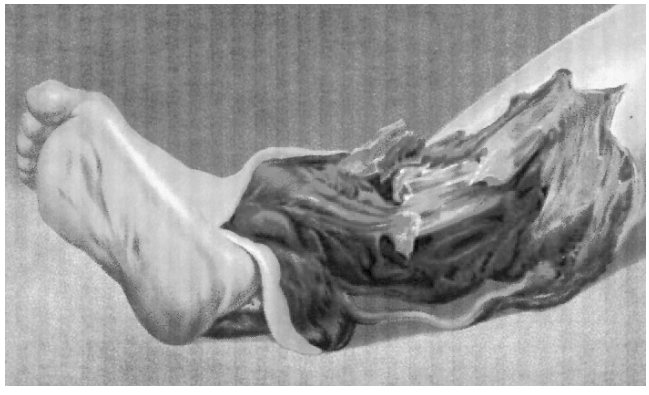
Low-dose Irradiation Therapy Cures Gas Gangrene Infections

by Jerry M. Cuttler

Seventy years ago, low-level radiation successfully cured gangrene and other lethal infections, without requiring amputation. It should be reinstated as a treatment.

Infection with clostridium bacteria, which live in the soil, is most often associated with war wounds, car accidents, complicated abortions, and so on. The incidence is highest in areas with poor access to proper wound care. Such infections lead to gas gangrene, a deadly disease that spreads very quickly in the body and causes rapid death. Present-day treatment consists of administering antibiotics and surgical removal of dead, damaged and infected tissue. Amputation is usually necessary to control the spread of the infection, which, once established, generally advances at the rate of six inches per hour. From the late 1920s until the early 1940s, this disease was treated successfully with low doses (approximately 50 rad), of radiation from X-rays in the area of infection.



A drawing of grapeshot wounds to the lower leg during the Civil War, from The Medical and Surgical History of the War of the Rebellion *by the Government Printing Office, 1870-1888. These were the sorts of wounds where quick surgery was once the only hope to thwart massive infection and rapid death.*

A review of 364 cases treated in this manner, from 1928 until 1940, indicated that patient mortality would be reduced from 50 percent (or higher) to approximately 5 percent if patients were treated *before* severe progression of the disease and with the correct technique. X-ray therapy stopped the infection without the need for amputation to control its spread. Furthermore, low-dose irradiation (LDI) therapy, given immediately, acted as a prophylaxis to prevent the onset of gas gangrene.

This is but one example of the extensive use of radiation treatment of many types of infections, before the advent of antibiotics. Low doses are not adequate to kill invading bacteria directly, but they will increase the activity of a patient's damage-control biosystem to destroy the infection. The observed beneficial effects are consistent with the large amount of scientific evidence of radiation hormesis—the stimulation by low doses of radiation of an organism's own defenses to destroy invaders and heal wounds.

In view of the ineffectiveness of antibiotics in many cases and the evolution of antibiotic-resistant strains of bacteria, current use of LDI therapy is needed, and many patients would benefit greatly.

