

Part VI

CONTRAINDICATIONS
TO X-RAY THERAPY;
REVIEW OF THE LITERATURE



Chapter XXII

CONTRAINDICATIONS

COMBINATION OF X-RAYS AND SULFANILAMIDE

As stated elsewhere, the exact changes which take place in the tissues when x-ray treatments are used for an acute infection are not understood. However, since the time of their discovery, x-rays have been used empirically in the treatment of acute infections with more or less success. Out of this trial and error method over almost half a century have come many technics which are unquestionably of great benefit to the patient, and are the methods of choice in the treatment of many serious infections because they produce consistently good results.

This was the situation when, at the beginning of 1938, cases were suddenly encountered in which the beneficial effects usually produced failed to materialize. Investigation showed that the patients who failed to respond to x-rays in the usual manner were receiving sulfanilamide or one of its early derivatives.

Since our knowledge of the beneficial effect of x-rays in infections is limited to clinical results and since results were found to be good when x-rays were used alone, the only course open was to use x-rays alone. No explanation is offered for the elimination of the sulfanilamide group from our therapeutic measures except that results are not as good when the two agents are used together as when x-rays are used alone. Again, this is simple application of the trial and error method.

When x-ray treatments are given, any measure which enhances the end-results should be used; or, if the other measure is less complicated than x-ray therapy and accomplishes the same result without x-rays, it should be used to the exclusion of x-ray therapy. When, in a given case, two therapeutic agents which experience has proved do not work well together are under consideration, each agent should be used as indicated to its best advantage, but they should not be used together. If they are used together, an injustice may be done the patient, and the therapeutic value of each agent may be distorted.

In December, 1938, we suggested before the Radiological So-

ciety of North America at Pittsburgh that the combined use of x-rays and sulfanilamide in the acute infections did not produce as good results as did x-rays alone. Early in 1939, after reviewing the hospital records of all infections treated at Creighton Memorial St. Joseph's Hospital during 1938, we commented on the matter as follows:

Small doses of sulfanilamide are still an uncertain element, but large doses, following which the patient becomes cyanosed, have, in our opinion, been definitely inhibitory to any beneficial effect the x-ray may produce. As a general rule, in the usual case, we get at least a temporary improvement following radiation therapy, slowing of the pulse probably being the most evident, but in those cases which have been saturated with sulfanilamide before any x-ray treatments are given, we have failed to note even the slightest improvement following the use of the x-ray. Whether the anoxemia, or other blood changes associated in the sulfanilamide-cyanosed patient prevent any effect from the x-ray or not cannot be stated definitely at this time, but we prefer to treat the patient without the aid of large doses of sulfanilamide.¹

We have not had sufficient experience with the local use of sulfanilamide and x-rays to form an opinion of such a combination. We have used x-rays and sulfathiazole internally and locally without any untoward results. We are certain, at this time, that the combination of sulfathiazole and x-rays is not as disastrous as the x-ray and sulfanilamide combination. We are using x-rays and administering sulfathiazole internally in many cases. The combination is still on trial, with the chances favoring their continued use simultaneously.

Our present view of the situation is summed up in the following comment:

With a mortality of 31 per cent in the group of cases treated with sulfanilamide and x-rays as compared with a mortality of 15 per cent in the group of cases treated with x-rays alone, the reason is obvious why we think the x-ray without sulfanilamide is the better therapeutic procedure.

The history of x-ray therapy, however, is filled with instances of failure of the x-ray with a given technic to influence a certain disease, but with the correct change in x-ray technic, it is found to give a favorable response in the same disease. So, it may be in combining the chemotherapeutic group of drugs with x-rays, possibly a large series of cases, closer attention to details, particularly to dosage of the drug, might give rise to the discovery of instances where the x-ray and such drugs could work very well together.³

CASE 87.—C. C., a man aged 43, was admitted to the hospital Janu-

ary 28, 1938, with a diagnosis of appendicitis. The white blood cell count was 26,950 and the temperature 101.6 F. Operation was done immediately, and revealed acute purulent appendicitis, with the appendix ruptured, and some thin purulent fluid in the abdomen. The appendix was removed and drainage was established by a Penrose drain through a stab wound far to the right.

Prontosil therapy was started the second hospital day. The following day x-ray therapy was started for gangrenous involvement of the abdominal wall around the incision and laterally at the site of the stab wound. This gangrenous process eventually extended down to the adjacent portions of the thigh and up over the chest and to the axilla. During extension of the process he was receiving adequate x-ray treatment to all of the involved tissues. Prontosil was given intramuscularly in 5 cc. doses three times daily during the entire time x-ray treatments were given. The patient died the twentieth day after admission.

Autopsy showed perforation of the small bowel, localized pericecal and pelvic peritonitis with cellulitis and gangrene, multiple fistulas of the right lateral body wall, herniation of the small bowel through the operative wound, perforation of the small bowel by the drainage tube and focal necrosis of the liver.

This was one of our early cases in which both x-rays and sulfanilamide were used. We were impressed by the fact that *the most thorough irradiation did not stop the spreading of the gangrenous infection, a failure of radiation therapy not previously observed by us.* The failure seemed all the more puzzling because the patient had an excellent physique and his surgeons were alert and competent. Yet he never showed any evidence of even temporary improvement.

