

The Classic

The Use of Sulfathiazole in the Treatment of Subacute and Chronic Osteomyelitis*

Frank D. Dickson MD (1882–1964), Rex L. Diveley MD, Richard Kiene MD
The 4th President of the AAOS 1935 (FDD)

Frank Drake Dickson was born in 1882, in Pittsburgh, PA. His paternal grandfather had opened the first soft coal mine in the western part of Pennsylvania and was one of the builders of the Pennsylvania Railroad [4]. He obtained an undergraduate degree from the University of Pennsylvania in 1902, and his MD degree in 1905. He then studied abroad for a year and a half, and subsequently took an internship in Philadelphia. He became a Professor of Orthopaedic Surgery at the University of Pennsylvania in 1912. In 1916, Dr. Dickson was offered a position at the new Christian Church Hospital in Kansas City. He stated, “My intention was to spend about two years in Kansas City, then return to Philadelphia” [4]. He was, however, a captain in the military reserve and when the United States entered WW I, he resigned his position at the hospital and his professorship at the University of Kansas Medical School, and went to England with the unit that Dr. Joel Goldthwait (Boston) had organized. He was transferred to France in late 1917. After the war he decided to return to Kansas City to resume his work at the University of Kansas and the Christian Church Hospital where he met Dr. Rex Diveley (who became the 15th President of the AAOS). The two later (1927) established the Dickson-Diveley Clinic and the following year moved their practice to the new St. Luke’s Hospital. He continued limited practice and served as a consultant at the Clinic up until the time of his death.

Dr. Dickson was one of eight individuals at the business meeting of the Clinical Orthopaedic Society, October 30, 1931, when the first concrete steps toward organizing the AAOS were taken [2]. (The Clinical Orthopaedic Society had originally been established as a regional association in 1912 as the Central States Orthopaedic Club with a name change in 1923 to the Clinical Orthopaedic Society [1].)

Dr. Dickson was involved in a number of organizations, and was President not only of the AAOS but also the AOA in 1940 (he later served as the AOA treasurer in 1951) and the Clinical Orthopaedic Society [4], the two organizations which founded the AAOS.

The article we reproduce here illustrates an early use of sulfathiazole to treat chronic osteomyelitis, coauthored with Dr. Rex Diveley [3]. They outline the four traditional treatments of osteomyelitis: débridement and packing to provide drainage, débridement and treatment with maggots, débridement and irrigation with Dakin’s solution, and the Orr method of débridement, packing with Vaseline gauze, and immobilization in plaster for long periods. Key and his colleagues [5], about the same time, had advocated the use of sulfanilamide in contaminated wounds. Dickson and Diveley decided to try sulfathiazole because it was more effective against staphylococcus (which at the time was the infective organism 90% of the time). (The sulfonamides had been synthesized in the 1930s in Germany, with the first publication in 1935. Hundreds of manufacturers quickly developed products, including Elixir Sulfonamide, which led to the deaths of at least 100 people from ethylene glycol in the product. The outrage led to the Federal Food, Drug, and Cosmetic Act in 1938, which greatly expanded the authority of the FDA [6].) Their approach was based upon a concentration shown by Key et al. [5] to kill any bacteria. Their 22 patients were treated by preoperative sulfathiazole by mouth for three days prior to surgery (monitoring blood concentrations from 1 to 13 milligrams per 100 cubic centimeters), then thorough débridement (after injecting the sinuses with methylene blue to identify their extent), and the application of 1 to 2 grams of sulfathiazole powder to the wound using



Frank Drake Dickson, MD is shown. Photograph is reproduced with permission and ©American Academy of Orthopaedic Surgeons. *Fifty Years of Progress*, 1983.

a nasal insufflator, followed by firm dressings and casting. The first patient was treated August 1, 1940, and the report (published in July, 1941) described the use of the approach in 22 patients, 18 of which had hematogenous osteomyelitic foci. Fourteen of the 18 patients healed within 23 days, and two were too recent to know the results. This was a remarkable outcome for the time. (Equally remarkable is publication in July of 1941, when the series began only in August of the previous year.)

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References

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This presentation is to be considered merely a preliminary report and in no sense as a finished investigation of the subject.

Hematogenous osteomyelitis is generally separated into three types,—acute, subacute, and chronic. This preliminary report deals primarily with the subacute and chronic forms, although two cases are included which might be considered acute.

