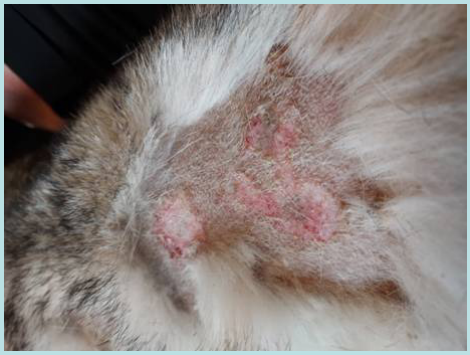
Bacterial Pyoderma and Resistance



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Appearance of Cutaneous Bacterial Infections

Clasification based on depth of infection:

Implications with respect to therapy.

1. ***Surface Bacterial Infections***

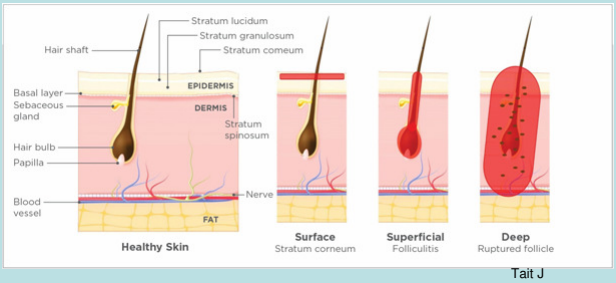
   Surface layers of epidermis only

2. ***Superficial Pyoderma***

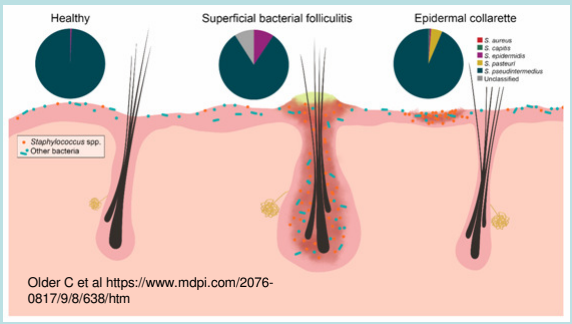
   Epidermis and hair follicles

3. ***Deep Pyoderma***

   Dermis +/- subcutis



Tait J https://todaysveterinarynurse.com/dermatology/pyoderma-in-the-dog/



Older C et al https://www.mdpi.com/2076-0817/9/8/638/htm

Principal Pathogens in Veterinary Dermatology

- Staphylococcus pseudintermedius (formerly intermedius)
- Coagulase –ve staph. Schleiferi and coagulans. If isolated in heavy growth from appropriate sample
- S aureus (consider ID method)
- Pseudomonas, Acinobacter (occasional)
- E coli and Enterococcus mostly passengers

S pseudintermedius is not a primary pathogen

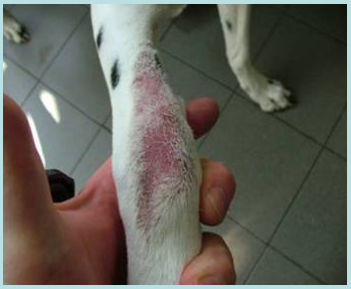
Effectively all cases are secondary to a loss of local immunity…see later

S. pseudintermedius is more like a sleeper terrorist

Surface Bacterial Infections

Pyotraumatic dermatitis

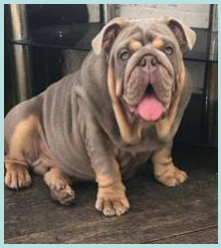
- **"Hot Spots"**
- **Often secondary to allergy**
- **Intensely pruritic**
- **Colonization and multiplication of bacteria on skin surface**



Surface Bacterial Infections

Intertrigo (fold dermatitis)

- *Anatomical disease*
- *Moist, warm and humid environment with friction predisposes infection*
- *Breed or obesity related*
- *Lip fold, vulval fold, face fold etc.*
- *Erythema, erosions and a foul smelling exudate*



