1945

Effects Of Infusion Of Penicillin In The Bovine Mammary Gland

D. E. Jasper
University Farm, St. Paul

F. J. Weirether
University Farm, St. Paul

Follow this and additional works at: https://lib.dr.iastate.edu/iowastate_veterinarian
Part of the Large or Food Animal and Equine Medicine Commons, and the Veterinary Physiology Commons

Recommended Citation
Available at: https://lib.dr.iastate.edu/iowastate_veterinarian/vol8/iss2/2

This Article is brought to you for free and open access by the Journals at Iowa State University Digital Repository. It has been accepted for inclusion in Iowa State University Veterinarian by an authorized editor of Iowa State University Digital Repository. For more information, please contact digirep@iastate.edu.
Effects Of Infusion Of Penicillin In The Bovine Mammary Gland*

D. E. Jasper, D.V.M., and F. J. Weirether, D.V.M.

Veterinarians have waited anxiously and patiently for the time when penicillin could be released for animal therapy. Practitioners and research men have had many conditions in mind which might be expected to respond to treatment with penicillin upon the basis of its known antibiotic activity. Foremost among these conditions was bovine mastitis. It has been fervently hoped that penicillin would be a valuable drug in the treatment of streptococcic and staphylococcic mastitis. Reports to date and the experience of many practitioners prove that we have not “hoped” entirely in vain. We know that a large proportion of streptococcic and staphylococcic mastitis can be cured by proper treatment with penicillin. We are also acutely aware of the fact that the optimum dosage and frequency for a given case of mastitis is not known as yet. A knowledge of the physiologic behavior of this antibiotic when introduced into the mammary gland is essential for a scientific application of the drug in therapy.

A series of experiments (9) have been conducted at University Farm to ascertain the rate of decline in concentration and the irritating effects of infused penicillin in the bovine mammary gland. Infusions were made via the teat canal in 5, 10, 30, 40, 50, 100, and 200 thousand unit doses in normal glands and in 10, 30, 50, and 100 thousand unit doses in pathologic glands. For the majority of experiments the sodium salt of penicillin was made up with sterile distilled water so that 1 ml. of solution contained 5,000 Oxford Units. In one series the penicillin was infused in quantities of water equal to the quantity of milk withdrawn. Small samples of milk were taken at intervals for penicillin assay and finally all of the milk was removed at intervals varying from 10 to 72 hours after infusion and the penicillin therein determined.

Concentration

In all cases where 30,000 or more Oxford Units were infused, the milk contained 0.5 or more units of penicillin per ml. 24 hours after the infusion was made. The rate of decrease is the greatest during the first 10 hours after which the disappearance of penicillin is at a slower rate. The rate of decrease is greater for each increment of the dose administered over the range studied which was up to 200,000 Oxford Units per quarter. At no time was there sufficient penicillin in the blood to be detected by the assay methods used (detects 0.031 Oxford Units per ml. in blood plasma), but that some of the drug found its way into the blood is evidenced by its presence in the urine. When a total of 100,000 Oxford Units were infused in all four quarters it was noted that the highest level of 11 Oxford Units per ml. of urine was obtained at 8 hours and 5 Oxford Units per ml. were found at the end of 24 hours after infusion. However, these cows were not heavy producers and the milk concentrations would probably be lower in a cow producing heavily. Injections of 25,000 Units at 12 hour intervals can be expected to maintain a
therapeutic level in most cases of streptococcic or staphylococcic mastitis in cows in average production.

The rate of disappearance from pathologic glands presented the same picture as for the normal except in coliform infections in which the rate of decline was much greater. This is very likely due to the production of penicillinase. In the second and third infusions in consecutive 24 hour periods, however, the rate of decline was progressively lower because fewer organisms were present. However, the organisms were not completely eliminated from any coliform infected gland in our series.

**Does Not Migrate**

In order to determine whether the rate of penicillin migration would be increased with water migration the penicillin was infused in quantities equal to the quantities of milk withdrawn in 7 quarters. It was noted that up to a 4-fold concentration was reached in one case 3 hours after the infusion was made. After the maximum concentration was reached the rate of decline presents much the same picture as for the experiments where smaller amounts of water were used. The concentrations in the urine were of the order of magnitude expected and indicate no greater absorption from the gland than when small amounts of water were used.

Water is rapidly absorbed from the mammary gland and most of the penicillin is evidently left behind so that its concentration in the mammary gland rises. Subsequent decreases in penicillin content can probably be accounted for chiefly by dilution with milk which is being secreted and by absorption from the gland. Absorption from the gland evidently takes place slowly for only when 455,000 Oxford Units had been infused could any penicillin (0.06 O.U. per ml.) be detected in the blood.

Hodgkinson and Nelson (3) recently reported that 24 consecutive cases of staphylococcic mastitis in humans had been successfully treated with penicillin injected intramuscularly. They believe that when penicillin therapy is initiated early, before the lytic action of the bacteria brings about suppuration, abscess formation can be avoided although it occurs in about 18 per cent of cases of human staphylococcic mastitis.

**No Value Intravenously**

Bryan, Horwood, and Huffman (2) were not successful in an attempt to treat a chronic *S. agalactiae* bovine mastitis by the intravenous route. In order to test the permeability of the lactating bovine mammary gland to penicillin in the blood, Seeley, Anderson, Plastridge and Pearson (8) made two trials on a Jersey heifer free of mastitis. In the first trial 80,000 Oxford Units of a calcium salt of penicillin in eight ml. of physiological saline were introduced into the jugular vein and in the second trial 500,000 units were administered. In each trial the cow was milked every one-half hour for 6 hours and a final sample was obtained after 24 hours. Penicillin activity was not observed in any of the milk samples obtained for assay during the 24 hour period following the injection of the 80,000 units nor following the injection of the 500,000 units intravenously.

