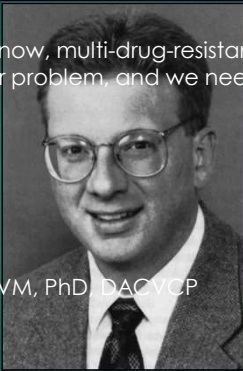


MULTI-DRUG-RESISTANT INFECTIONS

ELIZABETH A. SWANSON, DVM, MS, DACVS-SA
ASSOCIATE PROFESSOR, SMALL ANIMAL SURGERY

1


20 years from now, multi-drug-resistant infections will be a major problem, and we need to be ready



Mike Apley, DVM, PhD, DACVCP
Public Health
ISU 2000

2

IMPACT OF RESISTANT INFECTIONS

JAVMA 

Multidrug-resistant wound infections are associated with greater mortality, larger costs, and longer hospitalizations than susceptible infections in canine patients

2025;263(5):1-9

Deliana Allegretti, DVM; Scarlett M. Sumner, DVM; Laura Huber, DVM, PhD, DACVPM; Katelyn Huzsko, DVM, MS, DACVSI; Kayla M. Corriveau, DVM, DACVSI; Brad Matz, DVM, MS, DACVSI; Michael Tillson, DVM, MS, DACVSI

- ▶ Patients with MDR infections reported
 - ▶ 2.98 x longer hospitalization
 - ▶ 11.8 x greater mortality rate
 - ▶ 3.57 x greater cost

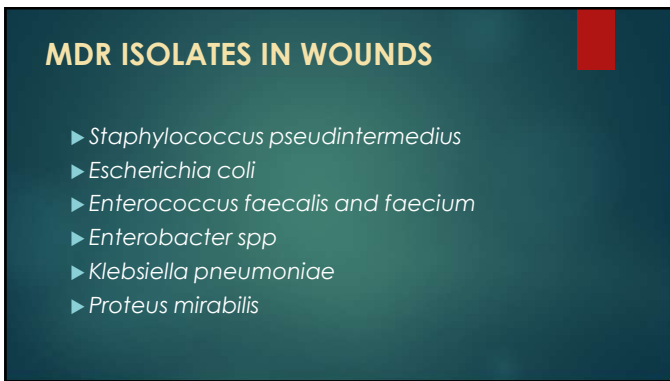
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6

ANTIMICROBIAL STEWARDSHIP

DEFINITION

Antimicrobial stewardship refers to the actions veterinarians take to preserve the success and availability of antimicrobial drugs through careful oversight and responsible medical decision-making while protecting animal, public, and environmental health.

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ANTIMICROBIAL STEWARDSHIP

- ▶ Prevent infection
 - ▶ Hand washing
 - ▶ Hospital hygiene/cleanliness
 - ▶ Patient and Surgeon prep
 - ▶ Appropriate PPE during wound care

8

ANTIMICROBIAL STEWARDSHIP

- ▶ Judicious use of antibiotics
 - ▶ Only when needed
 - ▶ Select most appropriate antibiotic for the infection and location
 - ▶ Prescribe correct dose/frequency/duration/route
 - ▶ Stay within owner/patient means

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ANTIMICROBIAL STEWARDSHIP

- ▶ Select antibiotic that penetrates target tissue
- ▶ Treat appropriate length of time for tissue/infection
 - ▶ Minimum 5-7 days is a course
 - ▶ Pyoderma = 3 weeks/7-14 days beyond resolution
 - ▶ "Hit hard and get out" - +/- pneumonia, wounds??
- ▶ Calculate correct dose
 - ▶ Ranges provided for most antibiotics
 - ▶ Time vs. concentration dependent
- ▶ Treat topically only if no systemic infection

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ANTIMICROBIAL STEWARDSHIP

- ▶ Resources
 - ▶ <https://www.avma.org/resources-tools/one-health/antimicrobial-use-and-antimicrobial-resistance>
 - ▶ <https://www.avma.org/sites/default/files/2020-10/AntimicrobialResistanceFullReport.pdf>
 - ▶ TARGET book
 - ▶ Drug Formularies



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INTERSECTION: BIOFILMS-MDR INFECTION-VET MED

- ▶ Biofilms cause recalcitrant infections
 - ▶ Develop slowly
 - ▶ Persistent
 - ▶ Resistant to immune response
 - ▶ Transient response to antibiotic therapy
 - ▶ → Resistant to antibiotics

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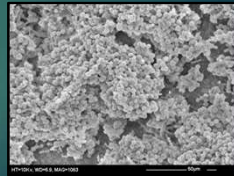
BIOFILMS IN CHRONIC INFECTION

- ▶ Transient response to systemic antibiotics
 - ▶ High MIC
 - ▶ 100x-1,000x higher than planktonic
 - ▶ Wolcott RD, et al. JAMA 2008.