Surface Bacterial Infections

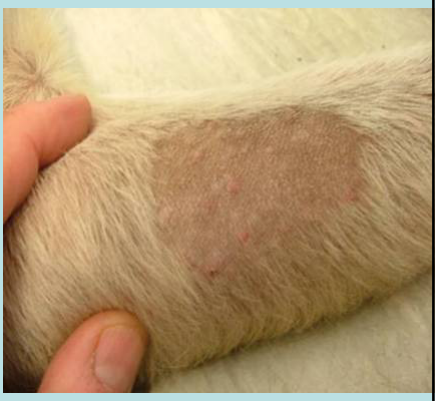
Treatment of Pyotraumatic Dermatitis and Intertrigo (fold dermatitis)

- *Identify and treat the primary cause*
- *Topical treatment sufficient in some cases 7-10 days of systemic antibiotics normally sufficient*
- *Antibiotic withhold strategy*
- *Short term corticosteroids may shorten course*
- *Rapid resolution expected if diagnosis correct*

Superficial Pyoderma

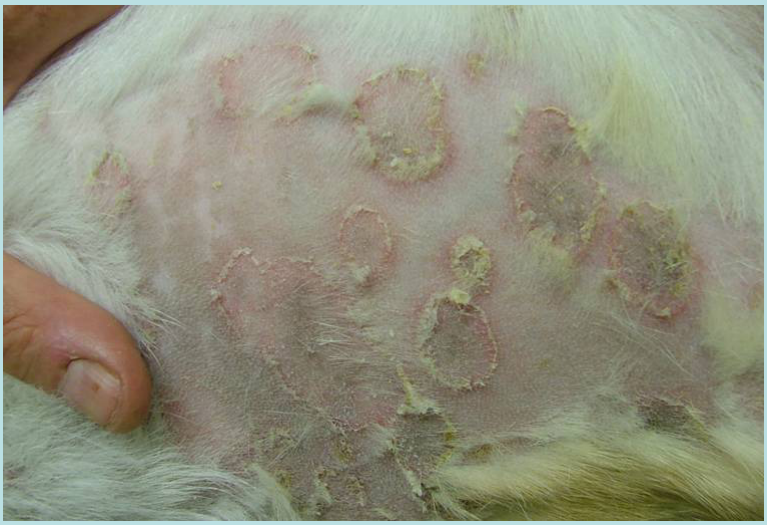
Folliculitis = Infection of hair follicle

- **Primary lesion is papule or pustule. These may rupture and expand as epidermal collarette.**
- **May break out and form furuncle (deep pyoderma).**
- **Usually pruritic**