CASE 88.—L. T. W., Jr., a boy aged 8, entered the hospital February 15, 1938, with a history of cough, pain in the left side of the chest, fever and chills of five days' duration. The rectal temperature on admission was 103.4 F., but three hours later it reached 105 F., with pulse rate 142 and respiratory rate 54. The white blood cell count was 12,600, with 69 per cent polymorphonuclear leukocytes. X-ray examination showed the entire left side of the chest to be opaque and the mediastinum displaced somewhat to the right. The right lung was quite clear. The series of x-ray treatments were withheld after fluid in the chest was noted on the x-ray film the day after admission. The chest was aspirated, and 200 cc. of fluid obtained. The patient also received fluids intravenously, calcidin and camphorated oil to the chest. Prontosil was given prior to admission to the hospital; it was also given in 5 cc. doses twice daily for seven days while he was in the hospital. Administration of prontosil was discontinued five days before he died.

An x-ray film of the chest on February 18 showed considerable fluid remaining in the left pleural space. The course continued to be stormy

(Fig. 113). Aspiration on February 19 revealed about 500 cc. of blood and purulent fluid. X-ray therapy was started on February 20 with two treatments, one treatment on the twenty-first, two on the twenty-second and one each on the twenty-third, twenty-fourth and twenty-seventh. February 24, 900 cc. of purulent material was removed through a trocar and a drainage tube was inserted. A film of the chest on February 25 showed the left pleural space completely free of fluid. Both lungs were partially collapsed. There was still some shift of the mediastinum to the right. The patient was given small blood transfusions on February 25, 26 and 27.

The blood study on February 18 showed a white blood cell count of 42,250, with 84 per cent polymorphonuclear leukocytes. Prontosil was stopped on February 23, and the white blood cell count on February 24 showed a drop to 18,350, with 96 per cent polymorphonuclear leukocytes.

This youngster failed to show improvement at any time, regardless of what was done for him. Toward the end, he apparently had no resistance, and at almost every site where a hypodermic injection was given or a needle inserted for intravenous therapy, a localized infection developed. He was watched closely. His absolute failure to respond to therapy at any time was so noticeable that some explanation was sought; the possibility that he might have had a vitamin deficiency prior to contracting the infection was suggested, but nothing could be found to support that theory.

CASE 89.—A girl aged 19, entered the hospital with a history of having had a boil on the left thigh three weeks previously and left inguinal adenitis of two weeks' duration. She had been confined to bed at home with a low grade fever. The swelling was apparently receding until about three days before entering the hospital, when she had chills and the temperature rose to 103 F. On admission, examination revealed a marble-sized lymph node in the left groin but no evidence of fluctuation. The white blood cell count was 24,250, with 77 per cent polymorphonuclear leukocytes. The blood culture was negative. Temperature was 101 F., pulse rate 108 and respiratory rate 28. Prontosil was given intramuscularly every four hours, and x-ray treatment was ordered immediately. The patient received one treatment on the second hospital day, one on the third and one on the fifth. No response could be noted, and since we were beginning to suspect that the sulfonamides and x-rays did not work well together, we refused to continue treatments. Death occurred several days later.

CASE 90.—C. H., a man aged 49, was admitted to the hospital November 5, 1938, with a diagnosis of acute appendicitis. He was operated on immediately. The appendix and the distal end of the cecum were gangrenous. The appendix was removed. X-ray therapy was sug-

