



The Cancer Chronicles

SERIOUS CONSIDERATION OF ALTERNATIVE IDEAS

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EDITORIAL

CANCER AND MICROBES

This issue deals in a detailed way with two treatments, Coley's toxins and MTH-68. One of them uses bacterial, the other viral, products as a treatment for cancer. Both rely on natural reactions of the immune system to fight the disease. Both have been tragically neglected.

The whole topic of micro-organisms and cancer is due for serious reconsideration. The current vogue for genetic manipulation is bound to run its course. People will once again be demanding a new therapeutic idea, and one that works.

The rise of AIDS, as well as antibiotic-resistant superinfections, has stirred the popular imagination. This interest is bound to eventually spill over into cancer research.

When scientists get around to exploring the relationship of cancer to microbes they will find that they have ample predecessors. In the 18th century, cancer was considered a contagious disease. But even after this idea was discredited, fruitful work was done on cancer and parasites or lower organisms.

This whole topic has been fraught with false alarms. For every scientist who claimed to find a particular micro-organism causing cancer, there have been a dozen arguing that the organism in question was not the cause but a mere "hitchhiker" or contaminant.

But theories of microbes and cancer persist. Most "spontaneous remissions" occur after some infectious process. And some of the most exciting treatments of today attempt to reproduce those "experiments of nature" in the clinic or to vaccinate against putative cancer-causing microbes.

In this special issue we present a detailed discussion of two such treatments. We hope it will contribute towards a more serious consideration of the many links between cancer and the microbial world. □

SPECIAL DOUBLE ISSUE: Treating Cancer with Microbial Products



Coley's Toxins



MTH-68: Newcastle Disease Virus Vaccine

THE SUM OF OUR HOPES

THE TREATMENT OF CANCER WITH COLEY'S TOXINS

Coley's toxins are a century-old immunological treatment for cancer. It consists of the injection into the patient of by-products of two common bacteria, *Streptococcus pyogenes* and *Serratia marcescens*. The treatment has also been known as "Coley's fluid," "Coley toxin," or "mixed bacterial vaccine."

It was developed by an eminent New York surgeon named William B. Coley, MD, who spent most of his long career as chief of the Bone Service at Memorial Hospital (now Memorial Sloan-Kettering Cancer Center).

The therapeutic idea was to deliberately and repeatedly invoke fevers, as high as 105° F, as well as chills and other "flu-like" symptoms in the cancer patient. The rationale was to provoke the immune system to attack and destroy the cancer.

HISTORICAL BASIS

This treatment did not come out of a vacuum. In the eighteenth and nineteenth centuries it was repeatedly observed that following serious infections cancer patients sometimes experienced "spontaneous remissions" of their malignancies. The diseases usually linked in this way to cancer were tuberculosis, malaria, and syphilis.

In 1866, a celebrated German surgeon, Wilhelm Busch of Bonn, reported on the spontaneous cure of cancer after an attack of erysipelas (*Berlin klin Wchnschr* 1866; 23:245). This is a serious skin disease which we now understand to be caused by the microbe called *Streptococcus pyogenes*.

Busch was well-respected and word of his observation spread rapidly. After that, many attempts were made to artificially stimulate either erysipelas or high fevers in cancer patients. As one of Busch's students, Willy Meyer or New York, later wrote, "A great

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variety of substances, from almost all the compounds of chemistry to plain water, have since then been injected, some of them with fever as a by-product" (*Cancer*, NY: Hoeber, 1931, p. 343).

The link between the onset of erysipelas and the "spontaneous" remission of cancer was noted in the 1880s. Even the Russian playwright Anton Chekhov, who was also a physician, noted the relationship in his diary in 1884.

In fact, over a dozen doctors on the Continent (mostly Germany) tried to induce erysipelas to bring about remissions in their patients. Most failed to even induce the disease; but some of these attempts appear to have been successful.

In a similar vein, a well-known French surgeon, Marin Tuffier, MD, brought about the remission of "terminal" breast cancer in a 37-year-old actress by giving her injections of a purified fraction of her own pleural exudate (lung fluid). Whether the woman benefitted from the fevers that ensued, or whether there was an enhanced immune reaction to some cancer antigens—or both—was never established. The woman left his care in greatly improved health, although there was no followup.

One big problem was that most fever-causing substances lost their potency after a short while. So, by the end of the nineteenth century, a worldwide search was on for a serum "of such range of dosage, without bad side-effects" which could put the patient "without fail and

"All therapeutic cures are obtainable only by the working of physiological forces and the first hope of therapeutic success comes with the observation of the efficiency of unaided nature to accomplish cure.... These cases, rare though they be, are the sum of our hopes." — Pearce Gould, MD, 1910

without interruption" in a state of fever (Meyer, p. 344). That serum turned out to be Coley's toxins.

NINETEENTH CENTURY LINK

Coley made his discovery without knowledge of these previous European findings. In 1891, he was a young man fresh out of Yale College and Harvard Medical School. His first bone cancer patient was a lovely 19-year-old girl named Bessie who had a sarcoma of the bone. (She also happened to be the girl friend of John D. Rockefeller, Jr.; on a personal level, many biographers say that this was the origin of the Rockefeller family's continued involvement in the cancer field.) Although Coley did everything according to the textbooks, the girl had a recurrence of her cancer and died.

Determined to find out why "orthodox" methods of

surgery had failed, Coley examined the records of 100 sarcoma patients who had been treated at New York Hospital. All advanced cases died. Eventually, however, he found the case of a man who had been operated on three times with no success; but the fourth incomplete removal of his tumor in 1884 resulted in a raging case of erysipelas, with its angry-red inflammation of the skin.

TRACES DISAPPEAR

Hospital records simply stated that all traces of the tumor had disappeared following the infection. Intrigued, young Coley traipsed up and down the tenements of New York's East Side and found the man, alive and well, in 1891. This was seven years after he had been "spontaneously" healed of his cancer.

Fascinated by the vistas that this "experiment of nature" opened up, Coley reviewed the evidence for erysipelas healing in the prestigious *Annals of Surgery* (1891;14:199-200). Thus began his life-long search for a cancer cure using the organism that causes erysipelas.

In October 1891, Coley took the fateful step of deliberately infecting a patient who had an inoperable cancer of the tonsils and neck with *Streptococcus pyogenes*, the organism that had only recently been discovered to cause erysipelas. Much to everyone's astonishment, after severe fevers and chills, the patient experienced a complete and prolonged remission of his cancer.

Coley thought he was the first person ever to do this, but we now know he was actually the fourteenth—but the others had all been in Germany, and Coley was unfamiliar with the world literature on the subject.

As usually happens with new cancer treatments, after the initial first success there followed a string of treatment failures. Coley's procedure was to put patients in so-called "erysipelas beds," which had recently been vacated by patients who had just died of the disease. But because live strep infections were potentially dangerous to both patients and health care workers, in 1893 Dr. Coley switched to injections not of live germs but of the non-infectious byproducts (so-called "toxins") of *Streptococcus pyogenes*.

At about the same time, a French scientist named G. H. Roger showed that if strep is grown together with a second microbe, now called *Serratia marcescens*, the virulence of the strep is greatly increased (*Séances et Mém Soc de Biol* Paris 1890;2:573-580). Roger was so impressed with its enhancing ability that he called this "Bacillus prodigiosus." For this reason, Coley added *Serratia* to the mix, creating the classical Coley's toxins.

The first patient to receive these toxins had an extensive and inoperable sarcoma of the abdominal wall and the pelvis, already involving the bladder. Coley injected his toxins for four months into and around the tumors. (In the early days, he generally favored intra-tumoral

and peri-tumoral injections.) Even without using live bacteria, he was able to cause a complete remission of the “incurable” cancer. The patient remained alive and well for 26 years, when he finally succumbed to a heart attack.