The Radiation Question

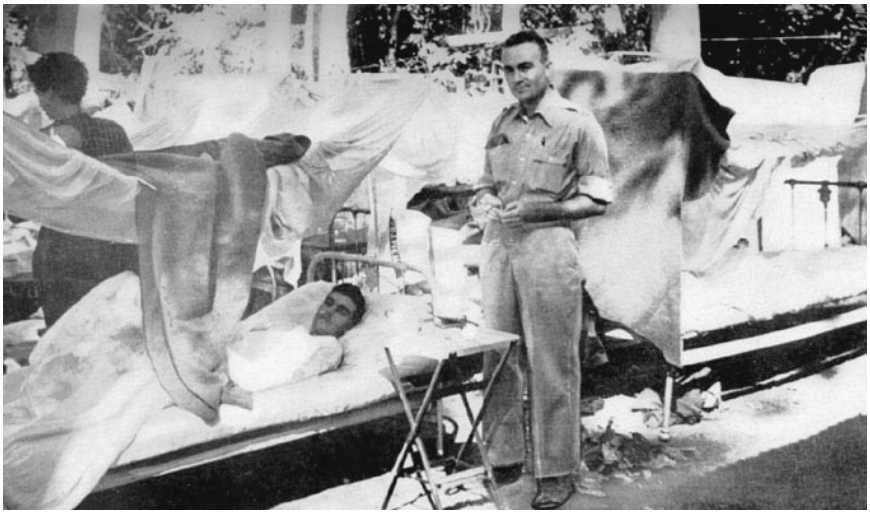
Low doses of radiation are rarely used today for treating infections because most people (and physicians also) believe that radiation in any amount is a significant cause of cancer. But this linear-no-threshold (LNT) model of radiation carcinogenesis is invalid. As this author and others have shown, low doses of ionizing radiation to the entire body will prevent and cure several types of cancer.[1] And for cancers that were not cured, the author pointed out that this low-dose irradiation therapy, which has no symptomatic adverse side effects, would likely give patients extra years of quality life.

The evidence did not consist of mere "anecdotal cases" but facts—many real people—organisms of 10 to 100 trillion living cells, struggling against the formidable attack of a relentless enemy.

Here I focus not on cancer but on another aggressive disease that is often fatal—gas gangrene—and a simple but very effective treatment to cure it: low doses of X-ray irradiation. It was first employed for this infection more than 70 years ago and was used with great success for about 12 years.

It began to be discarded after the mid-1930s—about the time that sulpha drugs and, later, antibiotics started showing dramatic success in a variety of applications (leading to the burgeoning growth of the highly profitable pharmaceutical industry). While "miracle pills" made other medicines seem outmoded, radiation treatment was discredited for political reasons: All radiation was associated with the destruction caused by the nuclear bombs used on Hiroshima and Nagasaki. The theory was put forward that no amount of radiation was safe, and that exposure to any amount of radiation would cause cancer.

Before antibiotics and before the bomb, radation was used extensively for the treatment of many types of infections, as documented by the historical review by Berk and Hodes.[2] Many radiation



Lt. A.N.C. Juanita Redmond (from her 1943 book: *I Served on Bataan*)

A military doctor is on duty in the gas gangrene ward at Bataan Hospital during World War II.

therapists of that era published substantial and consistent clinical evidence that demonstrated the ability of LDI, in the range of 75 to 300 rad, to cure a wide variety of infections; however, physicians were largely unaware of this, and the mechanism of action was unclear. One rationale held that the effect was caused by stimulation of the immune system by low level radiation damage, another that it was caused by the increase in local inflammation with resultant increase of blood flow. It was known, however, that these low doses did not significantly destroy bacteria directly.

More recently, Calabrese and Baldwin have defined hormesis as an adaptive response of biological organisms to low levels of stress or damage—a modest overcompensation to a disruption—resulting in improved fitness.[3] They point out that observation of this reproducible phenomenon has a long history (since the 1880s), and it has been widely reported in the scientific biomedical and toxicological literature. These scientists screened 20,285 papers that suggested a chemical hormesis effect and they extracted hundreds of dose-response relationships that met their special a priori criteria—the requirements for rigorous evidence of hormesis. They also carried out a review of the history of radiation stimulation on plants, as well studies on insects, bird eggs, salamanders, and so on.[4]

Their review includes a description of the clinical verification and application of the concept of "low-dose stimulation, high-dose inhibition" in the early decades of the 20th Century, in the treatment of human diseases and other conditions. Within one year of Roentgen's discovery of X-rays in 1895, 1,000 papers were published on their application.[3] The first therapeutic application reported (in 1897) the disappearance of inflammatory symptoms following treatment. Radiotherapy was then widely employed for the successful treatment of many inflammatory conditions and infections, including pneumonia. The magnitude of the clinical literature is substantial. It is interesting to note that the term hormesis was not coined until 1943.

