Mohs, 1956; Phelan 1962, 1963a, and 1963b). Nonetheless, AMA spokesmen, during their accelerated onslaught on Hoxsey in the 40s and 50s, discounted the fact that Mohs' paste and Hoxsey's were identical. In condemning caustic pastes as one type of frauds and fables in 1949, the AMA implied that arsenic was the chief ingredient of Hoxsey's paste, on the basis of their own testing of a sample pirated in the 20s (JAMA, 1926, 57; Young, 1967, 365). Apparently Mohs' use of surgery (which, along with radiation, constituted the entire range of what the Council considered "established treatment") made his method, in contrast to Hoxsey's, "scientific" and acceptable. The Council failed to grasp the central fact that both men were using sanguinarine, an alkaloid of bloodroot which has potent antitumor properties described in the medical literature as early as 1829 (Young, 1967, 365; Hartwell, 1960, 23-24).

The most controversial aspect of Hoxsey's method, in the eyes of orthodox medicine, was the dark brown liquid which he used to treat internal cancer. For many years Hoxsey refused to divulge the formula for this substance, generating a frenzy of vituperation in the pages of JAMA over a period of decades. He later gave several differing accounts of its origin (Young, 1967, 362). According to his autobiography (Hoxsey, 1956, 62-64), it was his great-grandfather, a horse breeder named John Hoxsey, who developed it at mid-nineteenth century, out of grasses and flowering wild plants which John took from the pasture where a favorite stallion, afflicted with a cancerous growth, grazed daily until the growth necrotized. According to Harry, John Hoxsey reasoned that the wild plants had caused the stallion's recovery. He therefore concocted a liquid out of "red clover and alfalfa, buckthorn and prickly ash" (and other plants which John could not identify), gathered from the area where the stallion had apparently cured himself.

John continued adding ingredients from old home remedies for cancer, until he found an herbal mixture that seemed to help similarly afflicted horses in the area around his farm, between Carlinville and Edwardsville, Illinois. According to Harry, John's reputation as a man with the "healing tetch" soon brought him business from horse breeders all over Illinois and as far away as Kentucky and Indiana (Hoxsey, 1956, 64).

As the autobiographical account has it, John Hoxsey bequeathed the formula to his son, who in turn presented it to Harry's father, John, a veterinary surgeon licensed under the grandfather clause of the Illinois Medical Practice Act of 1877. "Fired with the notion that a remedy effective in curing horses might be of equal benefit to human beings stricken with the same disease," John Hoxsey began "quietly treating cancer patients" under the supervision of two MDs in the region of Girard, Illinois, where he bought a livery stable shortly after Harry's birth in 1901. From the age of 8, Harry served as his father's trusted assistant, as growing numbers of human patients gradually crowded out his veterinary practice (Hoxsey, 1956, 66-71). Recognizing Harry's calling to be a doctor, John gave the family formulas as a deathbed legacy to Harry in 1919, charging him to go forth and heal the sick if need be, in defiance of the "High Priests of medicine" (Hoxsey, 1956, 65, 71-74; Young, 1967, 362-363).

Harry's initial unwillingness to disclose the formula, taken together with his peripatetic existence (Taylorville, Illinois; Chicago; Clinton, Iowa; Philadelphia; Detroit; Wheeling; Atlantic City; Dallas), his growing financial success, and his open taunting of organized medicine, led Morris Fishbein to label Harry (and his late father) as charlatans. This assault, entitled "Blood Money" and published in 1947 in the Hearst chain's widely circulated magazine section, *American Weekly*, provoked Harry to sue for libel. He won though the judgment called only for a token payment for injury to Harry's and his father's reputations (Young, 1967, 374-375).

By 1950, court decisions had sufficiently broadened the labelling requirements of the 1938 Food, Drug and Cosmetic Act to enable the FDA to act against Hoxsey's interstate shipments. In the ensuing litigation, Hoxsey revealed the composition of his long-secret preparation. He explained that, depending on the type and stage of cancer, and the individual patient's condition, he added to a basic solution of cascara (*Rhamnus purshiana*) and potassium iodide one or more of the following plant substances: poke root (*Phytolacca americana*); burdock root (*Arctium lappa*); barberry or berberis root (*Berberis vulgaris*); buckthorn bark (*Rhamnus frangula*); Stillingia root (*Stillingia sylvatica*); and prickly ash bark (*Zanthoxylum americanum*) (Young, 1967, 375; Hoxsey, 1956, 45-46; JAMA, 1951, 252; JAMA, 1954, 667; Farnsworth, 1988).