Around 1915, Coley became chief of the Bone Service at Memorial [Sloan-Kettering] Hospital, the world’s largest private cancer center, where he remained until his death in 1936. He was highly respected and honored, and over 400 scientific papers were written about his toxins. The treatment was used experimentally not just in the United States, but in Canada, the UK and Belgium. He kept giving it until 1936, when his son Bradley took over his position and practice at Memorial.

THE 896 CASES

In all, they and their colleagues in the US and Europe treated several thousand cases. Since 1939, Coley’s only daughter, Helen Coley Nauts, has been documenting the results of her father’s work and expanding on its meaning. Although she is in her late eighties, she continues to do so. Mrs. Nauts has now analyzed in detail the outcomes of 896 microscopically confirmed cases. Of these, 428 cases (roughly half) were found to be well from 5 to 92 years after treatment. The overall 5-year survival rate was 51 percent in operable cases and 46 percent in inoperable ones. This compares favorably to any treatment of the current day. Five-year-survival is the conventional definition of “cure.”

Amazingly, some of his cured patients may still be alive. I myself was speaking about alternative cancer treatments on a talk radio show in Scottsdale, AZ a few years ago. I received an excited call from a man whose voice revealed him to be quite elderly. He wanted to tell me about his cure from cancer of the shoulder back in 1912. He (and the audience, I presume) were quite amazed when I beat him to the punch and told him both the name of the doctor who treated him and the nature of the treatment!

In fact, Coley’s toxins were quite well-known and well-respected. In 1931, the New York cancer specialist Willy Meyer, MD, wrote, “Coley’s fluid...is so well known and has been so widely in use in cancer, and for so many years, that it appears superfluous to enter here until historical and other details regarding the same. There is a rich literature dealing with the results obtained with the fluid in numerous cases” (op.cit.).

James Ewing, MD, chief pathologist at Memorial Hospital, was both conservative regarding new treatments, and a powerful rival of Coley’s at that cancer center. He represented the least favorable end of the spectrum of evaluation. Yet he wrote, “[I]n some recoveries from endothelioma of the bone, there is substantial evidence that the toxins played an essential part”

(Neoplastic Diseases, 6th ed., Phila.: Saunders, 1941, p. 314).

LESSONS FROM HISTORY

The history of Coley’s toxins is thus both inspiring and instructive. It shows that in the past there were experimental treatments available that exceeded in efficacy some of the best modern treatments. Various forms of cancer that we today consider incurable were sometimes put into long-term, lasting remissions.

Patients understandably want to know how this can be. If a treatment was once effective why is it not now in common use? Answers vary. Some people continue to deny the reality of the claims. Or they state that Coley’s toxins are too dangerous to use. I have heard a researcher who is otherwise favorable towards alternatives tell a patient that since Coley’s toxins have been around for 100 years they would have been widely accepted if they were any good.

Coley’s toxins seem doomed to the “twilight zone” of effective but underexplored cancer treatments.

I deal in detail with these issues in my book *The Cancer Industry*. I think the barrier to their use is primarily economic. The production of Coley’s toxins is remarkably inexpensive. Making a six months’ supply comes to about one dollar! But the cost of working a new drug through the regulatory barriers average about \$230 million. Coley’s toxins are not patented, and there is simply no way to make back your investment, much less turn a profit, on this treatment.

Historically, the toxins were once produced by Parke-Davis and other companies. But they were forced out by chemotherapy. And although a number of pharmaceutical companies have occasionally expressed an interest in researching the toxins, this interest usually abates as they quickly understand the economics of the treatment.

There is now intense interest in Coley’s toxins among doctors in Germany, Sweden and China, as well as the United States and Latin America. Principal credit for survival of this treatment goes to Mrs. Nauts, as well as to Mr. Wayne Martin, an octogenarian science writer who has been researching this topic since 1932.

FOUR STAGES

The history of Coley’s toxins can be divided into four stages.

In the first stage, what we can call the “golden age” of treatment, 1891-1936, Coley used either erysipelas or the toxins to treat cancer at Memorial Hospital, and dozens of colleagues did likewise. The results were mixed: sometimes spectacular, sometimes failure.

In the second stage, 1936-1963, Bradley Coley, MD

took over the Bone Service of Memorial after his father's death. He and a few colleagues continued to give the treatment, but with increasing opposition from the forces representing both radiation and especially chemotherapy. The treatment was summarily banished from Memorial in 1955. Many patients were cut off from their medicine at that point. In the fateful year 1963, the Food and Drug Administration (FDA) refused to "grandfather" Coley's toxins, as a pre-existing medicine, the way it had done for aspirin and innumerable other products. That one act made it illegal to sell the toxins in the United States. At this point, the method was added to the American Cancer Society's "unproven methods" list, in effect declaring it quackery.

In the third phase, 1964-1994, Coley's toxins became virtually unavailable. After a decade, Mrs. Nauts and her scientific director Lloyd Old, MD of Sloan-Kettering Institute, did manage to have the method removed from the ACS list. Mrs. Nauts also completed publication of her historic series of 18 monographs on the true accomplishments of the treatment. She was able to find 896 such cases. Mrs. Nauts' greatest achievement was to meticulously document the outcomes of these patients. Anyone involved in evaluating non-conventional cancer treatments will appreciate the enormity of this job.

She completed many other great scholarly tasks, not the least of which was figuring out what the conditions were for the successful application of the treatment. During this period, Charles Starnes of Amgen, Inc. also took and interest in the toxins and published on them in peer-reviewed journals (*Pharmac Ther* 1994;64:529-564).

I first wrote about the toxins 20 years ago when I was still at Memorial Sloan-Kettering. It is prominently discussed in *The Cancer Industry*, as well as *Cancer Therapy*, where I attempted to give the public some idea of the successes that had been achieved with the method.

The current period began around 1994. During this period, Coley's toxins have become more widely used, especially in various parts of Latin America, thanks in good measure to the efforts of Wayne Martin.

THE SEVEN KEYS TO SUCCESS

Certain well-delineated factors made for success or failure in the use of Coley's toxins. Some of these are under the control of the treating physician. Others can be influenced by the patient. It may be possible, by carefully studying these factors, to optimize the chance of a long-term "cure" using this method.

Mrs. Nauts' careful analysis of the cases reveals seven factors that influence whether or not the patient is likely to be cured. We now know that many cases in the past were inadequately treated. These are:

1. Stage of disease and/or magnitude of tumor burden
2. Immune competence of the patient

3. Potency of various preparations
4. Site of injection, i.e. close contact with tumor cells, whenever possible
5. Dosage, frequency and duration of injections
6. Timing in relation to surgery, radiation and/or chemotherapy
7. Febrile reactions

We shall deal with each of these in turn.

1 STAGE OF DISEASE/BURDEN

As with any form of cancer treatment, the earlier in the disease process that the patient can be treated, the greater will be the chances of success.

Put another way, patients in the earliest stages of their disease (with small and/or non-disseminated tumors) do better than those who already have inoperable or metastatic disease.

Patients who began the Coley treatment when they had primary, operable tumors over-all had a 71 percent five-year survival rate. But when metastases were present, this was reduced to 28 percent.

Among moribund cases there were no long-term survivors, although palliation (reduction in pain, improvement in appetite and weight, better facial color, feelings of well-being, etc.) was usually achieved.

2 IMMUNE COMPETENCE OF THE PATIENT

Coley is regarded as a pioneer of cancer immunotherapy. Without fully functioning white blood cells there is less chance that Coley's toxins will work. The status of the patient's immune system is thus a major deciding issue.

Prolonged illness, advancing years, or the cancer itself may weaken the immune system. But nowadays it is more likely that the patient's immune system has been compromised by extensive surgery, radiotherapy and especially chemotherapy.

For that reason, we have to face the possibility that some of today's patients have less likelihood of being cured by this treatment than were patients described in the historical record.