Gangrene: What Is It?

Gangrene, which occurs in dry, moist, and a gas form, is the death (necrosis) of localized soft-tissue from prolonged blood-supply blockage.[5] It can occur in arteriosclerosis, diabetes, or decubitus ulcer, and after severe burns or frostbite.

In dry gangrene, gradual blood-supply decrease turns the part discolored and cold, then dark and dry. Treatment requires improving blood flow.

Moist gangrene comes from a sudden blood-supply cutoff: bacterial infection causes swelling, discoloration, and then a foul smell. To stop its spread, which can be fatal, requires antibiotics and possible tissue removal.

Gas gangrene, the most virulent form, is named for the gas bubbles under the skin produced by a highly lethal toxin from clostridium bacteria. The wound oozes brownish, smelly pus. Infection spreads rapidly, causing death. Treatment requires that all dead and diseased tissue must be removed and antibiotics given; an antitoxin can also be used.

In dry gangrene, healing usually takes place naturally at the junction between the living and dead tissue. In moist gangrene, some cells stay alive while surrounding cells begin to quickly die and leak fluid—an environment in which bacteria flourish.

Gas gangrene, the most deadly form, occurs in wounds that are affected by bacteria that live in low-oxygen environments and release gas and poisons into the body. Its incidence is highest in areas with poor access to proper wound care.

According to the National Institutes of Health, clostridium bacteria produce many different toxins, four of which (alpha, beta, epsilon, iota) can cause potentially fatal syndromes.[6] In addition, they cause tissue death (necrosis), destruction of blood (haemolysis) local decrease in circulation (vasoconstriction) and leaking of the blood (increased vascular permeability). These toxins are responsible for both the local symptoms—tissue destruction—and the systemic symptoms (those that occur throughout the body)—sweating, fever, and anxiety.

If gas gangrene is untreated, the person develops a shock-like syndrome with decreased blood pressure, renal failure, coma, and finally death. To prevent the disease, one must clean any skin injury thoroughly and watch for signs of infection: redness, discoloration, and puffiness. If the symptoms occur, medical care must be obtained promptly. The treatment consists of prompt surgical removal of dead, damaged and infected tissue (debridement); amputation may be necessary to control the spread of infection. Antibiotics, preferably of the penicillin type, should be given—initially intravenously. Analgesics may be required to control pain.

The complications include: disfiguring or disabling permanent tissue damage, jaundice with liver damage, kidney failure, spread of infection systemically through the body, shock, stupor, delirium, and coma. The infection progresses so rapidly that patients may die before any immunity could develop.

Since gas gangrene or clostridial myonecrosis is caused by a family of bac-

teria that live under low-oxygen (anaerobic) conditions in the soil, hyperbaric oxygen treatment has been employed to kill the bacteria, with varying degrees of success. The action of hyperbaric oxygen is based on the formation of oxygen free radicals. An oxygen pressure of 250 mm Hg is employed to stop alpha-toxin production and inhibit bacterial growth locally, thus enabling the body to utilize its own host defense mechanisms.

The onset of gas gangrene may occur within six to eight hours after injury, and presents itself with severe and sudden pain in the infected area. A delay in recognition or treatment may be fatal. Since the acute problem is the rapidly advancing phlegmon caused by alpha toxin in infected but still viable tissue, it is essential to stop alpha toxin production as soon as possible. Recent clinical studies indicate that the lowest morbidity and mortality are achieved with initial conservative surgery and rapid initiation of hyperbaric oxygen therapy.

The infection can advance through healthy muscle and destroy it at the rate of several inches per hour in spite of antibiotic treatment. Even with modern medical advances and intensive care, amputation is often the only choice and even then, 40 to 70 percent of victims will die. Research is now under way in Idaho, using an enzyme to fight gangrene "that would rely on the body's own immune system and reduce the need for amputation."