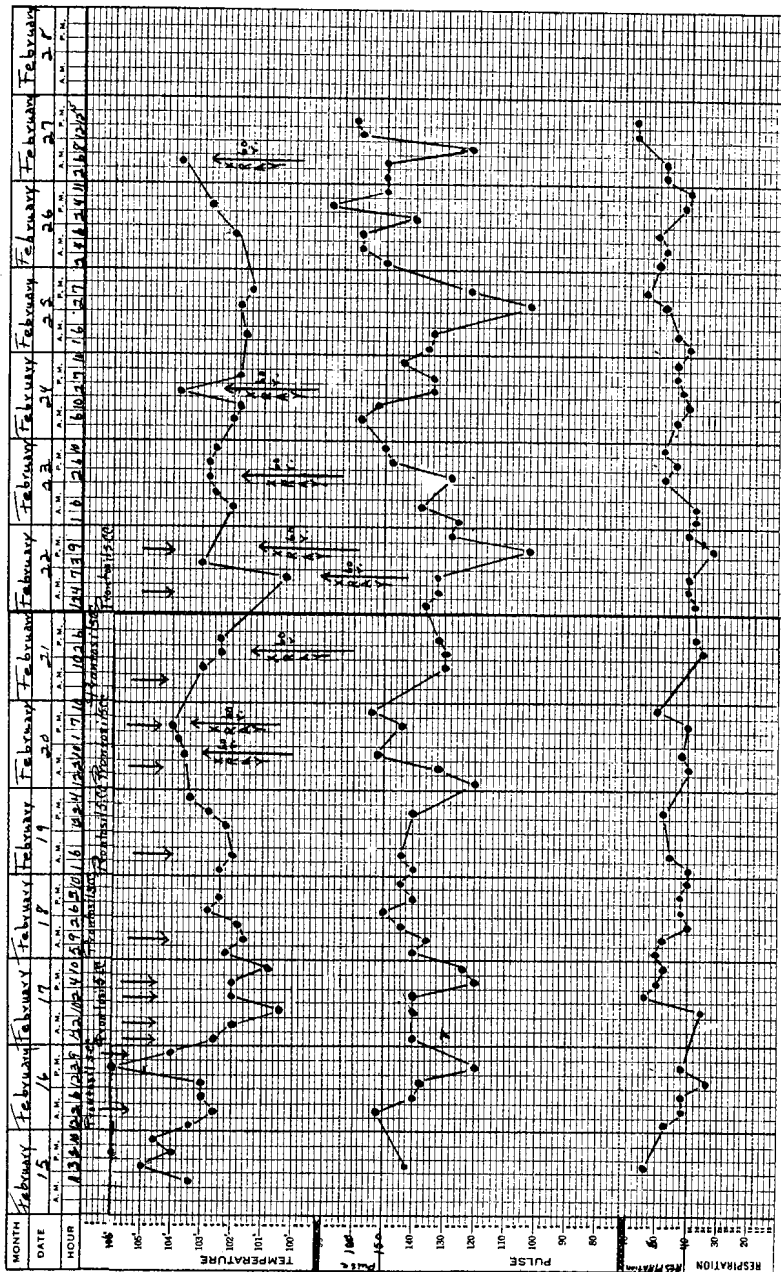


Fig. 118.—Case 88. Doses of prontosil are indicated by upper arrows directed down, and lower arrows show time when x-ray therapy was given. This was one of the early cases lost with the combined therapy, and although failure to respond to x-ray therapy was most noticeable, the simultaneous use of chemicals was not suspected as the cause. Technical factors were: 110 kv.; 5 ma.; 50 cm. distance; 3 mm. Al filter; anterior chest as port. Result was poor.

gested, but the surgeon elected to use prontosil, 10 cc. three times a day. The fourth postoperative day the patient's condition was desperate. He was markedly cyanosed. Prontosil was discontinued and x-ray therapy was requested. He received two x-ray treatments daily for three days, and then one on the fourth day, when he died (Fig. 114).

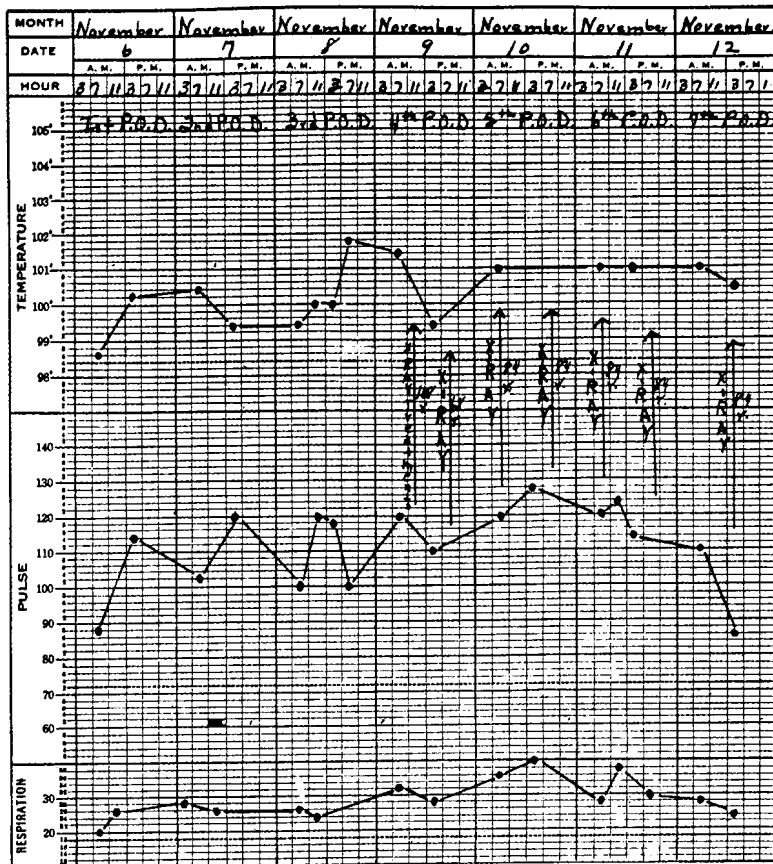


FIG. 114.—Case 90. Complete absence of response to x-ray therapy. The patient was saturated with prontosil when x-ray therapy was started. Technical factors were: 110 kv.; 5 ma.; 50 cm. distance; 3 mm. Al filter; entire abdomen as port. Result was poor.

Despite the poor condition of this patient when we started x-ray treatment, he did not die until four days later. We feel sure we could have done better in this case had x-ray treatment been started sooner. The temperature chart (Fig. 114) shows how poorly the patient reacted to radiation; the drop in tem-

perature and pulse rate usually noted after the start of x-ray therapy is not seen here.

CASE 91.—A boy aged 15 had a gunshot wound of the right hand. He received prophylactic serum the day of admission. Operation for reduction of a fracture was performed the day after admission to the hospital. The next day he showed evidence of gas bacillus infection. Sulfanilamide and x-ray therapy were started immediately. The next day the right hand was amputated just above the wrist because of gangrenous changes. He continued to receive sulfanilamide and x-ray therapy but three days later another amputation just below the elbow was required due to additional gangrenous changes. A total of six x-ray treatments and 175 gr. of sulfanilamide was given, and the boy recovered (Fig. 115). He was ready for a skin graft about a month after injury.

The fact that in a period of three days two amputations were necessary to remove the dead tissue from the infected area, during which time x-ray treatments were given, is entirely inconsistent with the usual response of a gas bacillus infection in a compound fracture. The tendency of the tissues to become gangrenous usually stops with the first two or three x-ray treatments if given a few hours apart, but such is not the case when two agents are combined.

Although this lad recovered, we believe that sulfanilamide and x-rays did not work well together and that more tissue was lost than would have been the case with x-ray therapy alone. This statement is based on the fact that *some areas which appear gangrenous when the x-rays are started regain their normal function.* (See cases in first series, p. 157 ff.).

When sulfanilamide is used with x-rays, extensive gangrene is generally the result. More tissue is lost with this combination than with any other method of treatment that has come to our attention. This had been so in our locality, and it is so in the small amount of literature available (see Cases 92 and 94). The reasonable conclusion seems to be to use x-rays and omit the sulfanilamide (see Cases 4 and 7).