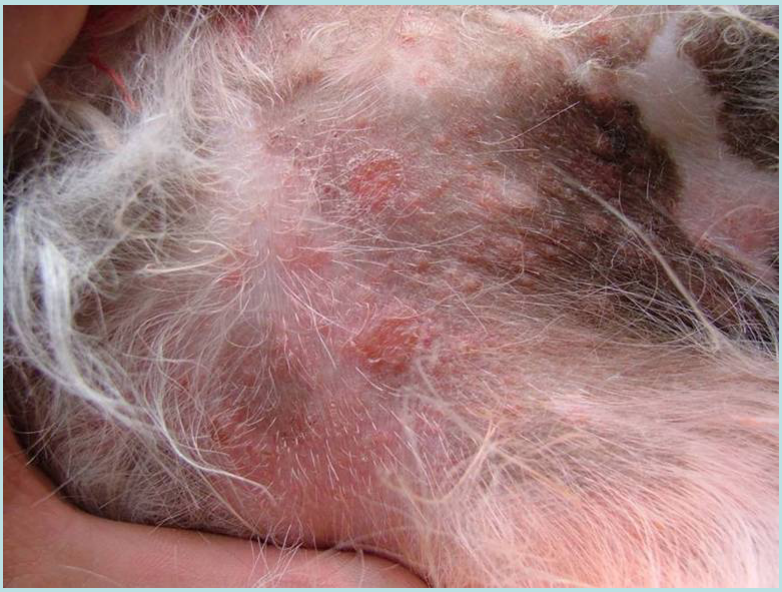
Superficial Pyoderma

Classical epidermal collarettes



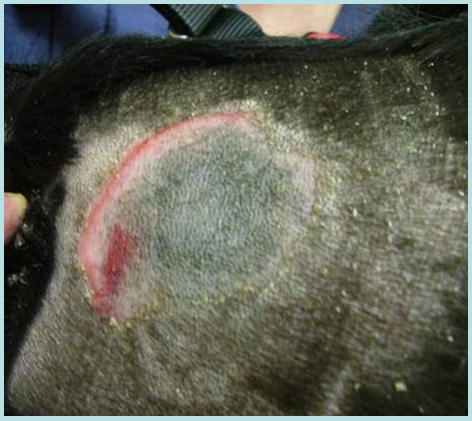
Superficial Pyoderma

Papules and collarettes - Impetigo



Superficial Pyoderma

Long haired breed

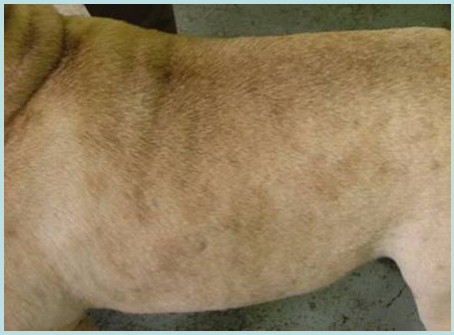


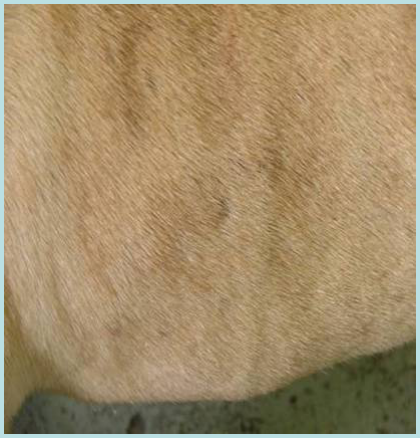
Collarette formation +/- scale.

•May be hidden by the coat.

Superficial Pyoderma

Folliculitis in a short haired breed





- Moth eaten appearance
- Small follicular papules

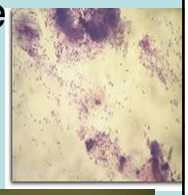
Superficial Pyoderma

Mucocutaneous Pyoderma

- ***Erosions crusts and fissures involving the lips and other mucocutaneous junctions (nose, eyelids, vulva, prepuce and anus)***
- ***Any breed but German Shepherds predisposed***
- ***DDX immune mediated diseases***

Superficial Pyoderma

Bacterial Overgrowth Syndrome



Overgrowth of Staphylococcus pseudintermedius

Looks like "yeast"

- Marked pruritus
- Greasy seborrhoea with offensive odour,
- Skin often thickened and hyperpigmented
- NO papules, pustules, epidermal collarettes or crusts
- Vast no's of cocci, few leukocytes

Deep Pyoderma

- Extension of superficial pyoderma into dermis => subcutis
- Direct inoculation into dermis.

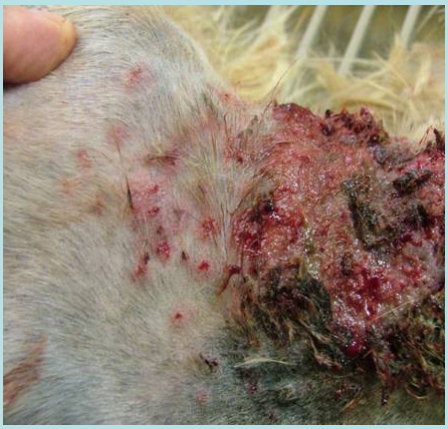
Signs:

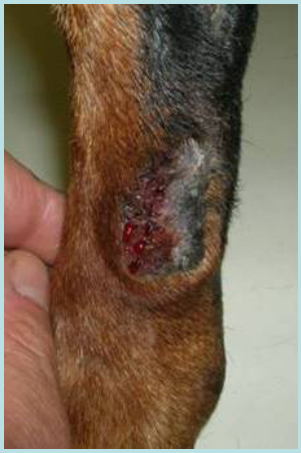
- ***Draining sinus's***
- ***Ulcers***
- ***Haemorrhagic bullae***
- ***Possible systemic signs and or cellulitis***
- ***Free keratin ⇨ foreign body reaction and nidus***

