

The Use of Bacterial Toxins in the Treatment of Cancer

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Introduction

For over two hundred years spontaneous cancer cures or regressions have been observed and recorded. They have been discussed in standard textbooks of surgery and medicine with the omission of a very important observation, i.e. that they were not spontaneous. Many of them, if not most, were preceded by a bacterial infection such as erysipelas. Many early physicians were aware that there was a relationship, but because there was no scientific explanation the connection did not become generally known. It had also been observed that the bacterial infection was even more beneficial if it was accompanied by fever. Helen Coley Nauts (1986) collected this imposing clinical data in the files of the Cancer Research Institute Records (1953-1982), and in her publications (1990).

Thus Vautier in 1813 discussed the cure of cancer by natural means after he had found several patients who were cured after they had developed gangrene. Nauts collected 22 such cases. The mixture of bacteria probably induced the formation of tumor necrosis factor. She published 449 cases found in 1032 worldwide references in the medical literature. Modern medical scientists ignore this material because it is considered anecdotal, not double blind. Physicians in the 18th and 19th century induced "laudable pus, selons or issues" in their inoperable cancer cases. Two case histories are given by Nauts (1989). Prior to 1744 Schwenke described a woman whose breast cancer progressed in spite of all treatment. After she had lost hope and stopped trying she developed an abscess on her leg. As this became worse the cancer began to regress and vanished. Against advice she allowed the ulcer to heal whereupon the cancer recurred. The ulcer was restarted and once more the cancer disappeared. This is an interesting example

of the first immunotherapy and would be classed as a spontaneous cure the first time, but there was nothing spontaneous about it the second time since the ulcer was induced mechanically. The second case was described by a French physician who applied gauze dressings soaked in gangrenous discharges on an ulcerated breast cancer. The ulceration destroyed the tumor in 19 days and she was healed. The gangrene replaced the live cautery, caustics and the scalpel. Other physicians recorded some remarkable cases of antagonism between bacterial infection and cancers. Busch (1866) reported the cure of a sarcoma of the face by recurrent episodes of erysipelas. Bruns (1887) saw a terminally ill patient with malignant melanoma with metastases recover after repeated attacks of erysipelas associated with fever. Rhodenburg (1918) reviewed 166 cases of spontaneous regressions of human tumor. Of these 72 had intercurrent high fevers, heat applications or infection. Everson and Cole (1956) found that out of 1000 cases worldwide, 130 were cured by fever or infection. But Dr. Coley was the first physician to follow up this new treatment approach systematically. The clinical data was assembled by his daughter Helen Coley Nauts in a series of very useful reports.

Just over 100 years ago William B. Coley operated on a 19 year old woman for a breast sarcoma. She died. This event, which would be accepted by most surgeons as an unfortunate natural event, changed his life. He concluded that surgery was at best a partial answer and he began to search for a better one. He studied about 100 charts of sarcoma patients treated at his hospital the previous ten years, and discovered one case of a patient with recurrent round cell sarcoma who developed erysipelas following surgery and was cured. Here was another partial answer which Dr. Coley pursued with undiminished vigor the rest of his life. He induced erysipelas in ten terminal patients but concluded this could not be acceptable treatment, since this might hasten

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death or not induce an infection. I doubt modern physicians would be tempted to try such a treatment, but today with the use of antibiotics this would be a much safer treatment than it was in 1900. It might be much more acceptable today since antibiotics could be used to terminate the infection after enough fever had been generated.

Realizing that infection could not be used Dr. Coley turned to bacterial vaccines. About 100 years ago bacteriology and the use of vaccines was being investigated with great enthusiasm. Dr. Coley prepared a vaccine from heat killed streptococci mixed with the toxin of bacterium *Serratia Marcescens*. This was the first use of a mixed vaccine in medicine.

He treated a 19 year old male with inoperable sarcoma of the abdominal wall and pelvis involving the bladder. The mass measured 16 by 13 cm. The vaccine was injected directly into the mass daily for four months. Fever to 40 degrees C was induced. The patient recovered and died 26 years later from a coronary occlusion. Dr. Helen Coley Nauts assembled 896 cases treated by this mixed bacterial vaccine (MBV). She found that of 523 inoperable patients, 238 recovered (46%), while from 373 operable cases 190, or 51%, recovered.

Considering how little was known about the optimum use of the vaccine, these results are remarkable and surpass the results obtained by any modern treatment using only surgery, chemotherapy or radiation. The quality of the vaccine was not standardized, the best site of injection not yet determined, and the optimum frequency of injection unknown.