CASE 92.—J. B., a man aged 39, was admitted to the hospital November 12, 1939, after he was injured in an automobile accident. Two hours after admission, the left leg was amputated 4 in. below the knee. He was given 3,000 units of tetanus antitoxin. The temperature was 98.4 F., the pulse rate 92 and the respiratory rate 20. Sulfanilamide, 15 gr., was started at noon. At 3:00 P. M. the same day, he was given an x-ray treatment of 75 r units. At 4:00 P. M. the temperature was 99 F.,

pulse rate 96 and respiratory rate 18; at 7:00 P. M. the temperature was 100 F., pulse rate 104 and respiratory rate 20. Two x-ray treatments of 75 r units each were given on both November 14 and 15. November 15, culture of the stump showed gram-positive encapsulated

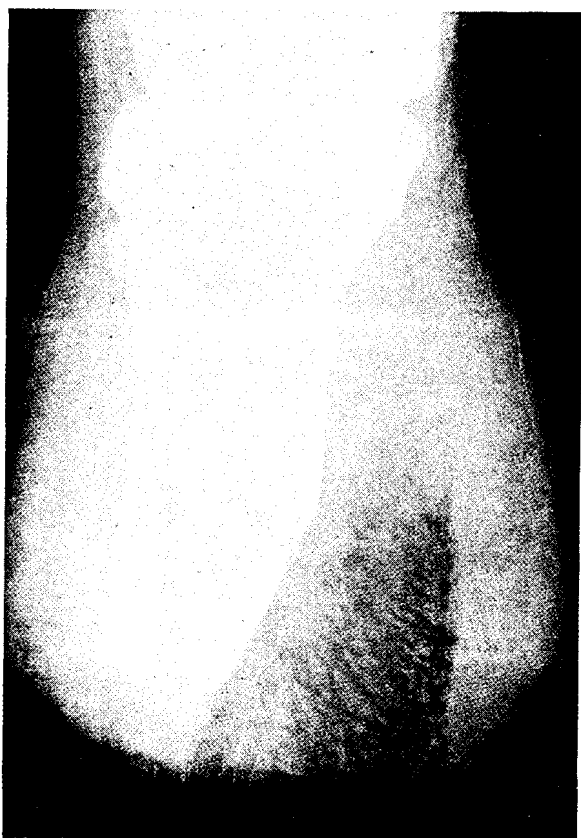


FIG. 116.—Case 92. Area of gas developed despite early x-ray therapy, which was given simultaneously with sulfanilamide administration.

bacilli in pairs and short chains. A film of the stump on November 16 showed considerable gas in the soft parts (Fig. 116). He was given two more x-ray treatments that day.

We were called in consultation at this time, and our first impression was that some area of infection had not been included in the treatment. When we learned that all of the area up to the thigh had been treated, we advised that sulfanilamide be stopped. X-ray therapy was continued, two treatments being given on November 17 and one each on November 18 and 21.

A line of demarcation was present November 21. A second débridement for the removal of areas of gangrenous tissue up to the line of demarcation was performed that day, and the patient had no fever after November 22 (Fig. 117). There was a normal amount of odorless drainage until November 25, and the patient was dismissed the following day.

It is noteworthy that on the tenth hospital day it was necessary to cut away some gangrenous tissue which showed a line of

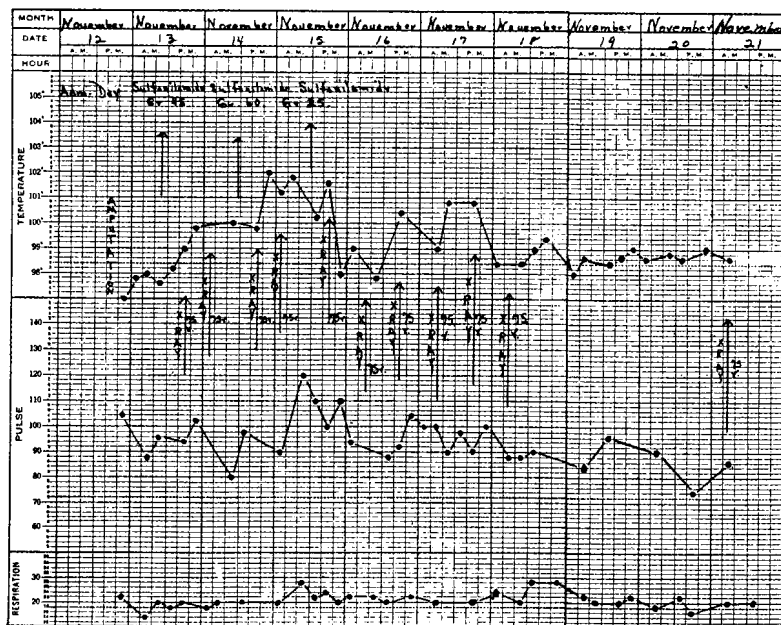


FIG. 117.—Same case as preceding. The patient received sulfanilamide and x-ray therapy from the time of his injury. Despite this early start, his temperature rose steadily during the first three days and the gangrenous process on the leg progressed. When sulfanilamide was stopped, improvement began. Technical factors were: 90 kv.; 5 ma.; 30 cm. distance; 1 mm. Al filter; right thigh as port. Result was fair.

demarcation. In our experience, a secondary operation to remove gangrenous tissue has never been necessary with x-ray treatment of gas bacillus infection; nor have others found secondary operations necessary when x-ray therapy is used. There have been few instances of demarcated gangrene, and then only in cases well advanced when x-ray therapy was started.