Of course, we must remember that patients respond in an individual way to treatments, and it is difficult to say who is immune compromised and who is not. One sign of compromise, however, is that the patient can no longer react with a fever after the injections of highly antigenic material such as Coley's toxins. This is not uncommonly seen in today's advanced cancer patient.

According to Mrs. Nauts, "many of the inoperable or terminal breast cancer patients treated after Coley's death in 1936 received [Coley's toxins] after having had

Newcastle Disease Virus Vaccine (MTH-68)

What is Newcastle disease?

Newcastle disease (ND), also known as “avian pneumo-encephalitis,” is a veterinary disease characterized by respiratory difficulties and nervousness in both water-fowl and domesticated poultry. Some adult birds do recover from ND but the mortality rate is high, and infected chicks almost never survive. The disease is caused by the Newcastle Disease Virus (NDV), a Type 1 paramyxovirus, broadly similar to the one that causes mumps in children. While there is no effective treatment for this “fowl plague,” for decades preventative vaccines have been routinely available for veterinary use.

Does NDV cause any human diseases?

NDV itself is considered either apathogenic or just minimally pathogenic in people. According to the Encyclopedia Britannica, “humans can become infected by handling sick birds but usually develop only a temporary conjunctivitis (inflammation of the mucous membrane lining the inner surface of the eyelid.” In actual practice, “pinkeye” is a relatively rare effect (see below).

What is the history of using NDV as a treatment?

In the early 1960s, a form of Newcastle Disease Virus (NDV) was directly injected into several uterine cervical squamous cell carcinomas. These underwent partial necrosis (cell death) and sloughing of tumor, which unfortunately was followed by tumor regrowth (Cassel, WA and Garrett, RE. *Cancer* 1965;18:863-868). This regrowth might have been due to the formation of natural antibodies against the virus. W.A. Cassel and colleagues used the 73-T strain of NDV, which had been passed through mouse Ehrlich ascites carcinoma cells. It is possible that the original viral strain was modified in this passage, possibly by a natural “recombination” with a parvovirus from the mouse.

Who is the principal pioneer of NDV treatment?

The principal pioneer is an Hungarian-American physician, Laszlo Csatory, MD (pronounced LASS-low Sha-TAR-ee). Dr. Csatory became interested in this topic in medical school in Hungary. He was intrigued by the fact that Hungarian farmers rarely got cancer. He theorized that they not only lived a healthier life style, but that some agent might be present in their rural environment that either prevented or cured cancer. He reasoned that since the fatal human disease smallpox was

prevented through vaccination with the cowpox virus (harmless to humans), there could also be some unknown viral agent that could perform the same role in cancer.

When he came to the United States, Dr. Csatory had a chance to put his theories to the test. In 1968, as a physician at the Jefferson Memorial Hospital in Alexandria, VA, he began to treat advanced cancer patients with a modified strain of NDV. He published a letter in the *Lancet* (1971;2:7728;825) about the spontaneous remission of metastatic stomach cancer in a Hungarian chicken farmer at the same time as an epidemic of Newcastle Disease in his flock. Dr. Csatory believed this remission was due to interference by the NDV with another cancer-causing virus. With his wife, Eva, Dr. Csatory eventually produced a medicine called MTH-68, which a carefully crafted variant on the NDV virus vaccine.

Csatory has since published a number of other articles on this topic (e.g., *Cancer Detection and Prevention* 1993;17:619-627). This reports on a phase I/II double-blind clinical trial performed in Hungary under the direction of Sandor Eckhart, MD, past president of the International Union Against Cancer. Dr. Csatory is currently the director of the United Cancer Research Institute, which was founded to promote research into viral therapies of cancer.

Supporting animal work has also been done in the US by Dr. L.N. Tauber as well as by R.M. Lorence and colleagues at Rush-Presbyterian in Chicago. These have been published in the *Journal of the National Cancer Institute and Cancer Research*, and were favorably reviewed in an editorial in the *JNCI* in 1994 (Kennedy, S and Pagano, JS. *JNCI*, 1994;86:1185-1187).

What is MTH-68?

MTH-68 is a biological product derived from the “H” strain of the attenuated NDV vaccine. The “H” strain was attenuated (somewhat weakened) in Great Britain in the 1930s by serial passage of a more virulent strain through eggs. This particular strain was originally obtained from the Veterinary Research Institute of the Hungarian Academy of Sciences.

It is sometimes erroneously stated that MTH-68 is nothing but a commercially available strain of NDV. This is not true. Csatory’s vaccine has been made in Hungary through a specially designed manufacturing process, which includes restriction enzyme analysis, cloning, purification and concentration, and lyophilization. One should therefore not identify MTH-68 as ordinary NDV. Even subtle differences in strains can produce profoundly different effects. Some strains are

ineffective. Others have variable effects on the growth of tumors in the presence of antiviral antibodies (Sinkovics, JG and Howe, CD. *Experientia* 1969;25:733-734). Yet others could conceivably be deleterious.

By contrast, MTH-68 has well-defined genetic and biological characteristics. Work on this was done by Hungarian scientists and the product is manufactured there. It meets the stringent World Health Organization (WHO) standards for such products. The final product is a purified version of the virus which is suitable for use in human cancer patients.

Could MTH-68 be harmful?

There is no indication that it is. But remember that MTH-68 is an experimental treatment, which by definition means that no one knows the full panoply of all its possible effects. We do know that conventional chemotherapy can and does cause many harmful side effects, sometimes including cancer itself. MTH-68 is not chemotherapy and does not work in the same way or share any of its other characteristics. However, one must always consider the risk vs. benefit ratio in utilizing this or any other treatment.

Does MTH-68 cause side effects?

MTH-68 sometimes does cause one particular side effect in patient, i.e. fevers. In one placebo-controlled study in Hungary, two thirds of the vaccine-treated patients had no negative side effects. But fever (in the range of 37° to 39° C, i.e. as high as 102.5° F.) was seen in 8 out of 33 patients following inhalation of the virus. This fever subsided within 24 hours. In the majority of such cases, repeated inhalation then caused only a moderate or low-grade fever. Two patients had low grade fever for 24 hours following inhalation of the virus. Fever is not necessarily a bad thing in cancer. Other treatments, such as hyperthermia and Coley's toxins (mixed bacterial vaccine), hope to raise the body temperature in order to disorganize and destroy cancerous tissue.

Conjunctivitis is the side effect most commonly discussed in relation to NDV exposure. But this is rarely seen in the clinical setting. One Healing Choices consultant did develop "pink eye" after taking the virus, but this may have been coincidental, since he was a child who had been exposed to other children with this condition just prior to this incident.

Can MTH-68 be injected?

In 1968, Csatory injected the vaccine intravenously (IV) and there were outstanding clinical results when it was

used in this way. Unfortunately, they had to abandon the use of this IV vaccine after one patient developed a severe anaphylactic (allergic-type) reaction from it. Only recently have they been able to purify the vaccine to make it safe enough for intravenous use. This could open up a new era in the use of safe and effective injected Newcastle Disease virus treatment.

At the present moment, however, the medicine is being taken either nasally as a spray or drip, or rectally as a suppository. (Final approval of the IV form in Hungary is in process.) The medicine comes in a powder form, which is mixed with a saline solution before one takes it. It takes only minutes to administer.

An intravenous version of the medicine has been developed according to World Health Organization (WHO) specifications. Toxicological and phase I (safety) studies are now underway on this in Hungary. This should be a big advance: presumably more effective, with smaller doses and lower prices for the patients. The IV form of the drug is sometimes given by nebulizer. Once Phase I studies are completed, this is promised to be available and will probably be sold in Hungarian pharmacies. Under no circumstances should patients attempt to inject the MTH-68 meant for application by inhalation.

How credible is this work overall?