With this astonishing record, why did this treatment not become the standard treatment of the day and even today when so much more is known about vaccines and their use? After his death in 1933 his son continued to use the Coley toxins, but the treatment was destroyed by the declaration of the American Cancer Society that this was quack medicine, and the decision of the FDA to classify the vaccine as a new drug even though it had been in use over 60 years. Only in the past few years, due to the heroic efforts of his daughter, Dr. Helen Coley Nauts, and due to increasing understanding of the role of the immune system, have vaccines become more respectable and are being used more and more. Thus B.C.G. has become an acceptable additional treatment for cancer.

Dr. Coley lost his first cancer patient. Luckily, double blind methods for examining treatments were far into the future and did not deter him from pursuing his investigations. Next he infected a patient with erysipelas who had repeated inoperable myosarcoma of the neck. The patient recovered. In 1893 Coley reported this case and 9 others, together with 28 who had accidentally developed the infection. In 12 the tumors vanished, and in 19 there was some improvement. But he realized that inducing infection was not a reliable way and was potentially dangerous. He therefore turned to vaccines using streptococci and later combining this with the toxin from *Serratia Marcescens*. His first case recovered. This recovery must have impressed Fr. Coley as much as had his first surgical failure, because from that moment on he did not waver in his research nor in his use of the Coley toxins for the treatment of a large variety of cancers. But he also used other treatment including surgery. He was the first to demonstrate that using the Coley toxins before surgery could prevent recurrences. Of 128 cases where amputation was avoided, 51 percent remained well, compared to 32 percent out of 166 cases after amputation only.

There were many problems with these early vaccines which were unavoidable, considering this was major pioneer work. The early preparations were variable in potency. Nor was the best injection site known. Surgical colleagues in England urged Dr. Coley to restrict the toxins to sarcomas, because the weaker preparations they had used seemed to be most effective for sarcoma, and had not worked with advanced cancers and melanomas. But many of these cases were treated successfully by the vaccines by other surgeons, and Coley continued to use it for all the tumors. Animal studies confirmed these clinical observations. The results were better when the vaccines were used.

Dr. Coley also used radiation. Patients given the toxins before radiation responded better and had fewer side effects. But too much radiation nullified the therapeutic effect of the vaccine. In this report I will discuss: (a) the reasons for the near demise of a very successful therapy; (b) the historical development of the use of mixed vaccines; (c) Dr. Coley the surgeon; (d) what is known about the vaccine; (e) what I would consider an ideal

treatment for cancer, combining Orthomolecular treatment, the vaccines and, as a last resort, surgery, radiation and/or chemotherapy.

Why New Treatments May Require Forty or More Years to be Accepted

(a) Resistance to New Treatment Ideas

The introduction of new treatments into medicine appears to be the result of a series of random events which determine whether a treatment will be rejected, or accepted sluggishly or swiftly. The scientific merits of the treatment seems to play a minor role at the onset of what usually becomes a great debate before it is eventually accepted. Whether or not serious examination is given to a treatment depends upon such factors as the location and prestige of the investigator. Thus, a discovery coming out of Harvard Medical School will be given more attention than a discovery from the University of Manitoba, for example. It depends upon the journal in which the findings are reported, upon the urgency of the disease being treated and, most of all, on the current fashion surrounding the disease and whether the new treatment violates the current dogma. A recent example is the treatment of AIDS which, in spite of its rather sudden onset and brief history, already has a dogma which prevents a proper examination of the use of vitamin C. It also depends upon chance events which are unpredictable, such as Queen Victoria's use of ether for childbirth, which helped introduce this useful treatment into medicine. More recently it depends upon public pressure such as that provided by the gay lobby, which is seeking to bypass the rigid rules of the FDA in order to get access to newer drugs more rapidly. A major factor is whether the drug can be patented. Nutrients can not be patented and therefore there is no financial incentive to develop and promote the treatment. Patented drugs have their parent companies behind them and can be promoted by huge expenditures of money for advertising and development. Thus niacin, which is one of the most effective compounds for lowering cholesterol, cannot be patented, even though it was discovered to be a hypocholesterolemic substance in 1955. Only in the past five years has it received a good deal of attention. Atromid, a patented drug, introduced just a few years after

niacin's effect on cholesterol was discovered, came into use very quickly, and for many years was the favorite compound for lowering cholesterol. It is ironic that niacin saves and extends lives whereas Atromid has been withdrawn from the market in some countries because of its toxicity.