Case 92 and others in this group are evidence that the disease may progress to the gangrenous stage during combined

treatment with x-rays and sulfanilamide. More amputations have been required for gangrenous extremities in the last two years, when sulfanilamide was used in conjunction with x-ray therapy, than were necessary in the Omaha area in the previous 10 years of treatment of gas bacillus infection by radiation alone.

While the patient in Case 92 was receiving sulfanilamide and x-ray therapy, the temperature continued to rise steadily. There was no clinical evidence of improvement until the sulfanilamide was discontinued.

CASE 93.—A man aged 48 was admitted to the hospital August 12, 1939, 20 hours after having been severely injured in an automobile accident. He had a comminuted multiple fracture of the mandible, comminuted compound fracture of the left patella, comminuted fracture of the left acetabulum, a fracture of the right ulna and a basal skull fracture.

On admission, the temperature was 100.2 F., pulse rate 84, respiratory rate 18, red blood cell count 3,090,000, 60 per cent hemoglobin content and white blood cell count 7,100.

On admission intermaxillary wiring of the jaw was done in his room. A plaster cast was then applied to the left knee. On August 16 a spica cast was applied to the left acetabulum.

X-ray therapy was given to the head and neck region for the first time on August 20. A treatment was also given the next day, at which time one of the attending physicians ordered x-ray therapy discontinued. We felt it was rather early to stop treatment. However, the patient was in the best condition of his entire hospital stay; in fact, he was considered on safe ground.

X-ray therapy was requested again four days later, at which time the patient was receiving neoprontosil. We gave six x-ray treatments during the following five days. From August 25 to September 5 he received 30 gr. of neoprontosil a day, except on August 25 when he received only 5 gr.

The course was stormy (Fig. 118). On September 16, extensive cellulitis of the left thigh and knee was incised and drained. On September 20, he received 10 gr. of neoprontosil, and from September 21 to 29, he received 30 gr. each day.

An x-ray film on October 9 showed some gas in the soft tissues above the patella (Fig. 119). This was the day he died.

The patient received seven blood transfusions, varying in amount from 260 to 500 cc. In addition sulfanilamide crystals were placed in the wound at the knee, and he received morphine, fluids intravenously, sedatives, aspirin and neoprontosil.

A point to be noted in this case is that the patient failed to show any evidence of response to the second series of x-ray

treatments, given while he was receiving neoprontosil. Another point is that by the time the patient died, all of the sites of injury, including the pelvic fracture, showed evidence of secondary infection. It would appear that application of sulfanilamide

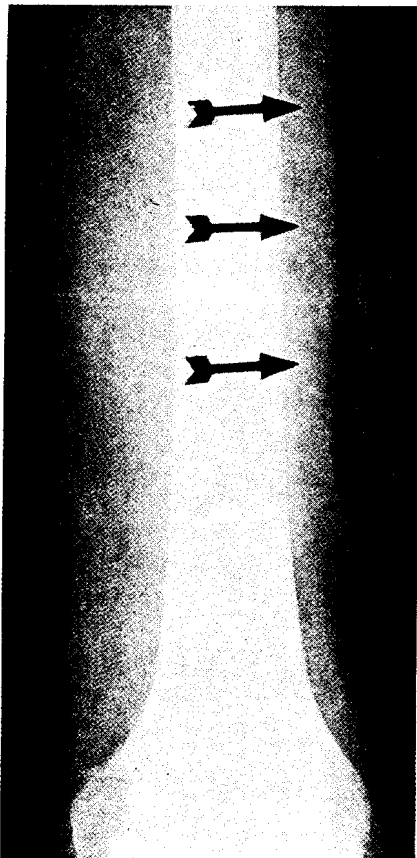


FIG. 119.—Same case as preceding. Area of gas in tissues on the day the patient died.

crystals locally in the compound fracture and its administration by mouth failed to have any antiseptic effect.

Without making critical reference to any of the other cases, this case lends itself well to a discussion of the means at our disposal of preventing and treating wound infections with x-rays, using the three types of injuries in this patient as ex-

amples of types of wounds which are met in every-day practice.

To us, the use of x-rays for prophylaxis and treatment is superior to all other methods. At least it can be applied to any area with equal ease. The injury around the knee is the most favorable for direct attack with external antiseptics. Even here, it is extremely difficult, because to sterilize an area or treat an infection with any local agent, it is necessary to reach all the infected tissues. This is usually an impossible task, or as in the oral injury—the fractured jaw—it is not practical.

To reach all the infected tissues with any agent through the blood stream may also be impossible if the area has circulatory obstruction or is gangrenous or for any reason is not receiving a normal blood supply.

X-rays, however, by their power of penetration, are able to reach all the tissues inaccessible to the other methods just mentioned. Nothing would prevent the x-rays from doing so except an external radiopaque dressing, and any obstruction of this type can easily be detected and removed. X-rays are easily applied, safe and extremely effective. These are real and practical advantages over other methods in the prevention and treatment of post-traumatic infections. In many cases the infection is ultimately more serious than the original injury, as in Case 93, in which the patient died of the infection, not of his injury. Here, x-ray therapy was not ordered until the ninth day after admission and only after chemotherapy had been used. The late use of x-rays and the administration of the drug were contrary to the best practice if x-rays were required. The excellent mobile apparatus now available makes it easy to treat this type of patient as frequently as seems indicated without disturbing him in any way.