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BIOFILMS IN CHRONIC INFECTION

- ▶ Transient response to systemic antibiotics
 - ▶ Proposed causes
 - ▶ Phenotype changes
 - ▶ Low metabolism
 - ▶ Charged particles in matrix
 - ▶ Low oxygen tension



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BIOFILMS IN CHRONIC INFECTION

- ▶ Antibiotic Resistance of Biofilms
 - ▶ Phenotype changes to cell membrane
 - ▶ Changes antimicrobial binding proteins and molecular targets
 - ▶ Low metabolism
 - ▶ Inhibits β -lactams
 - ▶ Senescence (Persister Cells)
 - ▶ Invisible to antibiotics

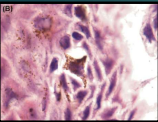
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BIOFILMS IN CHRONIC INFECTION

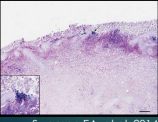
- ▶ Antibiotic Resistance of Biofilms
 - ▶ Negatively-charged particles in matrix
 - ▶ Repels aminoglycosides and β -lactams
 - ▶ Thick EPS decreases permeability
 - ▶ Low oxygen tension
 - ▶ Fluroquinolones, β -lactams, and aminoglycosides require O₂ for MOA or transport

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WOUND BIOFILM INFECTIONS



Freeman K, et al. 2009



Swanson EA, et al. 2014

- ▶ **Chronic Wounds**
 - ▶ Distal limb wounds in horses
 - ▶ Freeman K, et al. *Can J Microbiol* (2009)
 - ▶ Westgate SJ, et al. *Vet Microbiol* (2011)
 - ▶ Chronic elbow wounds in a dog
 - ▶ Swanson EA, et al. *J Am Vet Med Assoc* (2014)

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BIOFILM IN CANINE WOUNDS

- ▶ 4-year-old, SF, Old English Mastiff
- ▶ Dehiscenced incisions after elbow callus excision
 - ▶ Unhealed after 3 weeks



Left




Right

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BIOFILM IN CANINE WOUNDS

- ▶ Wound Appearance
 - ▶ Thickened, inflamed wound edges
 - ▶ Poor-quality granulation tissue
 - ▶ Not grossly purulent

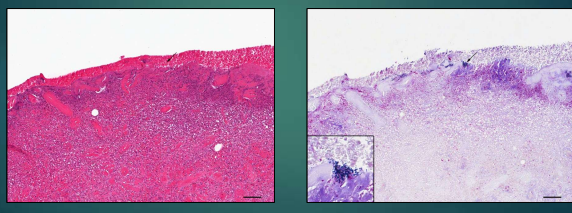


hyper textbook shop.com

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BIOFILM IN CANINE WOUNDS

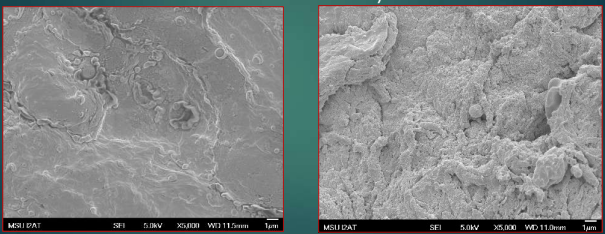
- ▶ H & E
- ▶ Gram



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BIOFILM IN CANINE WOUNDS

- Acute Laceration
- 5 Day Old Abrasion



MSH1.DAT SEI 5.0kV X5000 WD11.5mm 1um MSH1.DAT SEI 5.0kV X5,000 WD11.0mm 1um

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TREATING WOUND BIOFILM INFECTION

- ▶ General Guidelines
 - ▶ Prepare wound bed
 - ▶ Remove foreign material
 - ▶ Protect from repetitive injury
 - ▶ Improve circulation

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TREATING WOUND BIOFILM INFECTION

- ▶ Biofilm-Based Treatment Strategy
 - ▶ Frequent, aggressive debridement
 - ▶ To break up biofilm
 - ▶ Bacteria more susceptible
 - ▶ Antimicrobial therapy
 - ▶ Selective biocides
 - ▶ Antibiofilm agents




Wolcott RD, et al. Adv Wound Care [2010]

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TREATING WOUND BIOFILM INFECTION