CAUTION

May accompany neoplasia or auto-immune disease
Beware foreign bodies fungi and atypical bacteria

Deep Pyoderma

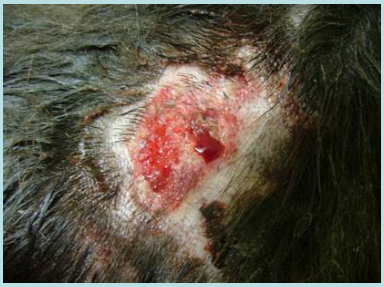




Deep pyoderma complicating a lick granuloma

Progression to deep pyoderma secondary to demodicosis.
Papule-> pustule-> furuncle-> ulcer

Deep Pyoderma



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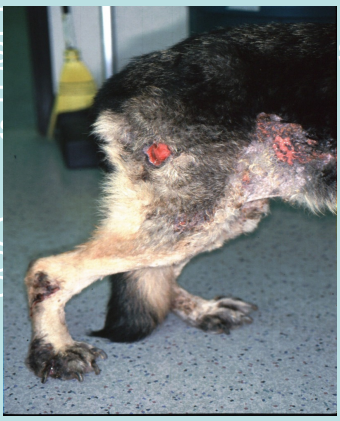
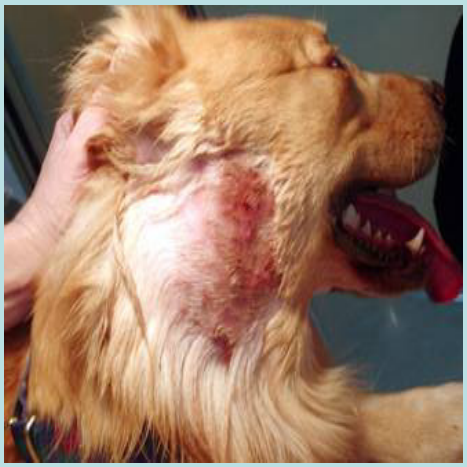
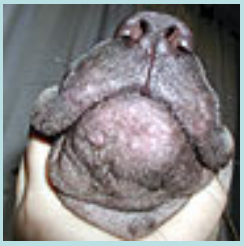


Deep Pyoderma



Pyotraumatic furunculosis
(Golden Retriever, Rotweiler)
DEEP PYODERMA
Pruritic and not a hot-spot !

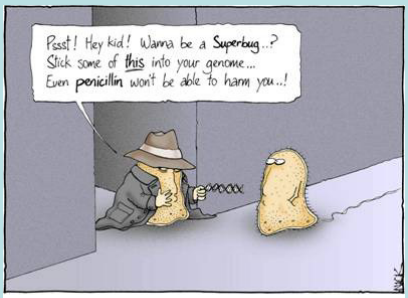


Canine Acne
Deep pyoderma

Transmission of Resistance

- Horizontal transfer via Mec-A gene coding for SCC-MEC chromosomal cassette
  - Codes for low affinity PBP-2a
  - Can carry other resistance genes
- Mutation
- Selection for resistance
- with antibiotics

- MRSP vs MDR-SP



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Rethinking the MIC

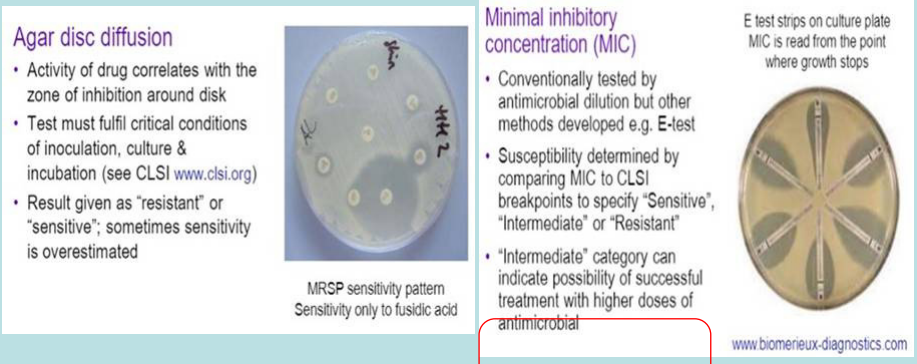
MIC - minimum inhibitory concentration

- Lowest concentration inhibiting growth following a standard inoculum $1x10^5$ cfu/ml
- Breakpoints of resistant, intermediate or susceptible based on MIC and tissue levels achieved
- Current basis of reporting