Broadly speaking, in the past four types of procedure have been employed in the treatment of subacute and chronic osteomyelitis:

1. The conventional method of thorough débridement of the focus or foci, followed by repeated packing of the cavity with some form of material to provide drainage.
2. The maggot method of Baer in which, after thorough débridement of the focus, live maggots are introduced into the cavity. The maggots, acting as scavengers, remove all débris and produce a clean wound, which is allowed to heal by granulation, or is closed by secondary suture.
3. The Carrell-Dakin method, which consists in thorough débridement of the focus, followed by irrigation of the

cavity with Dakin's solution every two hours, day and night, until the wound is free from infecting organisms, as demonstrated by laboratory methods. When the wound is sterile, secondary closure is made.

4. The Orr method in which, following thorough débridement, the cavity is packed with vaseline gauze and the region adequately immobilized in plaster and left undisturbed for long periods of time. This formula is followed until healing is complete.

It is not our intention to discuss the relative merits of these four methods of treatment, except to state that the first has been largely discarded by those who have had any considerable experience in the treatment of osteomyelitis. The Carrell-Dakin and Orr methods are those most generally followed today, with the Orr method decidedly leading in popular favor. Both the Carrell-Dakin and the Orr methods have definite disadvantages. The Carrell-Dakin method usually requires a long period of hospitalization and meticulous care in the daily dressings which are necessary. The chief objections to the Orr method, in the authors' opinion, are the long period required for healing, and the fact that healing is largely by scar tissue,—a real

disadvantage in many locations. Recognizing the disadvantages of the methods in use for the treatment of osteomyelitis, and having been impressed with the results reported by Key, Frankel, and Burford [1], following the implantation of sulfanilamide in contaminated wounds, the authors determined to try out sulfathiazole, administered by mouth and implanted in the wound, in the treatment of subacute and chronic osteomyelitis. Sulfathiazole was selected because it is a more effective agent than sulfanilamide against the staphylococcus, and so should be more effective in the treatment of osteomyelitis, in which staphylococcus is the infecting organism in 90 per cent. of the cases.

The plan of attack was based on the statement made by Key, Frankel, and Burford that powdered sulfanilamide in a wound is similar to a test-tube experiment in which a concentration of approximately 1,000 milligrams of the drug is brought into contact with any bacteria which may be present in the media. In such concentration, according to them, the sulfanilamide is effective against small numbers of staphylococci and of Welch bacilli, and against large numbers of streptococci. These authors, as the result of their work, concluded that when sulfanilamide is implanted in a wound, the drug exerts a neutralizing effect on the toxins present, thus minimizing the amount of tissue breakdown, and that the drug converts bacteria into a static or non-pathogenic phase in which they do not invade the surrounding tissues and do not multiply. In this static state, the bacteria are taken care of by the normal clearing mechanism of the animal and are destroyed. It was felt that if this premise was sound—and it seemed to be—a thorough débridement of the sinus and infected bone in subacute and chronic osteomyelitis, and the introduction of sulfathiazole powder into the wound should be effective in the same way against the comparatively small number of staphylococci and other contaminating organisms which would remain. An additional indication for the use of powdered sulfathiazole locally was the considerable evidence to show that pus is a definite depresser on the action of the sulfathiazole group, and that fibrous encapsulation of a focus makes it difficult for the drug to reach the focus through the blood stream in sufficient concentration to be effective. Both of these factors are present, to some extent, in subacute and chronic osteomyelitis; and consequently, the effect to be expected from sulfathiazole administered by mouth alone would be minimal.

The plan of treatment was: first, the administration of sulfathiazole for at least three days before operation in sufficient quantities to assure an average blood concentration of 4.7 per cent. (the purpose of this was to secure whatever benefit was possible from the presence of the drug in the blood stream); second, thorough débridement of the local focus and the introduction of powdered

sulfathiazole into the wound. The local treatment was carried out as follows:

1. A tourniquet was applied to the extremity to be operated upon and kept in place until a cast was applied following the operation.
2. The sinus tract or tracts were injected with methylene blue for the purpose of staining and so outlining all necrotic material in the soft parts and in the bone.
3. The sinus was completely dissected out down to the infected area in the bone.
4. The involved part of the bone was freely exposed and, using mallet, chisel, and gouge, all dead and necrotic bone, stained by the methylene blue, was removed, and the cavity saucerized as thoroughly as possible. The rough edges which remained were smoothed off by the use of an electric burr.
5. All scar tissue in the soft parts was dissected away as extensively as possible, thus providing healthy tissue which could be brought into contact with the bone cavity when closure was made.
6. One to two grams of sulfathiazole powder was then introduced into the wound, using a nasal insufflator.
7. The deep soft parts were then sutured with interrupted sutures in such a manner as to bring them into as close contact as possible with the denuded area of bone. Additional sulfathiazole powder was introduced into the wound and the superficial structures were closed with interrupted sutures. The skin was closed with cotton thread. A voluminous firm dressing was applied in such a manner as to press the soft parts firmly into the bone cavity. Finally, a plaster cast was applied, to adequately immobilize the extremity.