- ▶ Selective biocides
 - ▶ Ionic silver
 - ▶ Nanocrystalline silver dressings
 - ▶ Cadexomer iodine



diabeteshalthsupplies.com

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TREATING WOUND BIOFILM INFECTION

- ▶ Antibiofilm Agents
 - ▶ Lactoferrin
 - ▶ Bacteriostatic – binds Fe³⁺
 - ▶ Bacteriocidal
 - ▶ Binds to lipopolysaccharide on Gram negative membranes
 - ▶ Blocks planktonic attachment
 - ▶ Neutrophils
 - ▶ Hydroxyl radical production catalyst
 - ▶ Active in acidic environment



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TREATING BIOFILM WOUND INFECTION

- ▶ Antibiofilm Agents
 - ▶ LipoGel® gel
 - ▶ Propriety anti-biofilm gel
 - ▶ Lipid-based
 - ▶ Multi-functional
 - ▶ Xylitol
 - ▶ Inhibits biofilm formation
 - ▶ Unknown mechanism
 - ▶ Toxic to bacteria



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TREATING BIOFILM WOUND INFECTION

- ▶ Implications for patients
 - ▶ Faster healing
 - ▶ Wolcott RD, et al. *J Wound Care* (2010)
 - ▶ 22% faster healing rate
 - ▶ Wolcott RD, et al. *Plast Recon Surg* (2011)
 - ▶ Used molecular diagnostics to create specific treatment for wound

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TREATING BIOFILM WOUND INFECTION

- ▶ Implications for patients
 - ▶ Faster healing
 - ▶ Fewer amputations
 - ▶ Lower morbidity and mortality rates
- ▶ Why should we adopt these techniques?
 - ▶ Biofilms reported in >78% chronic wounds
 - ▶ Likely similar prevalence in veterinary patients

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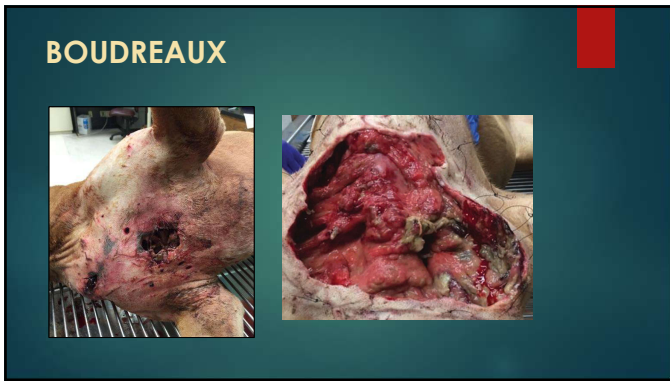
CASES

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MACK



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BOUDREAU


	<i>Escherichia coli</i>		<i>Corynebacterium sp.</i>		<i>Enterococcus faecalis</i>			<i>Escherichia coli</i>		<i>Enterococcus faecium</i>	
Amikacin	<=4	S	<=4	S	>32	R	Amikacin	<=4	S	>32	R
Amoxicillin/Clavulanic Acid	>1	NI	0.5	S	0.5	S	Amoxicillin/Clavulanic Acid	>1	NI	>1	NI
Ampicillin	>1	NI	0.5	NI	1	S	Ampicillin	>1	NI	>1	NI
Cefazolin	4	S	<=1	S	>8	R	Cefazolin	>8	R	>8	R
Cefuroxime	1	NI	0.5	NI	N/A	N/A	Cefuroxime	>4	NI	N/A	N/A
Ceftriaxone	8	S	8	NI	>16	NI	Ceftriaxone	8	S	>16	NI
Cefepime	<=2	S	<=2	NI	>16	NI	Cefepime	>16	R	>16	NI
Cefidroxime	0.5	NI	<=0.25	NI	>4	NI	Cefidroxime	>4	NI	>4	NI
Cefixime	>8	R	4	S	>8	R	Cefixime	>8	R	>8	R
Chloramphenicol	<=4	S	<=4	S	<=4	S	Chloramphenicol	>16	R	16	I
Clindamycin	>4	NI	>4	R	>4	NI	Clindamycin	>4	NI	>4	NI
Doxycycline	<=2	S	4	S	<=2	S	Doxycycline	<=2	S	>8	R
Ertapenem	>2	R	>2	NI	1	NI	Ertapenem	>2	R	>2	NI
Erythromycin	>4	R	>4	R	2	I	Erythromycin	>4	R	>4	R
Gentamicin	<=1	S	<=1	S	8	I	Gentamicin	<=1	S	>8	R
Imipenem	<=1	S	<=1	S	<=1	S	Imipenem	<=1	S	>8	R
Meropenem	>2	R	>2	NI	2	NI	Meropenem	>2	R	>2	R
Quacillin + 2 NaCl	>4	NI	2	NI	>4	NI	Quacillin + 2 NaCl	>4	NI	>4	NI
Penicillin	>8	NI	0.25	S	2	S	Penicillin	>8	NI	>8	R
Rifampin	>2	NI	<=1	NI	<=1	S	Rifampin	>2	NI	<=1	S
Ticarcillin	>64	R	<=8	NI	32	NI	Ticarcillin	>64	R	>64	NI
Ticarcillin/Clavulanic Acid	32	I	<=8	NI	32	NI	Ticarcillin/Clavulanic Acid	32	I	>64	NI
Trimethoprim/Sulfamethoxazole	<=0.5	S	>2	R	<=0.5	R	Trimethoprim/Sulfamethoxazole	>2	R	>2	R