MPC - mutant prevention concentration

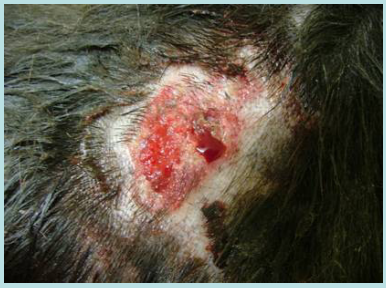
- Lowest drug concentration required to block the growth of the least susceptible cell in high density bacterial populations $1x10^9$ cfu/ml
- May be much higher than MIC
- **MSW-mutant selection window** lies between MIC and MPC

Culture techniques



- Breakpoint = concentrations **at which bacteria are susceptible to successful treatment with an antibiotic**.
- Resistance is increasing, long-time established breakpoints may underestimate antibiotic dosage levels, leading to undertreatment
- Minimum zone size defined to reflect the breakpoint. Sensitive = MIC>breakpoint. Select antibiotic with best BP/MIC ratio

Multiresistant infections:



- NOT deducible from clinical signs
- Increased likelihood with
  - Visits to vet clinics
  - Chronicity
  - Antibiotic use
- May be no registered systemic drug available

Bella Swab, Gel Skin

11/2/22

Staph. pseudintermedius Heavy growth

E. coli Heavy growth.

Staph. pseudintermedius E. coli Amox/Clav R R Amoxycillin R R Cefovecin R **S** Cephalexin R R Clindamycin **S** R Doxycycline **S S** Enrofloxacin **S S** Gentamicin **S S** Marbofloxacin **S S** Tri/Sulpha **S** R

7/5/22

Staph. pseudintermedius Amox/Clav R Amoxycillin R Cefovecin R Cephalexin R Chloramphenicol R Florfenicol S Clindamycin R Doxycycline R Enrofloxacin R Gentamicin R Marbofloxacin R Pradofloxacin R Tri/Sulpha R Fosfomycin S **Fusidic Acid S Rifampicin S**

Principals of treatment

Based on multiple consensus statements

- Could **topical treatment alone** be effective?
- **Always and without exception combine systemic antibiotics with topical treatment**
- Choose an **antibiotic based on culture and at the highest dose** safely possible to reduce the MSW
- Treat for **adequate duration** and review by cytology
  - Superficial pyoderma 7-10 (7!) days beyond visible cure (~ 3 weeks)
  - Deep Pyoderma 3-4 weeks beyond visible cure (~ 6-12 weeks)
- **Maintain** topical prevention if the **underlying cause** has not been identified and resolved (Atopic!)

Underlying cause of pyoderma needs identification:

Staphylococcal pyoderma is SECONDARY to a loss of local and/or systemic immunity:

- **Barrier defects associated with allergy**
- **Immunosuppressive drugs** (CORTICOSTEROIDS, cyclosporine, oclacitinib)
- **Endocrine disorders** Hypothyroid, Hyper A, diabetes
- FIV, FeLV, genetic (eg. German Shepherd), demodicosis
- **Idiopathic**