For most of his life, Dr. Csatory was a working physician, not a full-time research scientist. He paid for the development of this treatment out of his own pocket, from a humanitarian motive. For 25 years he only administered this treatment when and where he was legally entitled to do so, and never charged for the treatment.

His work has sometimes been criticized for lacking the kind of sophisticated detail that some more rigorous academic studies possess. With greater resources, however, such studies (e.g., on the precise immunological modifications caused by the treatment) could undoubtedly be performed. Nevertheless, in contrast to most "alternative practitioners," Dr. Csatory has all along published in standard medical journals, including the *Lancet*, considered one of the best medical journals in the world.

On a personal note, I was first led to the Csatorys' work by a former official of the Hungarian government, well known to me, who told me that he had been completely cured of a severe genital herpes condition by this treatment. His own father, he said, had been cured of prostate cancer on it. (The father recently celebrated his 84th birthday.)

I made a trip to visit Laszlo and Eva Csatory in the early 1990s and have spoken to them regularly over the

last four years. I have also spoken to many of their patients, and have been provided with summaries of the medical records of others. They have been extremely forthcoming in providing me with the data I seek. I believe they are credible and honorable people who are truly dedicated to the welfare of patients. The scientific evaluation of MTH-68 should be a high priority of the government's war on cancer

Can this approach be used to treat other illnesses?

Dr. Csatory presents credible data that similar products can also be used to treat other diseases of viral origin, including herpes infection and hepatitis B. The theoretical basis of such treatments is as follows: chickens are afflicted with a cancer-like illness caused by herpes viruses. This is called Marek's disease. Csatory and his colleagues gave both Marek's disease and a human myxovirus, influenza A, to birds in an attempt to study how they interfere with one another. Birds which had been exposed to both viruses recovered, whereas those which contracted only Marek's disease all died. The rate of cancer-like changes in the blood was cut in half. And of those that did develop cancer, there were "less severe lesions." (For more details, see *Cancer Therapy*, pp. 439-440).

To treat other illnesses other viruses are currently in use. Thus, they are using an attenuated variant of the Bursal Disease Virus (BDV), called MTH-68/B, to treat hepatitis B. In a placebo-controlled study of 84 patients Hungarian patients with acute B (43 patients) and C (41 patients) viral hepatitis, MTH-68/B reduced the frequency of relapses and decreased the number of cases progressing to chronic hepatitis. This work was reported at the Clinical Immunology Society meeting in February, 1996.

Of the 43 patients with Hepatitis B, 15 in the control group progressed to chronic active hepatitis, while none in the treatment group did so. There were long-term (six month or more) remissions in the control group, compared to 4/19 or 23 percent in the treatment group.

What is the relationship of viruses to cancer?

It is contradictory. On the one hand, it is well-established that many animal cancers are caused by specific viruses (e.g., the feline leukemia virus). More and more human cancers (e.g. Burkitt's lymphoma) are either known or strongly suspected of also being caused by viruses. It may be that viruses play a yet undefined role in initiating or promoting a great many human cancers.

At the same time, viruses are a two-edge sword, for it

appears likely that one can utilize viruses in the fight against cancer. It is an old observation, but a profoundly true one, that tumors tend to soak up infectious agents. ("The tumor functions as a sponge," according to C. Levaditi and S. Nicolau, writing in the French Annals of the Institut Pasteur 1923;37:1-3.)

The idea of using viruses to attack cancer is new to most people, but it has been repeatedly suggested and tried for over 100 years. As several researchers have written, this idea "repeatedly emerges reinvented anew and abandoned, just to reappear again in the most recent literature" (Sinkovics, JG and Horvath, J, *Medical Hypotheses* 1995;44:359-368).

There are many well-documented cases in the medical literature of cases of cancer that disappeared after natural viral infections with such diseases as measles or hepatitis A. In 1893, another Hungarian, F. Kovacs, described the regressions of leukemia that followed various kinds of viral infections (*Wien Klin Wochenschr* 1893;6:701). These have generally been dismissed as imponderable "spontaneous remissions."

A 1912 scientific article generated much interest when it reported on a woman whose carcinoma of the uterine cervix regressed after she received a vaccination with an attenuated (i.e., weakened) strain of the rabies virus (DePace, NC, *Ginecologia* 1912;9:82). In continental Europe, throughout the early decades of this century, sporadic attempts were made to treat advanced cancer patients with both native viruses and vaccines.

In the United States in the 1960s, Dr. Chester Southam, a celebrated immunologist at Sloan-Kettering Institute and colleagues, tried to use the measles and other viruses to induce remissions in Hodgkin's disease, Burkitt's lymphoma and acute lymphocytic leukemia (ALL). There were some good results, but one child with cancer may have died from the after effects of this measles treatment (Laski, B. *JAMA* 1973;225:1303). Following that, there was diminished interest in this approach.

Sporadic work still continues along these lines in a number of countries. In China it has been found that a combination of chemotherapy, BCG (a standard immune stimulant), and the measles vaccine brought about a complete response rate of 79 percent in leukemia compared to a rate of 31 percent using chemotherapy alone (Yu Zhifei, et al. *Chinese Med* 1981;94:31). This work has not been followed up on in the West. Perhaps the best-known use of viral therapy has occurred in Japan. There, starting in the 1970s, a Japanese scientist, T. Asada, used live mumps virus to treat 90 patients in an uncontrolled study. He claimed that 79 of these (87.7 percent) had

either regression or stabilization of existing tumors (Cancer 1974;34:1907-1928). Again, there is been no adequate follow-up of this work in the West.

Have other types of viruses been used as therapy?

Yes, other viruses have also been used successfully from time to time, including varicella (Bierman, HR, et al. Cancer 1953;6:591); attenuated yellow fever virus and hepatitis A (Weintraub, LR. JAMA 1969;24:1590); smallpox vaccination (Hansen, RM and Libnoch, JA. Arch Int Med 1979;138:1137 and DeStefano, AD and Buzdar, AY. Arch Int Med 1979;139:946). In fact, we now realize that many of the "spontaneous remissions" reported in the literature followed known or suspected viral infections (Sinkovics, J. Ann Immunol Hung 1986;26:271-290).

Is this work supported by laboratory studies?

Parallel to the clinical reports, and sometimes stimulated by them, have been some rather spectacular reports of both *in vitro* (test tube) and animal studies, starting in the 1920s (e.g., Molumut, N, et al. JNCI 1965;34:403 and Wheelock, EF. PNAS 1966;55:774).

Scientists have demonstrated a pattern of "interference" between common viruses and cancer-causing (oncogenic) viruses that could account for these effects (by the mid-1950s, 50 such papers had been published). Soon after the first cytokine, interferon, was discovered in 1957, it was recognized as a major mediator of such interference. Interferon itself was found to suppress the replication (reproduction) of both cancer-causing viruses and of cancer cells themselves. At the same time it has been found that cancer tissue itself exerts an interferon-suppressing effect (Sinkovics, JG, et al. Experientia 1968;24:927)

In still unpublished results from 1996, Hungarian scientists demonstrated pronounced antiproliferative effects when MTH-68 was incubated with different human tumor cells. The strains used were the HT29 human colorectal tumor, the MCF7 human mammary tumor and the PC3 human prostatic cancer cells. They were "altered remarkably" when they were infected by different doses of the live Newcastle disease virus, while the proliferation of normal human fibroblast cells was not affected by this treatment. In particular, it was found that the highest dose of the virus (107 EID50/ml) caused the destruction of 81.7 percent of the breast cancer cells, 75.8 percent of the colorectal and 32.2 percent of the prostate cancer cells after 48 hours incubation. By

contrast, only 11.6 percent of the normal human fibroblasts were killed by such incubation. □

For further information on MTH-68:

See Ralph W. Moss, Ph.D., *Cancer Therapy*, Equinox Press, Brooklyn, New York 1996, pp. 437-445. See also chapter on "Coley's Toxins," a somewhat related bacterial product, in Ralph W. Moss, Ph.D., *The Cancer Industry* (Equinox Press, 1996). To order these books, ask your bookseller or call the publisher at 1-718-636-1679.