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- # BOUDREAU
- ▶ Treatment
 - ▶ Debridement
 - ▶ Systemic antibiotics - many
 - ▶ Chloramphenicol and amoxicillin/clavulanic acid
 - ▶ Chloramphenicol and doxycycline
 - ▶ Selective biocide – none
 - ▶ Antibiofilm agent – poloxamer 407
 - ▶ Topical antibiotics
 - ▶ Vancomycin 20 mg/mL

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BOUDREAUX




- ▶ Hail Mary!
- ▶ No debridement
- ▶ 10 ml inserted into pocket
- ▶ Purulent drainage resolved in 24 hours
- ▶ No recurrence at 10 days

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Treatment of multi-drug resistant infections using poloxamer-407/antibiotic compounds vs. conventional management in veterinary patients
 Elizabeth A. Swanson¹, Gallaher HM¹, Rochat MC², Hixon LP¹

- ▶ P407 gel as delivery and antibiofilm agent
- ▶ Mean tx duration prior to gel: 26 days (6-68 days)
- ▶ Application frequency 2-7 days (q2-3 days)
- ▶ Mean gel treatment length: 10 days (1-17 days)
 - ▶ Overall duration: Mean 29 days
- ▶ Mean traditional treatment length: 46 days
- ▶ Time to complete healing for wounds treated with poloxamer gel-antibiotic compounds was significantly shorter than for those treated conventionally

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JAVMA 

Amikacin in 30% poloxamer 407 is a versatile local therapy with method of application and outcome documented in 29 dogs

Marjé Risselada, DVM, PhD, DECVS, DACVSI¹; Katie E. Spierl, DVM, Sui Young Kim, DVM, MS, DACVSI
 2024;262:1-7

Serum amikacin concentrations in dogs with naturally occurring open wounds treated with topical amikacin in carboxymethylcellulose hydrogel

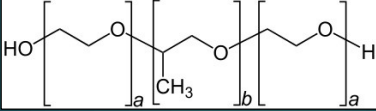

Zong H. Peng DVM¹ | Vanna M. Dickerson DVM, MS, DACVSI (Small Animal)¹ | Virginia R. Fajt DVM, PhD² | Emily N. Gould DVM, MS, DACVIM, PhD³ | Madeline Droog PharmD⁴ | Kelley M. Thieman Mankin DVM, MS, DACVSI (Small Animal)¹

Vet Surg 2025;54:453-460

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POLOXAMER 407 GEL

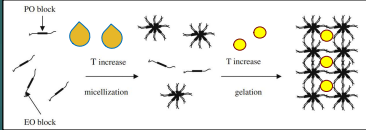
- ▶ Thermoreversible hydrogel
- ▶ Triblock copolymer (PEO and PPO)
 - (Talasaz AHH, et al. *J Appl Polym Sci* 2008; Dumortier G, et al. *Pharm Res* 2006)

40

POLOXAMER 407 GEL

- ▶ Poloxamer 407 gel
 - ▶ Micelles aggregate into cubes with increasing temperature



- ▶ Facilitates drug carriage

Dumortier G, et al. *Pharm Res* 2006

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POLOXAMER 407 GEL

- ▶ Increased wound contraction and faster closure in rats
 - (Du L, et al. *Wound Rep Reg* 2012; Dumortier JL, et al. *Pharm Res* 2006)
 - ▶ ↑VEGF and TGF-β1
 - ▶ Improved granulation tissue
- ▶ High concentrations
 - (Veyries ML, et al. *Antimicrob Agents Chemother* 2000)
 - ▶ Interferes with protein and bacterial adhesion
 - ▶ Enhances uptake of antibiotics and chemotherapeutics