Bad theory which becomes established also prevents newer treatments. The Howell theory of heparin's role in the body kept back serious examination of its clinical potential for many years. Another example is the use of vitamin B₃ for the treatment of schizophrenia which Dr. H. Osmond and I introduced about 35 years ago. It was instantly rejected because it was then known that schizophrenia was not a biochemical disease, and perhaps because we were the first psychiatrists to use the double blind technique for testing treatments and the method was too new to be examined seriously. Tranquilizers came in very quickly because they were promoted by many drug companies hungry for the fat profits which they yielded.

Another major factor is the innate conservatism of the medical profession. Almost every new discovery which eventually became a formal part of medicine was first rejected out of hand for many years. The history of medicine is a history of conflict of treatment ideas, from Harvey who was ridiculed because he thought blood circulated, to Sydenham who was nearly expelled from the medical association because he thought that it was better to lower fever in his smallpox patients, to the use of tranquilizers bitterly opposed by the psychoanalysts, and so on. There has always been a medical establishment, now more powerful than ever, which has fought against new ideas in medicine. They have used every technique to discredit and destroy the innovators, such as criticizing the research methods used, denying the diagnosis and questioning the person's competence and the conclusions.

(b) Belief that Medicine is a Science

There is a wide spread belief that medicine is a science. In fact, many scientific principles are involved and utilized, but unfortunately many physicians believe that being scientific means that we know why something works, in other words there has to be an acceptable explanation. Historically, medicine won over

some of the other healing arts because it covered itself under the cloak of science and thus defeated chiropractors, homeopaths and others. These professions were, and to many still are, considered quack medicine, because they do not provide explanations of why they work which are acceptable to the medical profession. The acceptable explanations do not have to be correct, but they do have to be acceptable. As a result, over the ages one explanation has replaced another as more information is obtained, and as theories of biochemistry and physiology are developed. Clinical descriptions of diseases are hard data for they do not change, whereas explanations are evanescent. The clinical description of epilepsy recorded two thousand years ago remains valid today, but the explanation of the disease two thousand years ago is totally inappropriate.

Because of this need to be scientific, i.e. to have an acceptable explanation, treatments which can not be understood are rejected. This has been one of the main problems in accepting Orthomolecular medicine, which emphasizes the use of large doses of some nutrients when these optimum doses are indicated. According to all the common theories in nutrition to which physicians adhere, there is no scientific explanation for the use of these doses. Linus Pauling in his basic report (1968), provided such an explanation, but no one seems to have read his paper in *Science*.

Medicine is a science because diseases treated by a given treatment ought more or less to respond in a predictable way, i.e. it is based upon the observations of many physicians whether these observations were made in the usual clinical sense, or by single blind controlled studies, or by double blind controlled studies. The use of the word anecdotal to denigrate observations has no place in the science of medicine. It is a practical science where observations take precedence over theory, even though these observations might have originated on the basis of theory. There should be no demand that no treatment is valid until it has been explained satisfactorily. I doubt that most treatments today have a valid scientific explanation except that they appear to work. For many years we used aspirin for the relief of pain, but only recently is there some understanding developing of how it might work, but aspirin has

not thereby become more effective.

Other healers are not as impressed with the need to understand. For example, herbalists freely use herbs which have curative properties even though we do not know why, nor what is the main therapeutic factor. Herbs comprise the original pharmacopeia. This does not mean we should not search for the correct explanations, which in time surely will be found. It does mean that we should not resist using newer treatment simply because there are no acceptable theories today.

Medicine is a pragmatic art which slowly incorporates scientific principles. But if we forget our pragmatic roots we have the situation we have today, where a lot of medical theory has become dogma and where practitioners can say, thinking they are scientific, "I do not believe in vitamins," for example. This dogma prevents serious examination of ideas developed which are outside the mainstream of medicine, and thus inhibits progress in medicine.

In an attempt to make medicine more scientific a new dogma has developed dealing with the way clinical trials should be run. I am partially responsible since, with Dr. H. Osmond, I conducted the first double blind controlled experiments in psychiatry when we began our trials in Saskatchewan in 1952. Modern medicine has adopted this technique as the ideal method for doing clinical trials, even though it has been severely criticized by Dr. Osmond and myself, and a large number of other theorists. Many of the early proponents have realized the errors inherent in this methodology. Today, double blind methods are used as a weapon against work which is not acceptable to the profession. If the new treatment tested by this method appears to work, it is criticized for not having been done well enough or by the right people. The originator is always suspect because he is bound to be biased. If it is not done double blind, it is rejected out of hand as being anecdotal. Thus, the *New England Journal of Medicine* rejected a paper which showed that 8 patients with idiopathic thrombocytopenic purpura (ITP) responded to vitamin C because it was not double blind. For ITP there is no useful treatment, apart from vitamin C. Double blind methods are being used primarily to promote treatments which have already been accepted, and to satisfy the dogma of research personnel

and editors of journals.