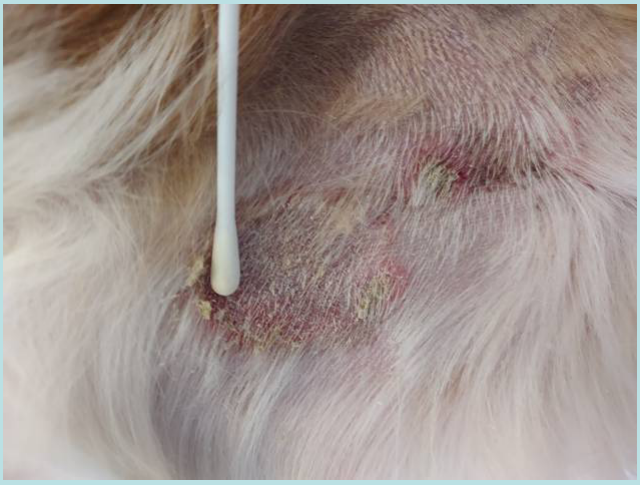
Always look diligently for the underlying causes of infection and control or eliminate these. When this is done effectively, it may even allow spontaneous recovery.

How to culture? When to culture?

- **More a question of when not to culture rather than when to culture**:
  - History of previous antibiotic use
  - Deep pyoderma
  - Generalized superficial pyoderma
  - Failure of first-line antibiotic

  How:
  - Superficial pyoderma. Pustule prick or multiple collarettes with a dry swab then put in the transport medium
  - Deep pyoderma. Draining sinuses or needle aspiration
  - Must go to a laboratory that is prepared to test for third line antibiotics.

Culturing an epidermal collarette



Systemic antibiotic prescribing cascade – 1st, 2nd 3rd tier antimicrobials

First line antibiotics:

•Cephalexin 25-35,mg/kg bid

•Clindamycin 10-12mg/kg bid with food (oesophagitis) 70%

Should we use broad spectrum drugs as first line treatment except in cases of intolerance or inability to dose???

•Amoxiclav 15-20mg/kg bid

•Cefovecin (Convenia©) Gen 3

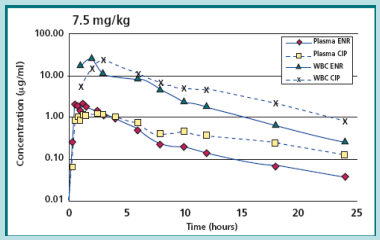
Second line antibiotics, not to be used without culture:

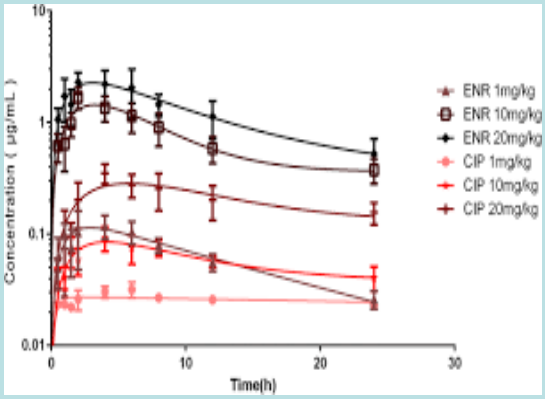
- **Doxycycline/minocycline** 5mg/kg bid. Immunomodulatory. Oesophagitis with HCl
- **Sulpha trimethoprim** 480 tab 1/20kg BID. Adverse reactions?
- **Fluoroquinolones** . Empty stomach. Concentration dependent. Use highest dose economically possible once daily. Use last
- **Azythromycin** 10mg/kg daily. Intracellular accumulation. Macrolide (clindamycin)

Enrofloxacin kinetics

Converted to active ciprofloxacin

Boechh A et al, 1999





Third line antibiotics. Not to be used unless no SECOND lines that will work:

- **Pradofloxacin** Empty stomach concentration dependent. Use highest dose economically possible
- **Rifampicin**. Liver and bone marrow 5mg/kg bid. Blood monitor 2 weekly.
- **Systemic fusidic acid** 25-30mg/kg bid
- Combination… ↓ Fusidic acid
- Combination therapy when dealing with single mutation potential?