This treatment was first administered on August 1, 1940, since which time twenty-two osteomyelitic foci have been treated by this method. The following is a summary of the cases:

The number of hematogenous osteomyelitic foci treated was eighteen. The duration of the osteomyelitic process in the individual varied from nineteen years to thirty-seven days. The average duration was four and eight-tenths years. The duration of the activity in the particular focus treated also varied. The longest period of duration was two years, the shortest one week, and the average duration twenty-three weeks.

The drug was administered by mouth on an average of five and nine-tenths days before surgery and fifteen days after surgery. The average daily dose of the drug by mouth was 0.11 grams per kilogram or five grams per 100 pounds of body weight. The range of blood concentration during administration by mouth was from one to thirteen milligrams per 100 cubic centimeters. The average blood concentration on the day of operation was 4.7 per cent.

The results were as follows: Fourteen of the eighteen cases, or 78 per cent., healed by primary union; two, or 11 per cent., did not heal; and two, or 11 per cent., have been too recently treated to report. The average length of time from the day of operation to healing was twenty-one days. In many of these cases, approximately 50 per cent., there was some superficial breaking down of the skin incision, not in its entirety but at one or two points. These areas healed within one to two weeks in all cases.

The two unhealed cases are of interest. The first of these was an osteomyelitis of the mandible, which apparently healed. Within a week following apparent healing, there developed a discharging sinus which, when probed, did not seem to lead down to bone, but which continued to discharge. The authors are unable to offer any explanation for this situation, since osteomyelitis of the mandible ordinarily heals rapidly. The second case was one in which the infection was due to the bacillus coli, determined before surgery was undertaken and at the time of operation. The inefficacy of sulfanilamide and sulfathiazole against bacillus coli is well recognized, and was certainly demonstrated in this case. The authors believe that a proved bacillus coli infection should not be treated by this method. This case is now being treated by the Carrell-Dakin method, and, as soon as the colon infection is cleared up, the wound will be closed by secondary sutures and powdered sulfanilamide or sulfathiazole introduced into the wound. In one acute case the wound was opened and drained for thirty-seven days, and then closed, using sulfathiazole powder. This wound closed by primary intention and has remained closed. A second case, which had some of the characteristics of an acute case, was of a boy whose original focus, in the lower end of the femur, had been healed for five months. The new focus was in the upper third of the femur, entirely separate from his original focus. When seen, the abscess had ruptured through the periosteum, and the thigh was distended with pus which had infiltrated between the muscle planes, forming many pockets. This case after débridement was treated by the Carrell-Dakin method for ten days. At the end of ten days, secondary closure was carried out, using sulfathiazole powder in the wound. This wound healed by primary intention in three weeks and has remained closed for two and a half months.

In addition to the eighteen osteomyelitic foci of hematogenous origin, four cases, in which the osteomyelitis followed a compound fracture, have been treated by this method. In these four cases, the longest period during which infection had been present was four years, the shortest was forty-one days, and the average was nineteen months. In all four cases healing was complete. The average length of time between surgery and healing was twenty-six days. The blood concentration of the sulfathiazole and the amount of powder used locally was the same as that in the cases of hematogenous osteomyelitis.

If the four cases of osteomyelitis following compound fracture are added to the eighteen cases of hematogenous osteomyelitis, the series reported includes twenty-two cases. Of the wounds in these twenty-two cases, eighteen, or 82 per cent., healed; two, or 9 per cent., failed to heal; and two, or 9 per cent., are too recent to report. The average length of time required for healing after operation in these twenty-two cases was twenty-three days.

Conclusions

1. A series of twenty-two foci of subacute and chronic osteomyelitis is reported in which the treatment employed was the administration of sulfathiazole by mouth, thorough débridement of the focus, and the introduction of sulfathiazole powder into the wound. In 82 per cent. of the cases in this series, there was healing by primary intention with an average healing period of twenty-three days following surgery.
2. This is a comparatively small series of cases, and no attempt can be made from it to arrive at a final conclusion as to the value of the method proposed. However, the results have been sufficiently satisfactory, both in regard to the type of healing and the healing period, to suggest that the method should be given a thorough trial.

Reference

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