Case Studies of Low Dose Irradiation

In a remarkable presentation before the Radiological Society of North America in 1931, Dr. James Kelly of Omaha, Nebraska, reported his three-year experience in the treatment of a group of eight cases of gas gangrene using low doses of X-rays.[7] The mortality rate for this disease up to that time had been 50 percent or higher, but in his group it was only 25 percent. No additional tissue was removed in any case, after radiation therapy was begun. In six cases involving the limbs, improvement followed immediately after the first X-ray treatment; amputations were unnecessary in three cases. The two patients who died had involvement of the trunk. For the treatment of such cases, Kelly advised that a higher X-ray voltage be used to increase the penetration. He reported that St. Catherine's Hospital in Omaha, Nebraska, started to use this method of treatment, in addition to other measures, on all gas gangrene cases.

Kelly urged other physicians to use this form of treatment for gas gangrene because everyone had access to X-ray apparatus and no special knowledge was required for applying the mild doses he employed. He pointed out that "[R]oentgen treatment of many localized infectious processes, due to other types of organisms, has been so definitely beneficial in the past that to neglect its use in gas bacilli infection may truly be considered poor judgment. In fact, X-ray treatment of these localized infections has been so successful and the results so widely published for the past twenty-five years or more that it seems unnecessary to make a plea for its use in such a fulminating and serious infection as gas gangrene usually proves to be. However, the use of the X-ray as an aid in the treatment of localized infections seems to have escaped the attention of many sincere practitioners."

Although there had as yet been no animal experimentation completed, Kelly advised that, in the treatment of a serious infection, any simple measure which did not interfere with other indicated measures, was not inherently dangerous, and appeared to be beneficial on all occasions, should be employed regularly, regardless of possible lack of confirmation from the laboratory.

With a mobile 80-kV X-ray unit (and a filter to prevent skin burns), Kelly described how he had applied a local dose of 50 rad (0.5 Gy) over a three-minute period. Most patients received this dose twice on the first day, twice on the second day, once on the third day, and once again on the fourth day. All tissues suspected of involvement were irradiated by moving the X-ray tube as needed, with overlapping on the areas.

Kelly said that he did not understand the action, but he mentioned some useful characteristics of X-rays, among them, their ability to penetrate, cause chemical change, and stimulate defensive powers of living cells or destroy them, depending on the amount of radiation received. The power to penetrate is very important, because he was attempting to reach an infection situated deeply in the muscles. He pointed out that a radiologist recommending the application of X-rays would often encounter objections from a surgeon, who would state that X-rays have no action—they could not destroy any organisms. The same physician would then explain to patients that X-rays would cause a burn. Kelly stated that the ability of radiation to exert a stimulating or destructive action on living cells, depending on the dose, was a scientific and clinical fact, beyond any possibility of question.

The discussion that followed this presentation mentioned other applications of X-ray therapy for inflammatory diseases—severe arthritis, which was identified in 1906 and diphtheria, identified in 1920. Progress in applying this treatment had been very, very slow because of the lack of scientific proof of the action of the X-rays in the

U.S. Army

Although X-ray treatment was not used to treat gas gangrene cases during World War II, the technology was certainly available, as can be seen in this photograph of a mobile X-ray unit operating in an evacuation hospital in France.

