

Dicloxacillin for Necrotizing Fasciitis in Virginia Opossums

AT A GLANCE

- Necrotizing fasciitis (NF), also called flesh-eating disease, is a rare, severe bacterial infection occurring in many species.
- Research conducted on pathogens isolated from Virginia opossums with suspected cases of necrotizing fasciitis with toxic shock syndrome (NF/TSS) has led to the identification of *Streptococcus didelphis*.
- Most of the National Opossum Society (NOS) literature cites oxacillin as the first-choice drug to treat NF. Both oxacillin and dicloxacillin belong to the penicillin class of antibiotics. Both have spectrums of activity similar enough to use oxacillin as a baseline for dicloxacillin sensitivity testing.
- Dicloxacillin is currently more readily available, making it a more realistic choice for NF treatment for modern rehabilitators.
- Treatment should begin as soon as possible, starting with oral dicloxacillin at an approximate dosage of 15 mg per pound of body weight.

Dicloxacillin General Information

Dicloxacillin is a narrow-spectrum antibiotic and second-generation penicillin. It is principally used off-label in veterinary medicine for dogs. It is prescribed infrequently in small animal medicine due to its limited spectrum of activity. It is not used in large animals due to poor absorption. Recommended dosage for small animals ranges from 11-55 mg/kg of bodyweight orally, three times a day.¹

Mechanism of Action

Like all penicillins, dicloxacillin works by weakening the cell wall of gram-positive bacteria. It is ineffective against gram-negative bacteria. It is most effective against staphylococci and is often used to combat penicillinase-resistant species, though it is inactive against methicillin-resistant species.^{2,1}

Necrotizing Fasciitis

Necrotizing fasciitis (NF), also called flesh-eating disease, is a rare, severe bacterial infection occurring in many species. NF progresses rapidly and requires immediate medical attention. It is thought to result from particular conditions which allow an opportunistic bacterium to propagate, such as a break

in the skin coupled with impaired host immune defense. Streptococci species are the typical pathogens responsible for infection. *S. canis* has been found in dogs, and both streptococci and staphylococci can be responsible for human cases.³ Bacterial penetration of the dermis, the thickest layer of skin, results in soft-tissue damage and eventual organ damage which can prove fatal. Treatment should therefore be started immediately if NF is suspected. While culture of the pathogen and sensitivity testing are important tools for treatment if available, one should not wait for results before instituting antibiotic therapy. If treatment is delayed or the infection is caught too late, prognosis is very poor. NF may present as asymptomatic with the exception of lesion development. Limbs and tails are common sites of infection in the Virginia opossum, with severe cases often currently requiring amputation. NF may be accompanied by Toxic Shock Syndrome (TSS), in which case fluids are advisable as part of treatment. Clinical signs of both NF and TSS in opossums summarized below:

Figure 1: Symptoms of NF and related TSS by Dr. Henness of the National Opossum Society (NOS)

Table 1. Summary of Chief Clinical Signs of Necrotizing Fasciitis (NF) / Toxic Shock Syndrome (TSS) in Opossums (<i>D. virginiana</i>)	
1.	Can occur at any age, in newly admitted up to long-term captive opossums.
2.	Opossums in general may appear anywhere from “normal” to very depressed and trembling.
3.	Wound may appear trivial or may be absolutely inapparent at first.
4.	<u>NF:</u>
	a. May occur anywhere on the body.
	b. Ecchymosis and erythema (bruised and reddened) area up to 1-2” from visible wound, or without evident external wound.
	c. Exaggerated pain at site with slightest touch (pain response of this degree not common in opossum, even at sites of mauling).
	d. <u>Heat</u> , pronounced, at site, possibly also with accompanying body fever.
5.	<u>TSS:</u>
	a. Predominant signs in the opossum <u>appear</u> to be limited to the head and neck (H/N).
	b. Rapid onset of <u>extreme edema</u> (soft tissue swelling), developing to fullest extent within 2 to 4 hours (may nearly double size of head and neck).
	c. Usually <u>no</u> visible wound. May <u>not</u> have bruising. May or may not be painful.
	d. Body fever unless deep shock.
	e. Extremely rapid heart rate, respiratory distress, cyanosis (blue-gray mucous membranes).

Henness, A., DVM. (1997). NECROTIZING FASCIITIS/TOXIC SHOCK SYNDROME in Opossums (*D. virginiana*) ... a.k.a. "Flesh-Eating Bacterial Disease." *POSSUM TALES*, 11, 4.