For all that the AMA and the FDA had been trying to force this revelation from Hoxsey for more than a quarter-century, they did not respond to it by investigating these botanical constituents for possible pharmacological properties. Instead, the AMA Bureau of Investigation dismissed the entire formula as worthless: "only potassium iodide has any recognized therapeutic activity." The Bureau added that "Any person possessing a modicum of knowledge of the pharmacological action of drugs should know that any combination of ingredients listed on the current label of Hoxsey Tonic. . . is without any

therapeutic merit in the treatment of cancer." Disregarding the most fundamental question in science -- i.e., What is the evidence? -- the AMA insisted that "Any intelligent physician" could testify that all of these substances were worthless in the internal treatment of cancer (JAMA, 1954, 667-668).

A specialist in pharmacological and experimental therapeutics from Johns Hopkins testified at the FDA trial that there was no basis for therapeutic claims for any of the contents, but he did not publish either laboratory or clinical data to support this conclusion. A noted cancer research scientist testified that, in an experiment he had conducted for the FDA (also apparently unpublished), malignant growths in mice appeared larger at autopsy than before the mice received the Hoxsey tonic (Young, 1967, 375-376). The FDA and the NCI merely reviewed cases. In the public warning issued against Hoxsey in 1956, Commissioner George P. Larrick stated that the FDA, after what he called a thorough and long-continuing investigation, had "not found a single verified cure of internal cancer effected by the Hoxsey treatment." Larrick's warning said an NCI review of case histories submitted by Hoxsey likewise failed to provide evidence of therapeutic effect (Larrick, 1956).

In addition to an extensive literature attesting the folk use of Hoxsey's herbal ingredients in the treatment of cancer (Hartwell, 1967 and 1971), the orthodox medical literature at that time contained at least one suggestive article about one of them, based on empirical observation by a regular, orthodox practitioner. In 1896, in the *Medical and Surgical Reporter* (Philadelphia), a surgeon described the action of poke root as retarding the growth of epitheliomas and increasing the patient's survival time, if it was given before ulceration became extensive (Millard, 1896, 421). Despite bibliographic tools that make it easy to search the medical literature back through the 19th century and beyond, this article had apparently escaped the attention of the AMA, the FDA, and the NCI.

More recent literature leaves no doubt that Hoxsey's formula, however strangely concocted by modern scientific standards, does indeed contain many plant substances of marked therapeutic activity. In fact, orthodox scientific research has by now identified antitumor activity of one sort or another in all but three of Hoxsey's plants and two of these three are purgatives, one of them (*Rhamnus purshiana*) containing the anthraquinone glycoside structure now recognized as predictive of antitumor properties (Kupchan, 1976). Between 1964 and 1968 four articles appeared in *Lancet*, *Pediatrics*, and *Nature*, describing the mitogenic activity of pokeweed, which triggers the immune system by increasing the number of lymphocytes, causing the formation of plasma cells, and elevating levels of immunoglobulin G (Farnes, 1964; Barker, 1965; Barker, 1966; Downing, 1968).

In 1966 two Hungarian scientists, engaged in a screening program at the University of Szeged, published their findings of "considerable antitumor activity" in a purified fraction of burdock, a plant which they included in their project because of its use as a folk remedy for new growths and ulcerations (Dombradi, 1966). In 1972 Kupchan described the growth-inhibiting activity of sesquiterpene lactones, a structural group which includes burdock (Kupchan, 1972). In 1984 researchers at Nagoya University, Japan, found in

burdock a new type of desmutagen: a substance uniquely capable of reducing mutagenicity both in the absence and in the presence of metabolic activation. So important is this new property that these scientists named it the B-factor, for burdock factor (Morita *et al.*, 1984).

Two recent studies from the Orient, one Japanese, one Chinese, have established the presence of antitumor substances in barberry (which Hoxsey also sometimes called berberis root). Testing tumor size in mice by the total packed cell volume method, Hoshi and his co-workers found strong antitumor activity in berberrubine, an alkaloid isolated from *Berberis vulgaris* (Hoshi, 1976). Also in 1976, Owen *et al.* derived from berberine a new antitumor substance which they have named Lycobetaine (Owen, 1976).