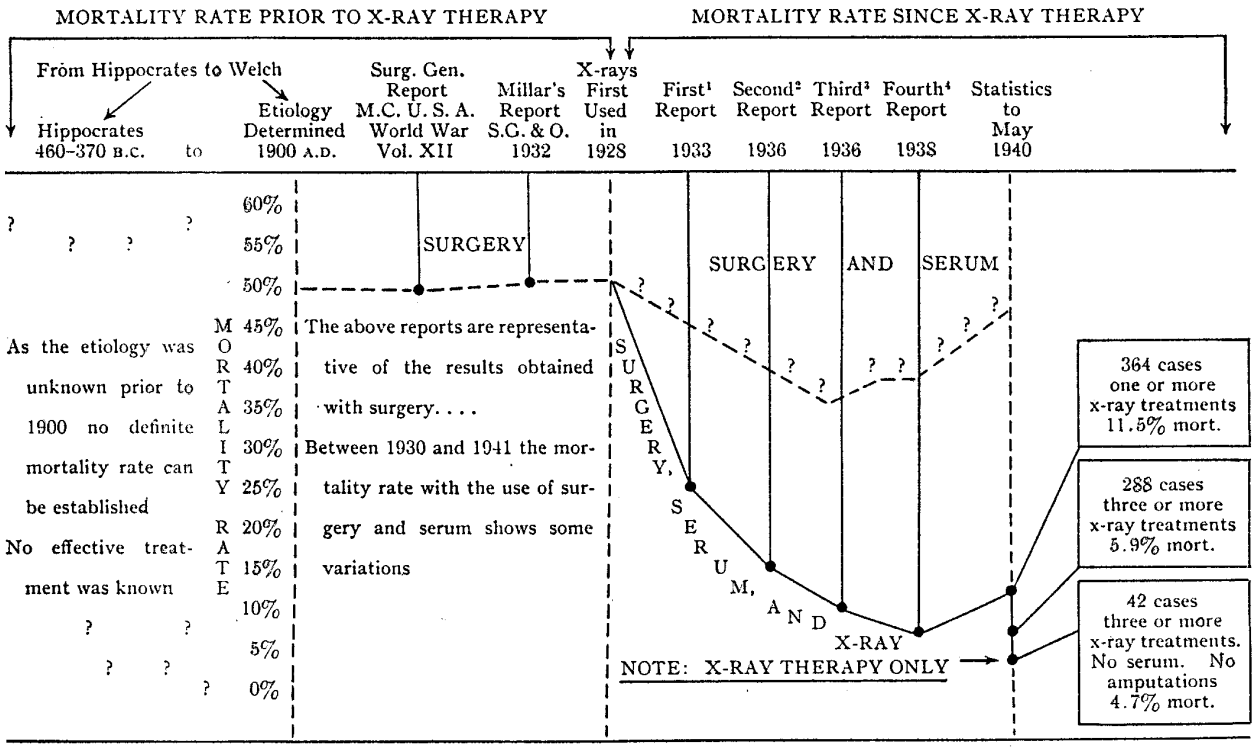


Figure 1
LOW-DOSE IRRADIATION THERAPY TO CURE GAS GANGRENE INFECTIONS

The original caption[8] stated: End of gas gangrene as a serious infection (if X-ray therapy is used). From Hippocrates' time (460-370 B.C.) to 1900 A.D., the aetiology of gas bacillus infection was unknown and as a result the mortality rate during that period cannot be accurately determined. Between 1900 and 1928, the mortality rate was 50 percent. Since 1928, the mortality has been reduced to 5 percent by the use of X-ray therapy without serum or radical surgical measures. X-ray therapy will prevent or cure the disease.

inflammatory tissue. One success that survived criticism, Kelly said, was the treatment of acne and boils.

Radiation Therapy Successs, 1928-1940

The mortality rate for gas gangrene up to 1928 had been 50 percent or higher, and that figure was attained only by the sacrifice of many arms and legs.[8] The reduced mortality of 25 percent in the first group of eight cases, reported by Kelly in the 1931 meeting, led many radiologists, a number of surgeons, and a few practitioners in the other specialities to try this therapy. Kelly and Dowell presented the data from a total of 364 cases, during the period 1928 to 1940, before the Radiological Society in 1941.

Figure 1 shows the drop in the mortality rate. It indicated, "gas gangrene need no longer be regarded as a serious disease. The X-ray has definitely removed gas gangrene from that group of diseases in which experimental therapy is any longer justifiable."