CASE 94.—K. M., a boy aged 12, fell from a cherry tree 48 hours prior to admission, sustaining a fracture of the left ulna and radius above the wrist, with protrusion of the bony fragments through the skin. There was a simple fracture of the right ulna through the olecranon process and of the right radius through its neck and also a simple fracture at the lower end of the right radius, with fragments in good position. The local doctor gave antitetanus serum, cleansed the wound and attempted reduction of the fractures. Splints were applied to the left arm and plaster to the right arm. The following day, increasing pain and elevation of temperature were noted. Sulfanilamide was started and continued for 36 hours prior to admission to the hospital.

Examination on admission revealed lack of sensation and motor function in the left arm below the elbow. The tissues were swollen and crepitant, and a foul, sanguineous exudate oozed from the wound. The hand was black and cyanotic. The fingers of the right hand were cold and discolored, and there was loss of sensory and motor ability below the wrist. The temperature was 102.5 F. and pulse rate 120 to 140. An x-ray film showed the fractures already enumerated and gas in the soft tissues around the left wrist extending up to the middle half of the forearm. *No definite break in the skin in the right forearm or wrist was seen.*

An x-ray treatment was immediately given over the entire left arm up to and including the shoulder, consisting of 75 r, with 100 kv., no filter, at 50 cm. distance. On the following day, two doses of 50 r each were given. *That evening it was noted that gas was developing in the right hand and forearm,* and 75 r was given to this area immediately and 60 r was given over a laceration on the scalp as a prophylactic measure. On the following three days, 50 r was given twice daily *over the right forearm, hand and shoulder and over the left arm* once daily; 50 r was given once daily *over both arms* during the following three days. From June 6 to 23, a total of 525 r units was delivered over both arms.

From June 16 to 19 the patient received 10 gr. of prontosil every four hours, and from June 19 to 22 he received 10 gr. of sulfanilamide three times a day. It was then discontinued. The temperature and pulse gradually returned to normal. On July 5, the temperature varied from 100 to 101 F. and pulse rate 90 to 110. At that time, the right arm was black up to the elbow and the left was gangrenous to the wrist. The left hand was amputated above the wrist and the right above the elbow. The temperature continued between 99 and 100 F. during the following week and gradually subsided to normal after about two weeks.

This is another case in which the use of x-rays and sulfanilamide failed to control a gas gangrene infection and the gangrenous changes continued after therapy was started. In fact, a new area of gangrene developed by hematogenous extension.

CASE 95 (Courtesy of Dr. J. A. Muggly).—T. M., a youth aged 17, was riding a mower carrying a 410 gauge gun. He bumped the gun, which accidentally discharged, and his arm which was over the end of the barrel was badly mangled and burned. Hemorrhage started, but pressure was applied and bleeding controlled and he was immediately brought to the hospital.

On admission, the temperature was 98.2 F., pulse rate 88 and respiratory rate 20. There was a facial expression of pain and shock. The abdomen was rigid and tender on the right side, particularly in the lower right quadrant. The ventral surface of the right forearm was badly mangled, the area extending from the proximal to the distal

third of the forearm. The flexor tendons were exposed, some of which were shot through. The ulnar artery was completely severed. X-ray films showed no bone pathology.

The patient was taken to the surgery, where the wound was cleansed as well as possible and the ulnar artery ligated. He was given a prophyl-



FIG. 120 (above).—Case 95. Film of arm at admission.

FIG. 121 (below).—Same case. Condition of the wound four days after x-ray therapy was started.

actic dose of tetanus and gas bacillus antitoxin. Sulfanilamide powder was placed in the wound. He was also given sulfanilamide by mouth, 90 gr. daily. The white blood cell count was 12,500, with 72 per cent neutrophils and 28 per cent lymphocytes, the red blood cell count was

4,610,000 and hemoglobin content 100 per cent. Urinalysis gave negative results.

Convalescence was satisfactory until the fourth day after the accident, when the temperature rose to 101 F. and the pulse rate jumped from 70 to 100; respiratory rate was 20. The wound had a foul, characteristic odor; the forearm was beginning to swell. Smears from the wound showed numerous *Bacilli welchii*. At this time, the radiologist in consultation advised that sulfanilamide and serum be discontinued and x-ray therapy started.

The patient received three minutes' radiation over the upper arm and axilla and three minutes' radiation over the forearm, using two different exposures. Packs of 1:4,000 potassium permanganate were used. The next morning the temperature was 99.4 F., but the pulse rate remained 100. He received six treatments of three minutes each, and a final treatment of one minute. The wound healed rapidly, and convalescence was uneventful (Figs. 120 and 121).

In this patient a serious gas bacillus infection developed despite use of serum and sulfanilamide locally and by mouth; but there was prompt response to x-ray therapy when the former measures, which failed to prevent or to control the progress of the gangrene, were discontinued. Despite the extensive destruction from the gunshot wound and further damage due to the action of the gas organisms, the entire extremity with the exception of a finger was saved. The futility of attempting to sterilize these tissues with any local antiseptic should be evident. Prior to the use of x-ray therapy, such an arm as this would have been amputated as high as possible as soon as the diagnosis was made. Amputation under such circumstances is unnecessary if x-ray therapy is used early and the sulfonamides are not given.

CASE 96.—A. W. F., a Negro aged 58, was admitted to the hospital at 7:00 P. M. September 25, 1940, with multiple injuries sustained when he was hit by an automobile shortly before admission. He was brought to the hospital in the police ambulance.

The most severe injury was a compound fracture of the left leg. An x-ray film showed transverse fracture of the left tibia just above the junction of the upper with the middle third, with comminuted fragments; comminuted fracture of the fibula at the junction of the head and neck; double fracture of the fibula just above the middle of the shaft, with a fragment about $1\frac{1}{2}$ in. long.