Along with the need to be scientific is the need to be certain. This is another reason double blind experiments are considered so essential. The magic 0.05 point indicating the difference is due to chance in only 1 in 20 experiments, is accepted as one of the elements of this certainty. But according to Foster (1992), "... the necessity of certainty is an inconvenient myth. Attempts to achieve this goal in medicine involves enormous suffering and unnecessary expenditure of time, effort and resources." He adds, "This does not mean progress is impossible, merely that society has to be willing to make decisions and take action on less than totally convincing evidence. To do this, it must accept lateral and other types of thinking as having a valid role to play in the search for solutions to its most pressing problems. To illustrate, despite enormous expenditure on cancer research which, in the United States alone, is approximately one billion dollars annually, cancer mortality generally continues to climb. The only significant exception to this generalization, of which this author is aware, has occurred in those regions of the Peoples Republic of China, where jiang-shi concretions have been added to drinking water. The decision to modify potable water in this way was not based upon irrefutable scientific evidence, conclusively linking esophageal cancer to deficiencies of one or more of the many bulk and trace elements found in jiang-shi, but rather was a lateral one, designed to test the efficacy of a traditional Chinese method of treating the disease."

(c) *Cancer is a surgical specialty*

Until the development of chemotherapy, the treatment of cancer was a surgical specialty. A few patients were cured, many more were not but there was no alternative treatment, and it made sense to remove the offending growth and stop its invasion of the body. Medical treatment would be counter to the prevailing ideas about treatment and take away the surgical monopoly. After he had developed the Coley vaccines, called Coley toxins, he found great difficulty in persuading other surgeons to use his treatment. Between 1891 and 1896 he published 16 papers describing his treatment. There was one critical report in 1894. In 1895 Dr. Coley read a paper to the New York

State Medical Association and published it the following year. After several adverse editorials Coley responded with, "... that a few physicians in a very limited number of cases with indifferent preparations of the toxins have failed to obtain good results will not... have great weight in the minds of the scientific portion of the profession in determining failure or success of this method of treatment of sarcoma."

Brief History

X-ray and radium treatments were introduced and were quickly accepted by surgeons, including Dr. Coley. As I see it, this was merely surgery by other means and so did not violate their basic beliefs. These treatments came into direct conflict with the use of vaccines, especially since it was impossible to explain how infections or vaccines could possibly have any influence on the tumors. Dr. Ewing, of Ewing's sarcoma fame, became medical chief of Memorial Hospital in 1915. He was an enthusiastic supporter of radium treatment and had no interest in Coley's vaccine. Coley, who was chief of the Bone Tumor Service, had to follow Ewing's rule that all patients on the service must receive radiation before surgery. Coley believed this to be very dangerous and in 1927 proved this. He published the results of 169 cases of whom none survived, while from his private patients given the toxin followed by surgery 50 percent survived. The Mayo clinic using his method also achieved a 50 percent five year cure rate, compared to the 10 to 15 percent reported by other surgeons not using the vaccine.

By 1909 Coley had published 66 papers, but the majority of surgeons ignored or criticized his work. January 1931 Dr. Coley retired after 40 years service. A testimonial dinner was held at the Waldorf Astoria Hotel on his 69th birthday. In 1935 he was made Honorary Fellow of the Royal College of Surgeons in England. Following his death, his son, Bradley L. Coley, became Chief of the Bone Tumor Service and continued to use the Coley vaccine. But after serving in the army from 1942 to 1946 he found on his return that the Medical Director, Dr. Rhoads, had advised Parke-Davis not to make any more vaccine, and in 1963 the FDA finally destroyed the use of the vaccine by declaring it to be a new drug, under the new powers given to the FDA. This effectively killed

the treatment with vaccine for a long time. At one time Coley vaccine was declared by the American Cancer Society to be quack treatment.