Kelly stated that chemotherapy had failed in well-developed cases because there was definite interference in the circulation to the infected area, and consequently the chemical did not reach the diseased tissue. The X-ray, however, had no difficulty in effectively reaching all cells and fluids in any infected area. Other ways of treating gas gangrene might be developed, he said, but there could be no question as to the status of the X-ray in the prevention and treatment of this serious infection. Since the mortality rate in cases treated with radiation was so much lower (4.7 to 11.5 percent) than that obtained by any other methods employed up to that time, Kelly suggested that those who refused to use irradiation should feel called upon to offer some explanation.

Kelly also noted that in the use of X-ray treatment for patients with acute spreading peritonitis (inflammation of the membrane lining the abdominal cavity), the response of patients was as prompt and convincing as it was in gas gangrene.

All but 1 of the 21 published reports on the roentgen treatment of gas gangrene that had appeared in the literature up until 1941 were favorable to the use of radiation, both as a preventative and as a therapeutic measure. The unfavorable publication reported 10 deaths in 14 cases, but no details of the cases were given. Based on his assessment of the 364 cases, Kelly stated that the mortality rate in the post-traumatic cases should not be in excess of 10 percent. "Any patient, no matter how far his disease has advanced, is entitled to a trial of X-ray therapy. Patients treated reasonably early and with the correct technique will respond favorably in most instances," he said.

Kelly gave more details of the treatment. The incubation, after injury, of gas gangrene in 134 available cases occurred in 15 percent of the cases within 24 hours—the incidence peaking between the 48th and the 72nd hour. X-rays were used successfully by several workers to prevent the onset of gas gangrene, and it was observed that the incidence of other infections also—osteomyelitis after compound facture in particular—seemed lessened by the use of X-rays.

Kelly did not suggest a reason for the action of radiation in preventing osteomyelitis, but if the rapidly growing organisms, such as the gas formers and the streptococci, can be kept from establishing an infection immediately after the injury, it was possible that the more stubborn, slowly growing secondary invaders would never have an opportunity to develop, as the wound might be well on the way to recovery before the usual period of incubation has been completed. The effect is prophylaxis in the same sense that cleansing the wound is prophylaxis.

Figure 2 shows a severe hand injury case, with multiple fractures and some gas in tissues (left X-ray). The same hand a few days after prophylactic irradiation (right X-ray) shows no gas in the tissue—no infection— with the hand on the way to complete recovery. The patient received antitetanus and antigas serum, but no sulphanilamide.

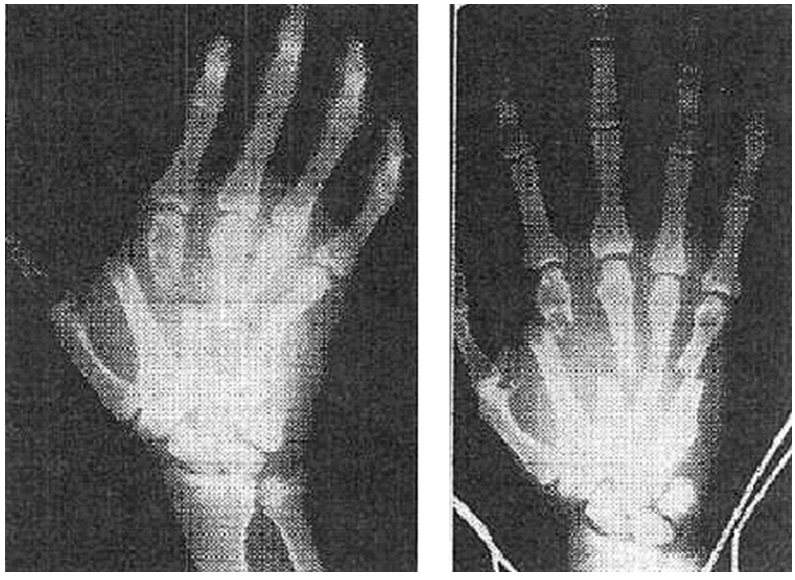


Figure 2
SEVERE HAND INJURY WITH MULTIPLE COMPOUND FRACTURES

For treatment, Dr. Kelly and his colleagues gave 150 rad per day in two doses of 75 rad or three doses of 50 rad to the area they believed to be infected. For prophylaxis, they gave 75 rad daily in one dose. The voltage varied from 90 to 130 kV, depending on the thickness of the body part. Filtration to prevent burns increased with voltage.