First line topical treatment:

- Sometimes topical is enough. Surface pyoderma hotspots. Some cases of superficial pyoderma. Allowing client pick up after 3 to 5 days.
- ·Chlorhexidine. Pyohex shampoo and lotion. Think do you need a shampoo? Malaseb less inappropriate for bacterial pyoderma due to strong surfactants. Residual action
- 2.5 % SOLUTION chlorhexidine dab on . Stability of made up?????
- BLEACH eczema bath protocol -> Pyohex/resichlor lotion
- 2% acetic acid (1 part white/apple cider vinegar : 2 parts water
- Silver sulphadiazine FLAMAZINE. Potential chlorhexidine synergy

Bleach – what we do and don't know

- Active ingredient sodium hypochlorite
- Varying concentrations in differing brands – 4.2% White King
- Degrades to sodium chlorate and may lose 50% efficacy by expiry date
- NaOH as stabilizer +/- perfumes, suds suppressors
- Uses for 200 years as a disinfectant
- Vast range of concentrations advocated 0.005% - 0.2% !
- **In vitro studies suggest effects may be beyond just bacterial suppression**
- High quality studies lacking
- **Consensus in humans** *Bleach bath improves clinical symptoms of AD and restores surface microbiome by eradicating bacteria, most notably Staphylococcus aureus. Many studies have noted that this antimicrobial effect has reduced the need for topical corticosteroids or topical antibiotics. In addition, bleach seems to have strong anti-inflammatory and antipruritogenic effects*.
- RCH -12-15 mL of plain White King / 10 litres of water = final bleach concentration of 0.005%) + 1-2 capfuls bath oil

Second line topical therapy:

- Chlorhexidine failures recognised
  - Resistance , biofilm or organic matter interference
- Topical fucidic acid (Fucidin human)
- Mupirocin topical bid. Should we use?
- Topical gentamycin

Reduced susceptibility to chlorhexidine in staphylococci: is it increasing and does it matter?
Carolyne Horner, Damien Mawer, Mark Wilcox
Journal of Antimicrobial Chemotherapy, Volume 67, Issue 11, November 2012, Pages 2547–2559,
https://doi.org/10.1093/jac/dks284https://academic.oup.com/jac/article/67/11/2547/711827

Autogenous Vaccines

- Evidence of efficacy in reducing incidence of re-occurrences
- Good personal results in some/most? patients
- Local reactions

- Tréidlia Biovet Pty Ltd
- PO Box 6563 Seven Hills NSW 2147
- P: 02 9674 1488 F: 02 9674 2488
- info@treidlia.com.au

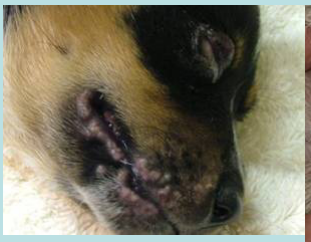
Stopping the itch of infection

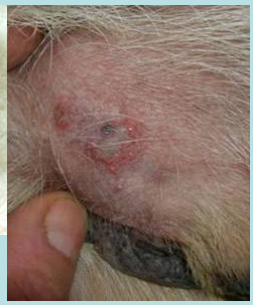
- In many cases, pruritus will dramatically reduce when infection controlled
- Apoquel (Oclacitinib) reduces local immunity
- Apoquel and Cytopoint act on the JAK-STAT pathway and may not be effective
- Prednisolone beyond 3 days is illogical in superficial or deep pyoderma.
- Long acting dex even worse

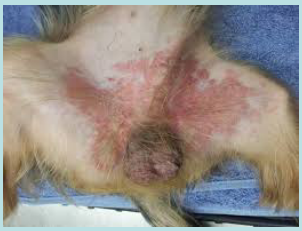
Staph infections are the result of a loss of local immunity

Treatment failures - why

- Compliance
- Inadequate dose
- Inadequate duration
- Resistance
- Development of resistance
- Failure to use topicals
- Failure control underlying cause
- Not a bacterial infection







Protocols to consider

- Reduce antibiotic use
- Simple stuff
  - Wash Hands
  - Clean tables
  - Disinfect clippers
- Barrier nursing
- De-colonisation ???

Recommendations for approaches to methicillin-resistant staphylococcal infections of small animals: diagnosis, therapeutic considerations and preventative measures. Clinical Consensus Guidelines of the World Association for Veterinary Dermatology

Vet Dermatology 2017;28: 304–e69

https://onlinelibrary.wiley.com/doi/epdf/10.1111/vde.12444

Questions, discussion

Thank you
Rob