Dr. Coley, the Surgeon

Dr. Coley was impressed by his observations but used them only to direct his further research. He was wide in his approach, using radiation and surgery as well as his vaccine, and he had enough faith in his own observations that he was not deterred from continuing his investigations. He made many contributions to his hospital and to medicine in general. Thus, at Memorial Hospital many of his patients could not afford to pay for the treatment, and between 1908 and 1913 60 percent of his operations were free. In 1901 he helped establish the Huntington Cancer Research Fund with a \$100,000 gift from Mrs. Huntington. He established the first x-ray department and ran it without pay for a year. In 1903 he set up a medical record system at the hospital. In 1902 he persuaded John D. Rockefeller to donate one million dollars to Harvard Medical School and he obtained another \$300,000 from Mrs. Huntington.

He developed acromegaly, which he self-diagnosed in 1913 but he told no one. He was at the same time under a lot of stress from Dr. Ewing's growing antagonism and Dr. Codman's Bone Sarcoma Registry. In 1920 Codman wrote, "... your treatment has a profound systemic effect but I am inclined to attribute the successful cases to errors in diagnosis. Yet I must admit you have more to your credit than anyone else." Codman did not want to include in the registry cases who recovered but died before 1920. He once accused Coley of not trusting him or of playing too much golf, because Coley did not send him enough data. Coley responded angrily but was hurt. He wrote, in referring to a letter he had written to Dr. Ewing, "You could at least have omitted your remark that you would regard the case as having gotten well in spite of Coley's toxins, instead of with the help of them." Codman apologized. Coley developed a very serious duodenal ulcer and hemorrhaged in February 1922. He never regained his former strength. The scar from his bleeding ulcer later stenosed and in 1930 required gastrointestinal surgery. But he continued to work. By 1926 he had assembled data on 170 cases of long bone

sarcoma and 69 of giant cell tumors he had treated from 1906 on, in two reviews. He published 25 more papers. By 1934 Codman, chairman of a Bone Sarcoma Symposium, summarized his paper on Ewing's sarcoma and he pleaded for further clinical examination of the Coley toxins.

Review of the Coley Toxins (Vaccines)

The optimum treatment using the vaccines depends upon the following variables.

(a) Duration of treatment. Up to six months of injections are needed before it is concluded that it will not help. There have been cases where the condition appeared to worsen with treatment and then finally improved, leading to recovery.

(b) Site and dose. The best place to inject is into the tumor. Next best is as close as possible to it, intramuscularly or subcutaneous. When injected at sites remote from the tumor much larger doses were needed to reach the required level of fever. The preferred sites are: intratubular> vascular tissue> intravenous> intramuscular> subcutaneous. The initial dose is 0.05 mL and is increased by 0.05 increments until a mild fever is obtained. Injections are given daily but may later be tapered off to less frequent administration.

(c) Fever. The greatest response rate was found when temperature rose above 39.4 degrees.

(d) Timing. The best results were found when the vaccine was started before surgery or radiation.

Other Vaccines

Vaccines prepared from other organisms have been used, such as the tuberculosis bacteria, B.C.G. or the SSM vaccine available from Japan.

Epidemiology

There is an inverse relationship between the incidence of infections and the incidence of cancer. For example, among the Native Indian population of North America where the infection rate is higher, the rate of cancer is lower, and in other populations where the infection rate is low the incidence of cancer has been six times as high. Helen Coley Nauts proposes the hypothesis that the use of antibiotics has increased the incidence of cancer, because it has removed from us nature's

way of fine-tuning our immune system by giving us an infection whenever it is down. This stimulates the immune system so it can deal with other invaders such as cancer. This hypothesis makes good sense to me. It suggests that antibiotics ought to be given only as a last resort, when it is pretty clear that allowing the infection to continue would be hazardous. It would be wise to allow simple bacterial infections to at least initiate the immune system activation with a slight degree of fever before suppressing it.

A Possible Ideal Program

The evidence from these vaccine studies going back 100 years, and from the Vitamin C studies going back 10 years, suggests that a combination of Orthomolecular medicine and vaccine therapy ought to improve greatly the outcome of cancer treatment when it is combined with the other treatments including surgery, radiation and chemotherapy.

1. Orthomolecular therapy, including optimum diets and optimum amounts of nutrients with a minimum of 12 grams per day of vitamin C.

2. Mixed Respiratory Vaccine or some similar vaccine, daily as described preferably into the tumor or into the abdominal wall subcutaneously. It should be started before radiation, surgery or chemotherapy to decrease the possibility of metastases. Avoid antibiotics as much as possible, avoid antipyretics.

3. Surgery, radiation or chemotherapy as indicated.

4. Other treatments may or will be used. This program is only a design which can be followed and which can be coordinated with any other treatment which has been found to be helpful in

cancer treatment. It is not meant to be the sole treatment which should be used. Too little is known about cancer and its treatment to become too narrow.

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