In Kelly's opinion, amputation during the acute toxic phase of gas bacillus infection that is receiving adequate and proper radiation therapy has never benefited any patient in the least. Whatever surgery is indicated because of the injury should be performed, he said, but there should be no extensive removal of muscle groups or other major surgery for the infection itself during the acute toxic phase. With radiation therapy, the tissue that is destroyed during the invasive stage becomes demarcated as the disease regresses, and the dead tissue, if there be any, may be removed after the acute toxic stage has passed.

In Kelly's judgment, there should not be more than 1 or 2 percent mortality because of deferred amputation and about the same mortality from the infection itself. In essence, he advocated a simple and effective measure to replace drastic measures that were ineffective. Previously, there had been no treatment for the infected part in gas gangrene, since amputation, or elimination of the infective area by surgical measures, can hardly be considered treatment. The area was not treated; it was simply removed. With radiation therapy, the infected part is actually treated and is removed only if it does not recover. X-ray therapy was far superior to any other method when it was available. Questionable and experimental measures of whatever character should not be substituted.

Sulphanilamide Should Not Be Used

The records of some deaths, particularly among diabetic patients, suggested that the use of "serum" (sulphanilamide, the early form of the "sulpha drugs"—the first use of the chemical antibiotics) might have been an important factor in the fatal outcome. The many instances in which serum had failed to prevent or cure the disease, while radiation therapy had been followed by prompt improvement, gave the impression that if radiation therapy was available, serum was unnecessary. Large doses of serum after the toxin of a gas infection had damaged the kidneys appeared to be more than some patients could withstand, and urinary suppression and death ensued. The mortality rate in 65 cases without serum was lower than in 248 cases with serum.

Kelly (and others) determined that sulphanilamide and radiation therapy could not be used simultaneously with good effect. Little was known about the interaction of these two agents, but it was clear that they should not be given at the same time. Serum was not effective in stopping the gas gangrene infection and, when used simultaneously with irradiation, completely degraded the effectiveness of the radiation therapy. In fact, it seemed that the destruction of tissue was accelerated.

What Turned Success into Failure?

The experience of Dr. Kelly and others shows that ionizing radiation provides a certain and definite means of prevention and treatment of gas gangrene that should have removed it from the class of acute diseases having high mortality and morbidity. His 12-year study should have been an important basis for the promotion of the general use of X-ray therapy for inflammatory disease at the bedside, with an apparatus of adequate voltage. The curative action of the X-ray in gas gangrene should have established beyond any doubt the fact that irradiation is of value in

treating infections, because the gas infections are uniformly resistant to other treatments, but responded consistently to LDI therapy. The antitoxic effect of radiation in acute infections was amply demonstrated in treating gas gangrene, acute spreading peritonitis, surgical mumps, erysipelas (local febrile disease), and other toxic acute infections. This general reaction as well as the favorable local effect was evident to many clinicians, years before gas gangrene was treated with radiation. So why was LDI therapy ignored and discarded after the mid-1940s?

Calabrese and Baldwin addressed this question in a 2000 paper.[9] The most critical factor was the lack of agreement over how to define the concept of hormesis and quantitatively describe its dose-response features. If radiation hormesis had been defined as a modest overcompensation to a disruption in homeostasis, as would have been consistent with the prevailing notion in the area of chemical hormesis, this would have provided the theoretical and practical means to blunt the criticism of this hypothesis.