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P407/ANTIBIOTIC GEL PILOT STUDY


- ▶ 2 Treatment Groups:
 - ▶ 25% Poloxamer Gel
 - ▶ 25% Poloxamer Gel + 20 mg/mL Vancomycin



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P407/ANTIBIOTIC GEL PILOT STUDY

- ▶ Treatment Durations
 - ▶ 4,8,12,16,20,24,36, and 48 hours
 - ▶ 3 coupons per time point in each group

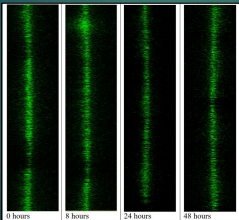


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P407/ANTIBIOTIC GEL PILOT STUDY

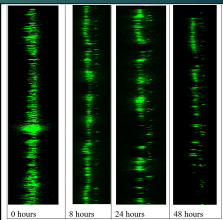
Results

Poloxamer-407 Gel



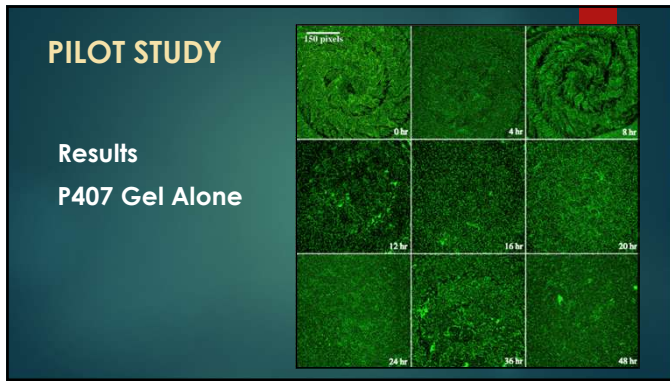
0 hours 8 hours 24 hours 48 hours

Poloxamer-407 Gel
+ 20 mg/mL Vancomycin

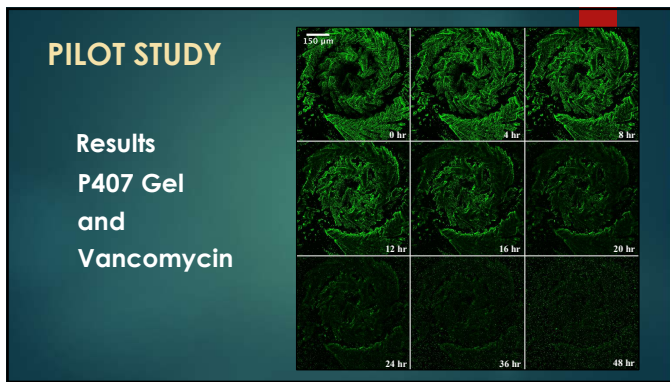


0 hours 8 hours 24 hours 48 hours

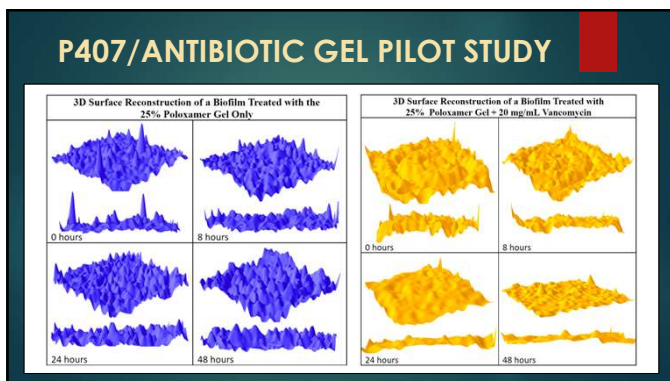
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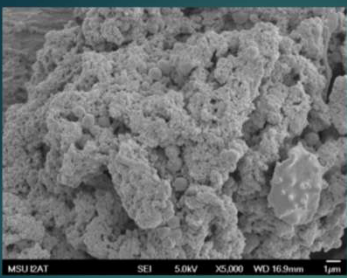


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P407 GEL TAKEAWAYS

- ▶ Application
 - ▶ Every 3 days
 - ▶ Or at time of bandage change
 - ▶ Can combine with other bandage materials
 - ▶ Silver alginate
 - ▶ Hydrocolloids w/ silver
 - ▶ Kerecis/Tilapia skin

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THANK YOU!

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