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Web site	http://www.walrus.com/~equinox/

radiation and/or chemotherapy. *Although no cures were obtained*, marked palliation, regression, decreased pain... and weight gain occurred in many of these patients” (italics added).

One possibility might be for the patient to take various immune-stimulating substances (such as the Chinese herb *Astragalus membranaceus*, which is widely available in health food stores) as a way of boosting the immune response.

Another confounding factor that could affect the outcome of Coley’s treatment is the widespread use of antibiotics in medicine and agriculture since the 1940s. Antibiotics, the “wonder drugs” of the postwar epoch, are clearly a two-edge sword.

Immunity is “a mechanism that has been acquired and perfected through millions of years of evolution” wrote B.A. Meyer and J.D. Benjafeld forty years ago. Yet incessant treatment with antibiotics may interfere with that mechanism.

“The antibiotics may absolve the body of the need to bring the normal immunological mechanisms into use” (*Med. Press* 1955:234:206-208). Such criticisms of antibiotics, once highly controversial, are now more common.

“The widespread and often indiscriminate use of antibiotics” has “created drug-resistant Gram-negative bacilli that readily acquire multiple resistance....” says a modern textbook. “Prolonged antibiotic therapy compromises this defense mechanism” (Baron, S., ed. *Medical Microbiology*, 4th ed., U. of Texas, Galveston, 1996:348).

It is thus also possible that optimal results with Coley’s toxins could be diminished by the side effects of long-term use of antibiotics.

Again, we should be prepared for the possibility of *less dramatic* results than were achieved 100 years ago.

3 POTENCY OF VARIOUS PREPARATIONS

Coley’s toxins are a manufactured item. And while making them is not “rocket science,” they do have to be prepared with both knowledge and care. To put it mildly, this has not always been the case.

Coley himself, while an eminent surgeon, was not a microbiologist, and always relied on others to make the preparations for him. When those others were knowledgeable and scrupulous technicians, clinical results with the toxins tended to be very good.

But when they were not, the preparations were either less effective or *virtually worthless*.

It was found that a weak preparation could usually be compensated for by an increase in the dosage. But some preparations actually appear to have been totally *inert* and the long-term remission rates achieved with them were virtually zero.

This one variable led to a great deal of confusion, skepticism,

and chagrin among Coley’s medical colleagues, even his erstwhile supporters. And this skepticism has been passed, like an infection, down through the decades.

Historically, there have been several different ways of making Coley’s toxins. First, as we have seen, Coley just injected *live* strep organisms (obtained from the laboratory of “microbe hunter” Robert Koch).

This was effective but too dangerous to use.

Following this, Coley’s colleague, Alexander Lambert, made preparations of toxins for him from killed streptococcal germs. Lambert made beef broth, grew the strep in the broth for several days, and then sterilized it with heat to destroy any living microbes (*Proc. Royal Soc. Med, Surgical Section* 1909-1910:1-48).

Coley was always interested in increasing the “punch” of his products and so he asked another colleague, B. H. Buxton, Fellow of Bacteriology at the Loomis Laboratory and later Professor of Experimental Pathology at Cornell University, to make up a mixture of strep and the aforementioned *Serratia marcescens*.

Buxton grew the two microbes together in the same flask. But one cannot just grow them together, however, because strep grows best at 36 °C (about 97° F), while *Serratia* likes to grow in a cooler medium.

Buxton therefore grew the strep by itself for ten days and only then added *Serratia*. The two were then grown together for another ten days at 25° C (about 77° F). After this total of 20 days, the germs were all killed by heat. But it was also observed that the lower the temperature used to sterilize the mixture, the stronger was the resulting product.

On the other hand, too little heat could leave the microbes, and especially the potent *Serratia*, alive and kicking. The injected mixture could theoretically infect the patient, with disastrous results.

Because of this fear, some technicians, then and now, overheated the product in order to make sure that they killed every last *Serratia* germ. But there was a price for such caution, for this overheated preparation also had little anticancer activity.

Thus, ironically, some technicians inactivated their own preparation, out of excessive caution.

TRACY FORMULA

Coley used Dr. Buxton’s formula until 1916. Then he switched to a new kind of formula produced by Dr. Martha Tracy. As we have said, there was nothing critically wrong with the Buxton formula. Many long-term remissions were achieved with it.

But around this time, Coley became aware that *Serratia* itself instead of being just a remarkable helper might be a potent anticancer agent in its own right. In fact, through experiments on animals, he began to suspect that it was even more powerful than the strep itself.

Martha Tracy's formula was designed to take advantage of this new information on *Serratia*. In the Buxton formula, no one could tell just how much *Serratia* was actually present in the mixture.

But *Serratia* turned out to have an extremely variable rate of growth. For this reason, unlike her predecessor Buxton, Tracy grew the two microbes *separately* and only mixed them together at the very end.

Tracy took a few cubic centimeters (ccs) of strep and added these to small flasks of sterilized beef broth. She allowed these to grow in an incubator for three weeks. She then spread some *Serratia* on sterilized agar solution and allowed it to grow at room temperature in daylight (but not direct sunlight) for ten days. She then scraped off some of the thick red growth of the *Serratia* with glass rods and ground these germs in a mortar and pestle into a smooth and thick suspension.

She then mixed this with physiological saline (salt) solution, bottled it and sterilized it at 75° C (167° F) for one hour.

Tracy then used what are called 'nitrogen determinations' to figure out how much *Serratia* was actually present in the medicine. In this way she was able to achieve "a definite standardization of dosage," wrote Coley.

All this was admirably precise. However, there was and is also a rough-and-ready way to know whether or not any given ampule contains much *Serratia*. That is simply to observe its color. *Serratia* is "chromogenic," i.e., shows up as bright red in the vial. The redder the solution, in fact, the greater the concentration of the microbe. Reddish products, not surprisingly, were also found to have greater anti-cancer effects.

Although Tracy could measure *Serratia* by measuring the nitrogen content, initially she did not know just how much *Serratia* to include in the final product. She guessed—and guessed wrong.

"Very severe reactions were obtained by minute doses," Coley reported in 1919, "and in one case, in the hands of another physician, death resulted within a few hours after an injection...into a very vascular tumor in the mediastinal region."

The amount of *Serratia* was hurriedly reduced by half, and then was used safely for decades. There were no more deadly reactions.

But we see that this essentially non-toxic product must be produced and administered correctly or serious consequences can result.

While the Tracy product is admirably scientific, it is also somewhat impractical to manufacture under less-than-optimum conditions, e.g. in Third World countries. And, for political reasons, it is most likely that Coley's toxins will be made and used in such countries for the foreseeable future. While such countries do have labora-

tories that, with a small investment, can produce the toxins, nitrogen determinations are trickier.

And since live microorganisms like *Serratia* cannot be shipped across national borders, sending away for nitrogen determinations is also ruled out.

For that reason, under some circumstances, the Buxton method is still used. The manufacturer has to simply "eyeball" the pinkness of the final product to judge its potency. This seems adequate.

However, before it can be injected into humans, each batch has to be tested in animals.

Patients start their treatment with very small doses to test the reaction. They then gradually increase the dose, using the fever/chill reaction as a guide. The proper dose basically depends on the amount necessary to raise the desired fever. I hesitate to talk too much about dosage, because this is a medical question that requires close attention to the individual patient. However, recent experience has been that the best way to get people on the road to being clinically well is to give them a great deal of vaccine. They will spell this out for you in great detail.