These observations would seem to indicate that the intravenous route will not prove to be a practical method for the treatment of chronic or subacute cases of bovine mastitis. However in acute cases, particularly those in which bacteremia is threatening, penicillin intravenously and intramuscularly may be of value.
Penicillin has proved to be without doubt the least toxic agent that has been used to date in the treatment of bovine mastitis by udder infusion. The reports by Kakavas (4), Bryan et al (2), Klein et al (5), Murphy and Pfau (6), and Barker (1) all indicate little or no unfavorable reactions manifested by the mammary gland. Our observations are essentially in accord with those of other investigators. Weirether, Jasper, and Petersen (9) noted that as measured by physical examination of the gland, body temperature effects and changes in the character and quantity of milk, infusion into the normal quarter of 5,000 to 200,000 units of penicillin in small quantities of water had but a slight irritating effect. In some cases no swelling could be detected. In others a slight swelling occurred within 3 to 4 hours after the infusions were made which completely subsided within 10 hours. In no case was any temperature rise noted. In the experiments where the cows were milked at regular intervals after infusions, no demonstrable decrease in the quantity of milk was observed. In all cases observed

by us there were changes in the character of the milk which varied in general with the quantity of penicillin infused. A few small flakes, with increases in chloride and leukocytes, were noted, as well as a slightly yellow color. According to Murphy and Pfau (6), the secretion in glands infected with Streptococcus agalactiae may become temporarily abnormal macroscopically or more abnormal in case the milk was abnormal before treatment. They also noted an increased leukocyte count, a few flakes, and a marked increase in chloride content following infusion into normal glands. There was no adverse effect on milk production.

**Water vs. Saline**

The sterile penicillin powder is most commonly dissolved with sterile distilled water or sterile physiologic saline solution. Dr. Petersen (7) of the University of Minnesota has shown that physiologic saline is much more irritating to mammary tissue than distilled water and for that reason we prefer to use distilled water as a solvent. Penicillin has also been suspended in oil for the purpose of intra-mammary infusion and has the advantage of being comparatively stable in such a suspension. The oil is non-irritating to udder parenchyma, and by using such a preparation the danger of contamination and the inconveniences of transferring the solvent to the penicillin bottle and back again into the syringe are avoided. The oil preparations used to date have only 20,000 units in a 20 c.c. bottle so that several must be used and a fairly large amount of oil must be injected if a high concentration is desired in the gland. The oil suspension has the further disadvantage of being very hard to shake up so that all of the penicillin is loosened from the bottom of the bottle. There is no evidence to indicate that the migration of penicillin out of the gland is increased or retarded when oil is used as a vehicle in place of distilled water.

In conclusion, it may be stated that: penicillin is relatively non-toxic and large amounts may be infused without danger of disturbing reactions; that the concentration in the gland is reduced most rapidly during the first 10 hour period following the infusion, and that this decrease in concentration is brought about by dilution with milk being secreted and by migration out of the gland. In view of its low toxicity and low cost, it is probably desirable to give a dosage which is well above the minimum required for
bacteriostasis to allow for: unequal distribution in the gland; organisms which may be extraordinarily resistant; and increased dilution in high producing cows.

LITERATURE CITED


Barnette Wins National Dog Week Bond

G. W. Barrette, editor of the Peoria (Illinois) Journal-Transcript, has been awarded a $100 Victory Bond by the Gaines Dog Research Center, New York, as author of the “best editorial on a dog topic appearing in an American newspaper during the 1945 National Dog Week,” it is announced. Mr. Barrette’s editorial, titled “A Dog’s-Eye View,” appeared in the Journal-Transcript on September 17.

Mr. Barrette’s editorial was chosen by a committee of judges which included Sydney H. Coleman, president of the American Humane Association, Albany, N. Y.; Capt. Will Judy, editor of Dog World Magazine, Chicago, and Harry Miller, executive secretary of the Gaines Dog Research Center, New York City.

Following is the Journal-Transcript editorial in full:

“This being National Dog Week, we wonder what a dog’s eye view of mankind would be. It might be . . .

“Well, the war is over, we dogs have proven our usefulness as sentries, message carriers, Red Cross helpers, guards, agricultural workers and aides to disabled soldiers. We think we’ve done our part as morale builders during the conflict. We have guarded prisoners. We have learned to lead the blind—men who had eyes, once, but whose eyes were put out by other men. We didn’t invent the atomic bomb. But since we live with human beings we were its victims, too. We never won or lost a war, but we gave our lives in war service—just because humans set us the example. We are dependent upon you humans for food and care, particularly in the city, but if that food and care is not given us we do not turn and rend you like people might do. We just become stray curs, an obligation of yours and a reproach to your humanity.

“We serve your children by teaching them that inferior creatures deserve their kindness and protection. In return, we give protection to you. We are the first to give notice of danger and to detect the presence of a marauder. We have an instinctive urge to rescue those who are drowning. We smell fire smoke sooner than you do. We enjoy running and playing, but don’t enjoy standing people up against the wall and shooting them or beating them to death in concentration camps. Indeed, perhaps, our morality is the morality of loyalty—loyalty to you human beings.

“All we ask in return is that you be a little loyal to us—that you recognize the ancient alliance between dog and man. This alliance is so old in the human race that we don’t resent it, one whit, even when you abuse us. But we don’t know how to abuse you, unless you desert us and ignore us, forget us and starve us, destroy our morale and neglect us.

“To us, you are pretty close to God. Indeed, you’re the only God we know. We sometimes wonder why you don’t behave like God—both in your relations with human beings and with us.”