The patient was taken to the surgery where severe trauma to muscle and other soft tissues was noted. A free end of bone protruded and was exposed for 6 in. and the wound was filled with debris and grass. The skin was thoroughly scrubbed with green soap and sterile water and antiseptic applied. Under local anesthesia, the wound was thor-

oroughly cleansed and irrigated with large amounts of sterile water. Bleeders were ligated, the fracture was reduced and sulfanilamide crystals were dispersed around the fracture fragments and throughout the wound. The soft tissues were approximated with catgut and the skin edges with dermal sutures. The leg was then immobilized in a plaster cast which was split on the anterior surface to allow for swelling.

Films taken after reduction and after the plaster cast was applied showed the fragments in good position and alinement. The patient was given "combined tetanus serum" (type and amount not indicated on the record), caffeine sodium benzoate and morphine $\frac{1}{2}$ gr. When the patient was returned to his room, the blood pressure was 60/0; at 12:30 A. M. he was given 1,000 cc. of normal saline with 10 per cent glucose and 8 units of histaminase. This was repeated at 10 A. M. the next day, and the blood pressure was 76/50. The patient had a chill at 11 A. M., but the highest temperature recorded for the day was 99 F. and the pulse rate 120. The patient complained continually of severe pain in the leg, and the abdomen became distended. Culture on September 27 revealed gas bacillus of the *B. welchii* type.

Dr. J. W. M. saw the patient in consultation on September 28, and his comment on the chart was: "This is unquestionably a gas bacillus infection. Precaution against dissemination of the infection should be taken. Would use H₂O in wound at frequent intervals and leave the wound exposed to air. X-ray treatment would be of help; also transfusions."

The patient died at 11 P. M. on September 28. The temperature just previous to this was 99 F., pulse rate 110, respiratory rate 30. No sulfanilamide was given by mouth or by hypodermic injection; it was used only in the wound, but failed to prevent onset of the disease.

In this case sulfanilamide was placed in the wound immediately and it was relied on to prevent gas bacillus infection. However, infection developed and the patient died the third day. Serum was given only at the time of admission, and no x-ray treatments were given at any time either to treat or to prevent the development of gas bacillus infection. This patient died in a local hospital 10 years after a sure method of treating gas bacillus infection was advocated in the Omaha area. Experiences in this vicinity with sulfanilamide have not been such as to warrant its use in preference to x-rays in the prevention or treatment of gas bacillus infection. A brief survey of the literature suggests that others have had similar experiences elsewhere.

CASE 97.—H. B., a Negro aged 6, entered the hospital May 10, 1941, with an infected third degree burn of five days' duration involving the anterior aspects of the right thigh and leg. The temperature on admission was 101.8 F. and the white blood cell count 13,800.

Sulfanilamide, gr. 10, every four hours and continuous hot epsom salts packs were started, but the patient grew worse instead of better. A débridement was done, and x-ray therapy was started on the third hospital day, with the understanding that sulfanilamide was to be discontinued. But the patient still failed to show improvement; through an error, sulfanilamide had not been stopped. On the fifth hospital day,

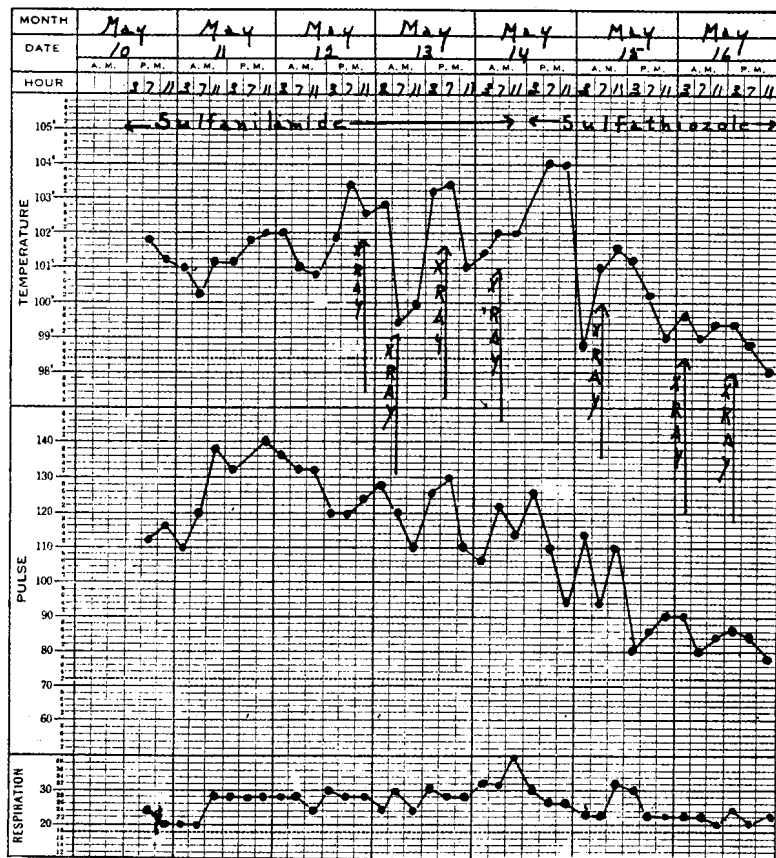


Fig. 122.—Case 97.

sulfanilamide therapy was actually discontinued and sulfathiazole was substituted. Combined x-ray and sulfathiazole therapy was continued, and the temperature and pulse dropped steadily until the eighth hospital day. Recovery from then on was uneventful (Fig. 122).