This has led some clinics to adopt the following general guidelines: they start with a minute amount .01 cc (i.e., one-hundredth of a cubic centimeter) IM (intramuscularly). They increase this on each successive day by 50 percent and in 13 days they level off at 1.00 cc (one cubic centimeter). They then continue on 1.00 cc for a total of four weeks. They then rest two (2) days and if possible start IV (intravenous) injections at .01 cc increasing this each day by 25 percent for a period of one (1) week. On the following week they return to intramuscular injections (IMs), starting at .05 cc and continue increasing this by 50 percent until they reach a MAXIMUM of 1.00 cc. After two weeks of IMs they return to IVs if possible, starting at the same .01 cc, etc.

Again, this is an empirically derived formula, but is not writ in stone. It is likely to be modified by further clinical experience.

What if live bacteria are still lurking in the mixture? Could this cause a blood infection (septicemia)?

In Coley's day, the bacteria were usually heated to 58° C (137° F) and no such problems were encountered. But more recent experience has shown that even at 60° C (140° F) some *Serratia* was still left alive in the mixture. Therefore, today the product is generally heated to 65° C (149° F) for two hours. The resulting product is strong and has always proved sterile.

In Coley's day, they also added a little bit of thymol, a phenol preservative derived from the volatile oil of the herb thyme. In recent years, some manufacturers have used synthetic thymol for this purpose, while others have used butyl alcohol.

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COLEY'S TOXINS, *continued from page 6*

Somewhat more controversial is the fact that today's mixture tend to be *filtered*. This upsets some Coley purists. Coley himself feared that filtering might weed out some of the most desirable bacterial by-products. However, in Coley's day it didn't much matter if a few larger particles were included in the mix, since most injections were either into a muscle (I.M.) or directly into the tumor (I.T.) Intravenous injections (I.V.) were not widely used in those early days.

For that reason, both heating and filtering was like 'wearing belts and suspenders.' However, today, if solid particles were to be injected into a vein, this could indeed cause serious adverse reactions, even shock. (This is a largely theoretical concern; to our knowledge it has not happened within living memory.)

It seems quite prudent, for this reason, to filter the killed product through a five micron filter, as a precaution against any stray particles. This should not affect the potency of the mix, since the bacterial by-products themselves are smaller than five microns.

Once this is done, the mixture is ready for use.

DIFFERENT PREPARATIONS

There were great differences in the results achieved when different versions of Coley's toxins were used. While excellent results were often achieved with both the Buxton and the Tracy preparations, there was also an ineffective *commercial* preparation of the toxins made at the Lister Institute of Preventive Medicine in England, from about 1895 until 1944.

This is designated Lister VIII in the literature. (All preparations were given Roman numerical designations by Mrs. Nauts.)

Something was definitely wrong with the Lister method of preparation. Even today it is painful to read how British supporters of Dr. Coley repeatedly wrote to him complaining about the weakness of these British preparations. Injections of this product elicited no fever/chill reactions and consequently proffered no clinical benefit. They were essentially inert. But poor Coley, without our modern means of communication, was unable to remedy the situation.

Many of those writing to him had started out as enthusiasts, but became disillusioned or even opposed to its development. It is perfectly understandable why skepticism about this American innovation grew under the circumstances. It was based on such repeated stories of failure that Sir Frederic Eve, a senior surgeon at London Hospital, denigrated the use of Coley's toxins in print. Eve was highly regarded in the field and his article in the prestigious journal, the *Lancet*, doomed the

treatment from receiving further serious consideration in British medicine and consequently in many places around the world.

In the United States, a similar situation prevailed with the formula known as Parke-Davis IX. Although the Parke-Davis company had started production with the Buxton VI strain of strep, this strain had apparently lost most (or even all) of its potency over time.

Nor did the company attempt to standardize *Serratia* in the manner of Dr. Tracy.

Again, American colleagues wrote to Dr. Coley. What they said was a giveaway that Parke-Davis was asleep at the switch. For some of the bottles were reddish in color, but others were *perfectly clear*, almost a sure sign that there was little if any *Serratia* present in the mix.

This is one of the major reasons that there was a 58 percent five-year survival rate using Buxton formulas IV, V and VI and a remarkable 67 percent using Tracy X and XI. But there were *zero cures* with Lister VIII or using the later Sloan-Kettering XIV formula. (Sloan-Kettering has never had much luck with alternative treatments of any kind.) Everything depends ultimately on the inherent power of the toxins. A weak or inactive preparation will yield minimal, if any, results.

4 SITE OF INJECTION

In chemotherapy, oncologists often attempt to deliver toxic drugs as close as possible to the site of the tumor. The same principle applies to Coley therapy. By doing this, one increases the 'antigenicity' of the tumor (i.e., its visibility to the immune system), elicits an inflammation reaction, and activates the macrophage cells, which are a key element of the immune system.

In animal studies, the injection of immunological agents such as BCG (bacillus Calmette-Guérin) directly into a tumor produces a tumor suppressive response, whereas little or no response is seen when it is given systemically (Baldwin, RW. In: Steffin, C and Ludwig, H., eds. *Clinical Immunology*, Elsevier, 1981).

Initially, Coley himself injected the toxins into any tumor that could be reached by a needle. In this way the inflammatory reactions could be set to work. But Coley suspended intratumoral injections in 1906, and did not resume them until a year or two before his death. By that time, he understood that he had made a tragic mistake in suspending them, and that by doing so he had decreased the success rate of his treatment.

The reason he did this was to prove to skeptics that the toxins exerted a *systemic effect*, and did not just act by locally poisoning or eroding the tumor. This was an important academic point, but should never have been allowed to overshadow the therapeutic needs of the individual patient.

5 DOSAGE, FREQUENCY AND DURATION

A sufficient amount of toxins must be given in order for the patient to mount a proper immune reaction. But how much is enough? Generally, as we have stated, the patient should be given the dose that causes a strong fever and/or chill reaction.

We have given one formula in use. But basically the dose has to be established by trial and error, and it can also be expected that a certain tolerance will develop.

One cautionary note, however, is that too small a dose of Coley's toxins, "given either intramuscularly or subcutaneously, may actually stimulate the target tumor cells rather than inhibit them" (Nauts, HC. *Breast Cancer*; 1984, citing Prehn, RT, *Science* 1972;176:170-171).

Following the injection, especially intravenously, the patient often experiences fever and chills for two hours or more. Some doctors (and family members) may have ambivalent feelings about allowing such reactions and want to promptly reduce it. But through it all one must always keep in mind that *this unpleasant fever is the main point of the treatment*.

Historically, if the patient's fever averaged 102° to 104° F or even reached as high as 105° F, and especially if this was accompanied by chills, *there was a 60 percent chance of 5-year survival*. This doesn't even take into account other factors that could increase these odds.

But when fevers averaged below 102° F, the survival rate in otherwise comparable patients dropped to 28 percent. And if there were few if any fevers, the 5-year survival rate fell further to 20 percent.

Duration of treatment is another especially important factor. In fact, it cannot be emphasized enough.

- When the toxins were given for just 1 week, there was *no* survival advantage to the treatment.
- When they were given for 2 weeks, there was 14 percent 5-year survival.
- When treatment was continued for 2 months, there was 42 percent 5-year survival.
- And when they were optimally delivered for 6 months, 80 percent of the patients survived 5 years or more.

Further treatment after that time did not increase the survival rate, although a periodic booster shot was considered desirable.

We can conclude that for optimum results the treatment should be given for a minimum of five or even six months.

Even many doctors who gave the treatment were unaware of the need to give the treatment aggressively *at least three times per week initially*.

6 TIMING IN RELATION TO SURGERY

Understandably, because it never was accepted as a conventional treatment, Coley's toxins were generally given

in far advanced, so-called "terminal" or "moribund" cases. In such cases, although it still could possibly cure, more frequently it palliated the condition.