Treatment: Dicloxacillin vs. Oxacillin

Most of the NOS literature cites oxacillin as the first choice drug to treat NF. Dr. Henness recommended oxacillin treatment (administered either orally or subcutaneously) at 15 mg per pound 3 times per day or 20 mg per pound 2 times per day. She advised starting oxacillin as soon as NF was suspected and continuing the regimen for at least two weeks.³ While *S. didelphis* was found to be sensitive to amoxicillin and nearly every other (unspecified) antibiotic tested in vitro, treatment was unsuccessful when instituted in vivo,^{4,5} and so Dr. Henness' oxacillin regimen remained the recommended treatment. Rehabilitators reported success to the NOS with this treatment, as well as with dicloxacillin, though it is unknown if they maintained the dosage recommended for oxacillin.⁴ Both drugs belong to the penicillin class of antibiotics and have spectrums of activity similar enough to use oxacillin as a baseline for dicloxacillin sensitivity testing.¹ At the time of this publication, neither dicloxacillin nor oxacillin is used frequently in veterinary medicine. Dicloxacillin remains more readily available, making it a more realistic choice for NF treatment for modern rehabilitators.

In addition to antibiotic therapy, proper wound care is essential. Dr. Henness recommended the wound be cultured, debrided if necessary, and dressed as soon as the opossum is stable. Lesions should be kept clean and free of fecal contamination.

Suspected Pathogen

Research conducted on pathogens isolated from suspected cases of NF/TSS in nine opossum led to the identification of a novel species of streptococci likely to be responsible for the infections, *Streptococcus didelphis*.^{4,5} This species has a similar appearance to other streptococcus species but behaves more like members of the staphylococcus genus.^{1,5} This unique mix of characteristics may explain dicloxacillin's efficacy against *S. didelphis* despite its genus.

Conclusion and Recommendations

When necrotizing fasciitis is suspected in an opossum, time is of the essence. Treatment should be started immediately, starting with oral dicloxacillin at an approximate dosage of 15 mg per pound of bodyweight. This dosage is our best estimate based on (a) the dicloxacillin dosage range found in literature (5-25 mg/lb)⁴ and (b) Dr. Henness' oxacillin dosage (15-20 mg/lb).³ If possible, keep a detailed record with photographs of visible lesions to track healing of the affected areas. Keep wounds clean and maintain antibiotic therapy for at least two weeks. If no improvement is seen within two to three days, dicloxacillin should be discontinued and a trusted veterinarian consulted before starting another antibiotic. Note that some success has been had with clindamycin and Baytril in parallel.⁶

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References

1. Mark G. Papich, Dicloxacillin Sodium, Editor(s): Mark G. Papich, Saunders Handbook of Veterinary Drugs (Fourth Edition), W.B. Saunders, 2016, Pages 234-235, ISBN 9780323244855, <https://doi.org/10.1016/B978-0-323-24485-5.00205-9>.
(<http://www.sciencedirect.com/science/article/pii/B9780323244855002059>)
2. Dicloxacillin. (n.d.). Retrieved from <https://pubchem.ncbi.nlm.nih.gov/compound/Dicloxacillin>
3. Hennes, A., DVM. (1997). "NECROTIZING FASCIITIS/TOXIC SHOCK SYNDROME in Opossums (*D. virginiana*) ... a.k.a. 'Flesh-Eating Bacterial Disease.'" *POSSUM TALES*, 11, 4.
4. Arms, P., MLT (ASCP). (2008). "Update on the Culprit." *POSSUM TALES*, 11, 4.
5. Rurangirwa, F. R., Teitzel, C. A., Cui, J., French, D. M., McDonough, P. L., & Besser, T. (2000). *Streptococcus didelphis* sp. nov., a streptococcus with marked catalase activity isolated from opossums (*Didelphis virginiana*) with suppurative dermatitis and liver fibrosis. *International Journal of Systematic and Evolutionary Microbiology*, 50(2), 759-765.
doi:10.1099/00207713-50-2-759
6. Mowrey, L. (2005). Necrotizing Fasciitis; Flesh Eating Bacteria. Retrieved from <https://possumlover777.wixsite.com/opossumcare/necrotizing-fascitishttps://possumlover777.wixsite.com/opossumcare/necrotizing-fascitis>
7. Penicillins By Dawn Merton Boothe, By, Boothe, D. M., & Last full review/revision Nov 2015 | Content last modified Nov 2015. (n.d.). Penicillins - Pharmacology. Retrieved from <https://www.merckvetmanual.com/pharmacology/antibacterial-agents/penicillins?query=dicloxacillin>