A residual area of denuded surface 2 × 2 in. was covered with Thiersch skin grafts 10 days before the patient was dismissed from the hospital. He was in the hospital for 10 weeks.

The course in this case only added to our opinion that x-rays and sulfanilamide together are of no therapeutic value, but that x-ray and sulfathiazole therapy given simultaneously may work very well.

As a routine measure in the prevention of infection in superficial and deep tissues and tissues with good and with poor blood supply, we have more confidence in small doses of x-ray than in any other measure we have seen employed. This is particularly true when it is impossible to reach the bottom of the wound and all of its various recesses with antiseptics or irrigating fluids.

Also, x-rays used prophylactically leave less local and general unfavorable reactions or sequelae than any other agent we have used. The minimum morbidity is always apparent when x-rays are used in prevention and in treatment. The effects of some other measures we have seen used are extremely uncertain and often cause disaster.

X-rays seem to raise the general level of the patient's resistance. This statement is supported by the fact that in many instances in which a reactivation of a gas bacillus infection occurs, a minimal amount of radiation controls the infection and it disappears almost immediately.

However, some of the other agents in general use may be of some value if they reach all of the exposed tissues at the site of injury; but if the infection is beyond their reach, they have no stimulating effect on the defensive mechanism of the blood and their use locally is worthless.

There are now on record in this country too many advanced cases with recovery following x-ray therapy without loss of tissue from gangrene to permit such an occurrence as that related in Case 94 without seeking an explanation. If some free oxygen is necessary in the blood and tissues receiving x-ray therapy before any beneficial effect is secured and the chemotherapeutic group of drugs in some manner combine all the available oxygen, it is obvious that no good can come from x-ray therapy and sulfanilamide. This is, of course, merely a guess as to a possible cause for the failure of x-rays and sulfanilamide to work well together, but it may have some support in the fact that not all patients do as poorly as others when receiving the combined treatment. Regarding this observation, it might be kept in mind that not all patients are affected in the same way by sulfanil-

amide; for instance, some promptly become cyanosed even with small doses, whereas others tolerate fairly large doses and remain free of toxic symptoms.

It is not unreasonable to assume that those who are most susceptible to sulfanilamide, that is, those who develop the most cyanosis and show other evidence of toxicity, give the poorest response to x-ray treatment, and that those less affected by sulfanilamide show better response, although still not as good as those who receive no sulfanilamide while receiving x-ray therapy.

From the few cases which have come to our attention locally and in the literature, we have not been impressed by the evidence that sulfanilamide is able to control the usual gas bacillus infection even when x-rays are not used. An extended review of the literature has not been undertaken, but in the cases coming to our attention the results have been poor. Among these is a case reported by Macey⁴ in 1939 and the cases of McNamee and Lulenski,²³ Sewell²² and Cantril.⁵ A report from Germany suggests that Zeissler is also doubtful of the value of chemotherapy locally in the prevention or treatment of gas bacillus infection. He stated:

Gas edema is a collective term for gas gangrene and malignant edema which frequently develop as mixed infections. The author maintains that local chemotherapy is ineffective, and warns against the injection of chemicals in the surroundings of the wound. Such injections may cause trophic disturbances in the tissues or even tissue necrosis and thus provide one of the factors favoring the development of gas edema.⁶

Furthermore, the literature, supporting the use of sulfanilamide therapy for gas bacillus infection carries reports of only a few isolated cases, and analysis of the results shows no great improvement over the results obtained previously by serum and surgery. In practically all of the cases, amputations have been necessary, and this is certainly a poor procedure during the acute invasive stage. It is rarely required at any time when x-ray therapy is used. The difference between treating a diseased area and removing a diseased area is apparently not clear to those who claim successful treatment when the part is removed.

For those who wish animal experiments to support our contention based on clinical observations that sulfanilamide and x-rays do not work together, the following remarks may be of interest:

In the *in vivo* experiment, it is surprising to note that the combined action of drugs and roentgen rays permitted less survivors than did either the drugs or roentgen rays alone. What the answer to this may be is not known. However, it has been noted clinically that patients with infections treated coincidentally with roentgen rays and sulfanilamide have not responded as well as similar patients treated with one or the other. Therefore, under the conditions of this experiment, no synergistic reaction between sulfanilamide and roentgen rays was demonstrated.⁷

The experimental work of Kendrick also failed to demonstrate any therapeutic efficiency for the chemical in the animal. Kendrick had this to say:

A series of experiments has been done to study the therapeutic value of Neoprontosil, sulfanilamide, and sulfapyridine in gas gangrene infection produced experimentally in guinea-pigs. The results obtained with the three drugs were very similar. In the doses used, whether the cultures were washed or unwashed, these drugs did not provide protection against the infection. In the treated group, there was a mortality rate of 89.5 per cent; in the control group the rate was 94.3 per cent.

Comparison was made between protective value of antiperfringens serum and sulfanilamide in gas gangrene infections in guinea-pigs. The antiperfringens serum was more effective.⁸

Those who wish to restrict the use of x-rays in man because they have not been effective in treating animals must bear in mind that no evidence has been produced that sulfanilamide has a therapeutic effect in animals. However, these same persons continue to recommend sulfanilamide in man and condemn x-rays which have been used successfully for several years by numerous physicians in this country and abroad.

Patients recover their strength and return to work much sooner following the use of x-rays than they do following the use of the sulfonamides. The effects of these two therapeutic agents on the patient's natural and acquired immunity seems to be worthy of further clinical and scientific study. The x-rays appear to act through a stimulation of the forces of immunity and the sulfonamides only by a temporary bacteriostatic action, probably with some disturbance of immunity.