It should be emphasized that Coley's toxins do not contradict the usefulness of adequate surgery. In fact, *it is particularly appropriate when used as an adjunct before and after conservative surgery*.

Mrs. Nauts points out that it is "particularly needed in all postmenopausal women to augment their response to adjuvant chemotherapy." It should be given during the time when recurrences or metastases are most likely to develop. It can be used to reduce the tumor burden and to protect against the harmful effects of chemotherapy and radiation "while potentiating the response of the tumor to these modalities" (*ibid.*).

7 FEVERS AND CHILLS

Fever and chills are the hallmarks of this treatment. They are certainly unpleasant, but are they bad for us? According to the authoritative *Merck Manual*, "whether to treat an elevated temperature that occurs with an infectious disease is the subject of an ongoing debate. Experimental evidence suggests that host defense mechanisms are enhanced by an elevated temperature; thus, fever is potentially beneficial and should not be routinely suppressed" (16th ed., 1992, p. 9).

In cancer, the existence of fever outside of Coley's toxins can be a serious complication. This is especially so when the patient is suffering from immune suppression following chemotherapy. We are not commenting here on the wisdom of antibiotic therapy in such cases. We are just trying to point out that there is a strong philosophical bias against not just allowing fevers but utilizing them as a therapeutic procedure in any cases.

It bears repeating that patients who had fevers which averaged between 102° and 105° F (39–40.5° C) had a significantly higher percentage of complete and permanent regressions. This was especially true in inoperable or metastasized cases. In addition, the responses were better when injections were given in or near the tumor; intravenously, or in larger intramuscular doses. The subcutaneous route was historically the least effective.

The largest number of "spontaneous remissions" also followed infections in which there was a high fever.

But fevers are not easy to endure. If the fever goes on beyond two hours it can be brought down within fifteen minutes or so by Tylenol suppositories or other anti-fever medications. (Since Tylenol can have side effects of its own, it is optimal not to have to resort to such agents.)

Prescription muscle relaxants are also sometimes used. Patients suffering from chills sometimes find warm baths to be comforting. Those who are troubled by headaches or other discomforts associated with the fever

might find some relief by taking an enema.

Some researchers believe that a coffee enema or two per day while undergoing vigorous cancer treatment decreases the amount of toxic buildup, and leads to an improved feeling of well-being. But more should only be undertaken while under medical supervision.

Fevers are still somewhat mysterious. We know that infections, real or simulated, can trigger the release of various chemicals called endogenous pyrogens in the body. (Endogenous pyrogens are varieties of cytokines.) Generally speaking, these are peptides or protein-like materials produced by many and varied cells of the body.

The names of some of these pyrogens are interleukin-1 and IL-6, tumor necrosis factor (TNF) and interferon- α .

You will notice that some of these are themselves being explored as cancer treatments. But they are usually tested as single agents in high doses. In Coley's toxins the patient gets them all in small to moderate amounts, with many agents working together in concert in a natural "symphony." Philosophically, Coley's toxins is worlds apart from the kind of immunotherapy now promoted by the National Cancer Institute.

An increase in these cytokines can in turn stimulate various important immune function cells including monocyte-macrophages, keratinocytes, and endothelial, B, epithelial and glial cells.

These cells in turn influence the heat-regulating center of the hypothalamus, which is sometimes called a "master gland" of the human body.

Macrophages (literally, "big eaters") themselves can kill cancer cells, but must first be activated by other factors. And the most effective way of activating them is simply to bring them into contact with "a variety of microorganisms and their structural components" (Heppner, GH and AM Fulton, *Macrophages and Cancer*; Boca Raton: CRC Press, 1988, p. 150).

Various high-tech and incredibly expensive ways have been devised of doing this. In fact, the sale of purified fractions makes up an increasing component in the worldwide anticancer drug marketplace (see the author's *Questioning Chemotherapy*, p. 76).

Coley's toxins, on the other hand, remains a relatively easy, inexpensive and natural way of getting the body to produce its own supply of these chemicals. It is natural because it simulates something that happens or at least used to happen on a regular basis in our species, i.e., severe bacterial infections.

(On a speculative note: I once knew a woman who tragically refused all treatment for breast cancer. The cancer predictably metastasized and killed her. However, before she died she developed an infection of the suppurating 'wound' that had become her breast.

At this point, the breast became inflamed and while she was bathing one day this primary tumor literally fell out of her breast, leaving a clean hole. As stated, however, the woman died of the metastases, and so this form of 'treatment' is certainly not recommended. However, one has to wonder if in those endless stretches of time before the development of modern cancer therapy, tumors that broke to the surface of the skin and became infected sometimes spontaneously healed with nature's own form of "Coley's toxins.")

TOXICITY

The unfortunate appellation "toxins" has certainly has done its share to scare people away from this treatment. But all euphemistic names (such as "mixed bacterial vaccine") have never really stuck. And so Coley's *toxins* it is.

Ironically, we have a right to ask whether Coley's toxins should really be considered a toxic form of cancer treatment. The answer depends on what one means by "toxic."

The goal of Coley's treatment is clearly to stimulate an intense immune reaction, such as one normally experiences when assailed by an intense bacterial infection. Fever, chills, sweats, or even headaches are very unpleasant, and in that sense one must acknowledge that *this is certainly not a treatment without its drawbacks.*

Plus, Coley was aiming for the maximum therapeutic effect and to get this he sought out the most "toxic" strains of microbes he could find. As he once said, "I obtained cultures from fatal cases of erysipelas in order to get the highest degree of virulence." The strep he preferred (from the Huntington Cancer Research Fund) was isolated from a fatal case of septicemia. "It is doubtful whether an organism from an actual case of erysipelas would give any better results," he wrote, enthusiastically.

However, the word "toxic" has changed its meaning in the intervening decades. Chemotherapy has added a whole new dimension of toxicity to the medical textbooks. Chemotherapy destroys a great many of the normal cells of the body, especially those of the immune system. Although oncologists routinely deprecate any concerns over this aspect of the treatment, it seems clear that attempts to resort to immunological treatments after chemotherapy are greatly hampered. To what degree the immune system really recovers from intensive chemotherapy (or radiotherapy) is uncertain.

By contrast, to our knowledge, Coley's toxins leave the various organ systems and tissues of the body in as good if not better shape at the end of the treatment than they were at the beginning. This seems particularly true of the immune system, which seems to be toned and enhanced by the treatment. As Mrs. Nauts summarizes:

“The available evidence suggests that Coley’s toxins are without harmful or dangerous effects to patients or animals suffering from various types of neoplasms, provided these toxins are administered properly as to dosage, site and the usual aseptic precautions.”

She does emphasize the following limitations on the treatment, however, which should be understood by all those considering this route:

“They should *not* be given to patients with severe *hepatic [liver] insufficiency* due to metastatic disease or other pathology, nor to patients who have had *severe heart conditions*, nor to patients who are *almost moribund*, because such patients do not respond.”

Any questions on the potential danger of the treatment must be referred to a competent medical doctor.

BARRIERS TO ACCEPTANCE

The history of Coley’s toxins presents some unusual features to students of alternative medicine. Oftentimes, proponents of unconventional treatments are themselves “outsiders.” Some are not cancer specialists or not even medical doctors. Their treatments may be marketed in various “underground” or even illegal ways. This guarantees that they are dismissed or attacked as arrant quackery by the regular medical profession. And no doubt some of them are classical quackery, with tragic consequences.

Under conditions in which alternatives are routinely dismissed as worthless, practitioners have little incentive or even possibility of documenting results with such treatments, much less long-term outcomes.

What makes Coley’s toxins stand out, however, are that Dr. Coley was the very opposite of a “quack.” He was a highly regarded surgeon at one of the world’s foremost cancer centers, with scores of scientific publications to his credit. He never attempted to go over the heads of his medical colleagues and directly address the public with either his claims or his frustrations. (He developed ulcers instead.) In that bygone era, he and his collaborators were highly honored for their work. In fact, no finer group of doctors could have been found at that time.