At the University of Virginia in the mid-70s, Kupchan and Karim isolated an antileukemic principle from buckthorn (*Rhamnus frangula*). Their discovery that the efficacy of this substance in leukemia is vehicle-dependent led these scientists to advise re-testing of other anthraquinone plant substances for similar antitumor activity (Kupchan, 1976).

The least studied of Hoxsey's herbs to date are *stillingia sylvatica* and prickly ash (*Zanthoxylum americanum*), but even these are represented in the scholarly literature. In 1980 two German scientists discovered several new diterpene-esters (a chemical group known to have antitumor activity) in *Stillingia* root, the portion of this plant used by Hoxsey (Adolf, 1980). At a symposium on folk medicine in 1986, Varro Tyler observed that, despite the wide use of northern prickly ash bark in folk medicine, it has been nearly 50 years since any studies were done of its chemical composition and there have never been activity-directed fractionation studies. Noting that pharmacological tests have revealed significant anti-inflammatory and anesthetic properties in several closely related species, Tyler urges scientists to study prickly ash for these and other therapeutic properties (Tyler, 1987, 106).

Whether there is therapeutic merit in Hoxsey's particular formula for internal use remains as much a question today as it was in 1925, despite provocative findings of antitumor properties in many of the individual herbs he used. Neither laboratory nor clinical reports have roused the AMA, the FDA, or the ACS to re-examine the possibility of efficacy.

In adding Hoxsey's remedy to its *Unproven Methods* list (ACS, 1971), the ACS used its customary phraseology about lack of evidence of worth. In actuality, except for work with mice done in the 50s by an outside contractor for the NCI, but never published in the scientific literature, it appears that Hoxsey's treatment has never been tested, either in animals or in humans. The only negative investigation cited by the ACS was a three-day visit to Hoxsey's clinic by several Canadian physicians, who failed to find merit in his methods (American Cancer Society; Moss, 1980).

As recently as 1965, Morris Fishbein, former long-time editor of JAMA, repeated in *Perspectives in Biology and Medicine* a rolling, melodramatic sentence he had first coined for a popular presentation of the AMA case against quackery on the March of

Time. In 1947, in a major JAMA editorial called "Hoxsey Cancer Charlatan", Fishbein reiterated this favorite phrase: "Of all the ghouls who feed on the bodies of the dead and the dying, the cancer quacks are most vicious and most heartless." Verbiage such as this, widely circulated by the influential writer who was the "Voice of American Medicine" for more than four decades, has done much to set the low level of discourse and the emotional rather than analytical tone that have characterized the American medical profession's response to unorthodox remedies.

In 1976, surveying the results of the plant screening program begun in 1960 by the Cancer Chemotherapy National Services Center at the NCI, Richard Spjut noted that the occurrence of activity was found to be higher in plants reported in folk literature than in plants collected at random, "suggesting a correlation between plants used in folklore and those with anticancer activity" (Spjut, 1976, 979). Jonathan Hartwell, the chemist who long directed this national program of drug development from plant products, also values folk usage as a guide to plants likely to yield therapeutically active substances. In his *Plant Remedies for Cancer* (1960), Hartwell quoted historian of science, George Sarton, on the recurrent phenomenon of initial medical hostility toward folk remedies that eventually become valued tools in conventional medical usage. Writing in 1947, Sarton had in mind chaulmoogra (for leprosy), cinchona bark (for malaria), and variolation (for smallpox): to these we can now add (for cancer alone) periwinkle, mistletoe (labelled a "promotion" by Morris Fishbein as recently as 1965), Mayapple, autumn crocus, and chaparral tea. Sarton counselled the profession to exhibit less intellectual arrogance and more open-mindedness: "The remembrance of these astounding folk discoveries should sober our thoughts when we criticize too freely the old pharmacopoeias. It is easy to make fun of mediaeval recipes; it is more difficult and may be wiser to investigate them. Instead of assuming that the mediaeval pharmacist was a benighted fool, we might wonder whether there was not sometimes a justification for his strange procedure." (quoted in Hartwell, 1960, 24).

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