The second critical factor pointed out by Calabrese and Baldwin was the total unawareness by radiation scientists of the concept of chemical hormesis, which had been more advanced, substantiated, and generalized than in the radiation domain.

The third factor was the major scientific criticism of low-dose stimulatory response that occurred when the United States was organizing a national research agenda on radiation that generally excluded the hormetic hypothesis. On top of this came the criticisms by the leading scientists of the 1930s, followed by the Linear No-Threshold (LNT) hypothesis of the late 1950s, which undermined the concept of radiation hormesis. These criticisms, limited in scope and highly flawed, were perpetuated over the decades by other "prestigious" experts, who appeared to simply accept the earlier reports.

These factors were then linked to a growing fear of radiation as a cause of birth defects, mutations, and cancer—factors all reinforced by later concerns over the atomic bomb. Findings on hormetic effects by Soviet scientists were either not available in the United States or disregarded.

Even in the 1940s, there were many physicians who had never heard of the X-ray as a means of prevention or treatment of gas gangrene, and others who insisted that there were not yet a sufficient number of cases in the literature to establish its true status. Today, with penicillin and more advanced antibiotics, it is easy to regard the 70-year-old LDI technology as primitive.

However, the current status of gas gangrene, as outlined at the beginning of this paper, is not encouraging. Even advanced antibiotics will not reach areas where there is no circulation, and antibiotic-resistant bacteria continue to evolve and proliferate. Hyperbaric oxygen is useful, but it cannot reach deep-seated regions of infection, and the availability of oxygen chambers is severely restricted. And when we consider the enormous influence of the pharmaceutical industry and the pervasive preference for chemotherapy solutions, it is not surprising that there is still no mention at all of LDI therapy.

How Does Low-Dose Radiation Work?

How are low doses (50 to 75 rad) able to destroy invading bacteria in a living organism? (For sterilization, radiation exposure in the range 10 to 50 kGy (1,000 to 5,000 kilorad) is necessary.) Like hyperbaric oxygen therapy, ionizing radiation creates oxygen free radicals. LDI delays the cell cycle, allowing the immune kill rate to exceed the bacterial proliferation rate. But the large amount of evidence in support of the radiation hormesis hypothesis provides a very high degree of confidence that the principal action of LDI therapy is to stimulate the patient's own defenses to destroy infections and mend wounds. The likelihood of delayed cancers resulting from such small radiation doses is negligible compared with the likelihood of cancer caused by normal metabolic processes.[1,10]

The ethics case in support of providing LDI therapy for gas gangrene can be understood by comparing it with the ethics case for local radiation treatment for cancer. Typically, a tumor volume is given 200 rad (2 Gy) per day, five days per week, for five to six weeks, and this is a universally accepted treatment; that is, the benefit/risk ratio is judged to be highly favorable. The doses in LDI therapy are much lower, and so the risk of causing a new cancer (some 20 years later) is much lower.

Moreover, while high-dose radiation decreases damage-control biosystem activity, low-dose radiation increases biosystem activity, causing lower than normal cancer mortality.[10,11] So, in addition to curing the infection, LDI therapy reduces the risk of cancer.

The potential benefits of using low-dose irradiation therapy on gas gangrene patients are enormous. When will physicians start again to provide such treatments—and save lives and limbs?

Dr. Cuttler retired from AECL (Atomic Energy of Canada) in July 2000, and is now President of Cuttler & Associates Inc., providing consulting services. He served on the Council of the Canadian Nuclear Society (CNS) for 10 years and was its president in 1995/1996.

For the past 12 years, Dr. Cuttler has been assessing the effects of ionizing radiation on health and has drawn widespread attention in Canada and abroad to the beneficial effects of low doses. A previous article "The Significant Health Benefits of Nuclear Radiation" appeared in the Fall 2001 issue of 21st Century.

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