And far from exploiting his treatment for financial gain, Coley was exceptionally generous towards all patients. In 1897, in fact, he established the Needy Patient Fund at Memorial Hospital. In 1898, records show that he handled some 40 of these charity patients himself and often paid their bills out of his own pocket. Indigent cancer patients were referred to him from all over the United States and he never refused to treat them. In fact, Coley himself performed up to 60 percent of the “free” operations at Memorial Hospital between

1908 and 1913 (Nauts, HC. *Coley’s Toxins: 1893-1995 and Beyond*. Speech to Pharmacia, Lund, Sweden, 5/15/95).

He did not attempt to patent or otherwise monopolize the treatment, and in fact spent a great deal of his own money sharing his knowledge with scientists around the world. There were no secrets, other than those that Nature has kept from the scientific community.

Alternative cancer practitioners are also often accused of disregarding the long-term outcomes of their cases. Dr. Coley kept good records, and made it possible for his intrepid daughter to compile the outcome of 896 cases who had been treated by either Coley himself, his son, Bradley, or their worldwide collaborators. This work was meticulously carried out by Mrs. Nauts.

Cancer alternatives are also often characterized as inordinately expensive. But the cost of Coley’s toxins has always been remarkably low, in fact just pennies a day for the medicine. They are simple to produce and may be ideally suited for very poor countries. (In fact, there is a Coley’s hospital in China.)

The starting broth, which today is generally a synthetic mixture called AOAC Depco, costs around \$10.00 and takes about 30 minutes to assemble.

This is then put in the incubator, where it is inoculated with the strep organism. The laboratory technician then goes away and comes back in ten days. A second inoculation is then done and he or she then goes away again for another ten days. The total labor time comes to about five hours, and this work produces about a quart (1,000 ccs) for a total cost of about \$100. Mass produced they might cost even less.

Naturally, the patients’ cost will be considerably more than this. There has to be some markup for the people producing the toxins, for the doctors and hospitals that administer the treatment, etc.

But, still, this is a potentially inexpensive “drug.” Ironically, this makes it very unattractive to those in power in the medical field. It has long been our contention that Coley’s toxins cannot compete in the drug marketplace dominated by patented chemotherapeutic agents. They are just too cheap.

SOME COMMENTS ON THE MICROBES

In general, the micro-organisms themselves are easy to come by. Various biological supply companies sell live cultures for research purposes for very little money. Clinicians have been known to obtain potent *Streptococcus* from the “strep throat” of their patients. In some places they are available from medical schools. They stay alive for a long time and usually do not lose their potency.

Streptococcus pyogenes is a Gram-positive, nonmotile round to egg-shaped coccus which occurs in either pairs or chains. Most *Streptococci* are anaerobes, i.e. flourish in the absence of air. They are generally encased in a cap-

sule made up of hyaluronic acid.

Although *Streptococci* are part of the normal flora of the nose and mouth (we all probably have some resident in such places), under certain circumstances they can cause a variety of human diseases. These include pneumonia, scarlet fever, rheumatic heart disease, and glomerulonephritis. Acute strep infections can take the form of pharyngitis, scarlet fever (rash), impetigo, cellulitis, and of course, more to the point, erysipelas.

Various factors can affect the ability of this microbe to cause disease. The immune system normally produces antibodies against what are called "group A" *Streptococcus*, which is the type that is commonly associated with human illness. Also, we know that gamma globulin (IgG) is produced by the mother in her milk to protect babies.

PLEOMORPHISM

Students of alternative treatments will be interested to know strep infections (and thus, Coley's toxins) may interdigitate with certain bacterial theories of cancer's origins. Even orthodox textbooks point to the existence of certain forms of strep that resemble those weird pleomorphic organisms seen by innovative researchers such as Gaston Naessens and Virginia Livingston-Wheeler.

According to the recent edition of a classic textbook: "Recently, nutritionally deficient streptococci (also known as [cell] wall-deficient, L form, etc.) have been recovered from a variety of clinical sources....These variants demonstrate bizarre pleomorphism microscopically...." (Baron, *Medical Microbiology*, 4th Ed, p. 202).

Strep also contains various substances which can prompt an immune response. These include peptidoglycan in the cell wall, pili M protein type antigen; lipoteichoic acid; and R and T proteins.

In addition, strep produces a wide array of products. These include the following: streptolysins, NADase, hyaluronidase, streptokinase, streptodornases, and pyrogenic exotoxins (the main source of fevers). These have been studied intensively, yet scientists are still not clear how or why strep causes disease (Baron, p. 204).

Streptokinase in particular has independent anti-cancer properties, although it may be destroyed when the Coley's product is heated.

SERRATIA MARCESCENS

Serratia marcescens is a Gram-negative bacillus that is normally found in the human intestines. In this regard it is similar to the *E. Coli* bacteria found in the gut. They are both called coliform bacteria (no relation to Dr. Coley).

Marcescens is one of 11 species of the *Serratia* genus. At one time it was dismissed as a harmless part of the intestinal flora. It was Coley who first pointed out its important biological (even curative) role, although this was not accepted in his own day.

Today, it is finally acknowledged to be one of the six

or seven bacteria that is responsible for most infections produced by this group. It is particularly found as a cause of pneumonia and of urinary tract infections following catheterization as well as infections complicating burns.

What do these microbes do in the body that could have such an effect on cancer? *Serratia* contains various markers on its surface, called H, K, and O antigens.

H antigens are derived from the numerous "tails" or flagella that stick out from many places on the microbe's cell surface. Some *Serratia* have K or capsule antigens, which are components of the polysaccharide capsule that surrounds the cell.

The outer membrane of the bacteria contain lipopolysaccharide (LPS), of which the lipid portion is particularly toxic. It was in the course of experiments with LPS (and a tuberculosis vaccine) that the anti-cancer substance, tumor necrosis factor (TNF) was discovered at Sloan-Kettering Institute in 1975.

If we don't really know which of these creates the anticancer effects do not be surprised. In fact, the process by which *Serratia* produces disease is itself still poorly understood. In fact, it rarely does cause disease unless the host defense system fails in some way. Humans with systemic infections from *Serratia* do display the common effects of bacterial toxins, which includes fever and chills.

These bacteria are normal to the host, and in fact generally keep each other in balance. The reason that *Serratia marcescens* is now often infectious (but was formerly rarely so) has to do with the fact that *Serratia marcescens* is frequently found in hospital-acquired (nosocomial) infections as well as community-acquired human diseases.

CONCLUSIONS

We have now had 25 years of the 'war on cancer.' Although Congress was promised a cure in time for the Bicentennial, there has been little progress towards that goal. It appears that chemotherapy has about reached the limit of its usefulness.

Coley's toxins (and related treatments) represent a different way of approaching the cancer problem. Admittedly, this is a difficult treatment for the patient, since fevers and chills are decidedly unpleasant. However, despite the name, Coley's toxins are far less toxic than conventional chemotherapy.

The historical record documents the frequent successes seen with this method. It thus is absolutely imperative that Coley's work be revived, reproduced, and extended. "Improvements" on this work should only be embraced when it can be demonstrated that they yield a higher five-year survival rate than the original method. In this way, we can reach into the past to find a viable treatment for the future. □

The Cancer Chronicles

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For further information on Coley's Toxins:

See Ralph W. Moss, Ph.D., *The Cancer Industry*, Equinox Press, Brooklyn, New York, 1996, chapter 7. See also the same author's *Cancer Therapy*, Equinox Press, Brooklyn, New York, 1995, pp. 407-413, as well as related chapters on MTH-68, Maruyama Vaccine, etc. To order these books, one can call the publisher at 1-718-636-1679.

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