

Updates on Treatment and Control of Bovine Mastitis

Abdul Samad

9969371999

drasamad11@gmail.com

Lecture Plan

- What is microbiome?
- How it is studied?
- Udder microbiome and significance
- Microbiome and current mastitis control measures
- New Paradigm
 - Barrier Technology
 - Post-milking Barridip
 - Green-T-Sealant
 - Leaky Udder Management

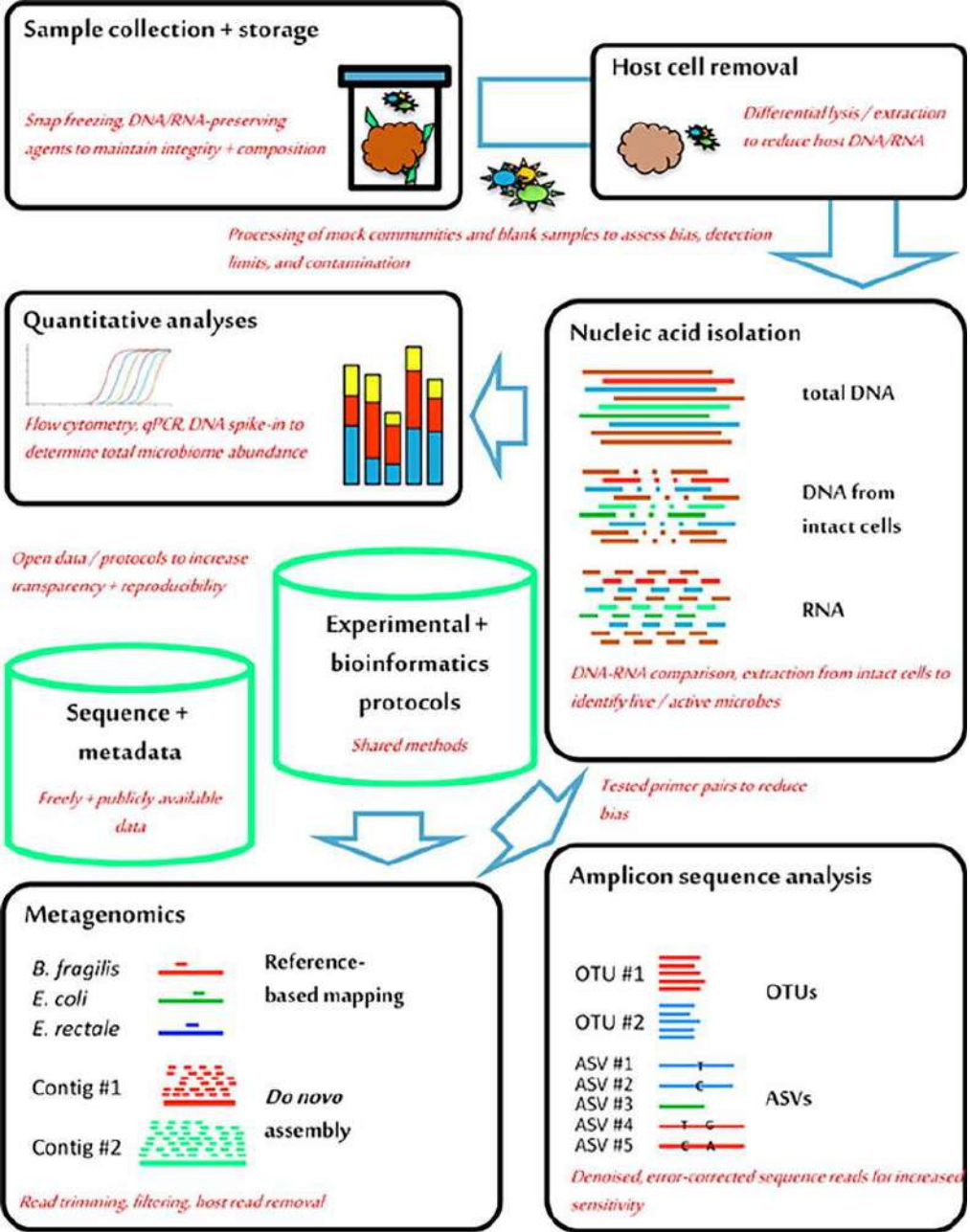
Microbiome

- Large and diverse populations of bacteria, viruses, and fungi occupy almost every surface of the human body / animal body
- It is estimated that there are nearly 30 trillion bacterial cells living in or on each human
- That is about one bacterium for every cell in the human body. These microbes are collectively known as the microbiome.
- Exposure to microbes first occurs during birth and is later influenced by environmental factors, such as diet and exposure to antibiotics.
- Due to differences in environment, diet, and behavior, the specific types of microbes that make up the microbiome can vary greatly between individuals
- It is thought that every animal's microbiome is slightly different.
- In fact, work is underway to investigate the use of microbiomes to identify individuals, much like fingerprints
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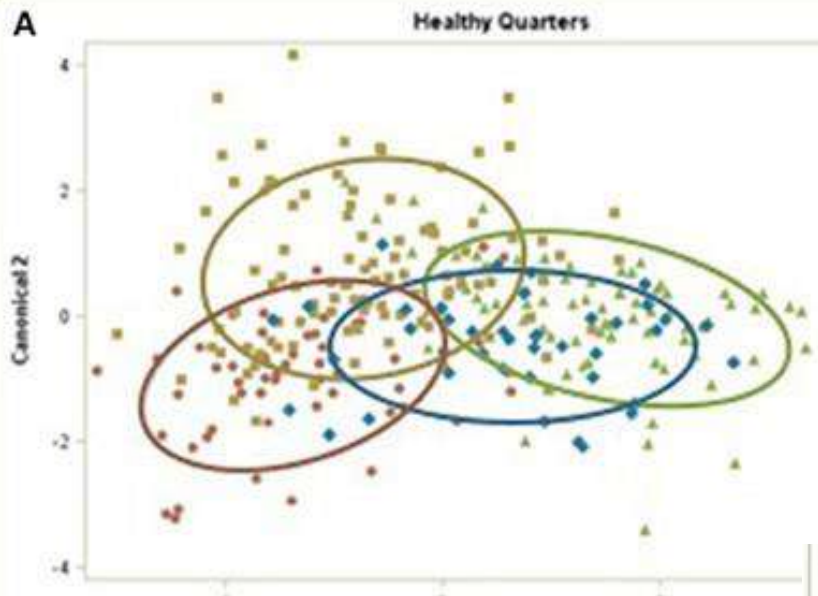
Microbiome and Health

- Scientists are just beginning to understand the link between the human microbiome and cancer development. Initially, epidemiological (population) studies suggested certain microbes played a role in cancer.
- These studies laid the ground work for laboratory experiments, which are ongoing. While these experiments have improved our understanding of microbes in human health and disease, there is still much more to uncover.
- *Helicobacter pylori* (*H. pylori*- gastric cancer
- The skin microbiome is diverse and differs by anatomical location. Experiments done in mice suggest the microbiome can have either protective or harmful roles in cancer development.\
- Mice treated with antibiotics (to kill their microbiome) have an increased risk of melanoma skin cancer and shorter average survival times.

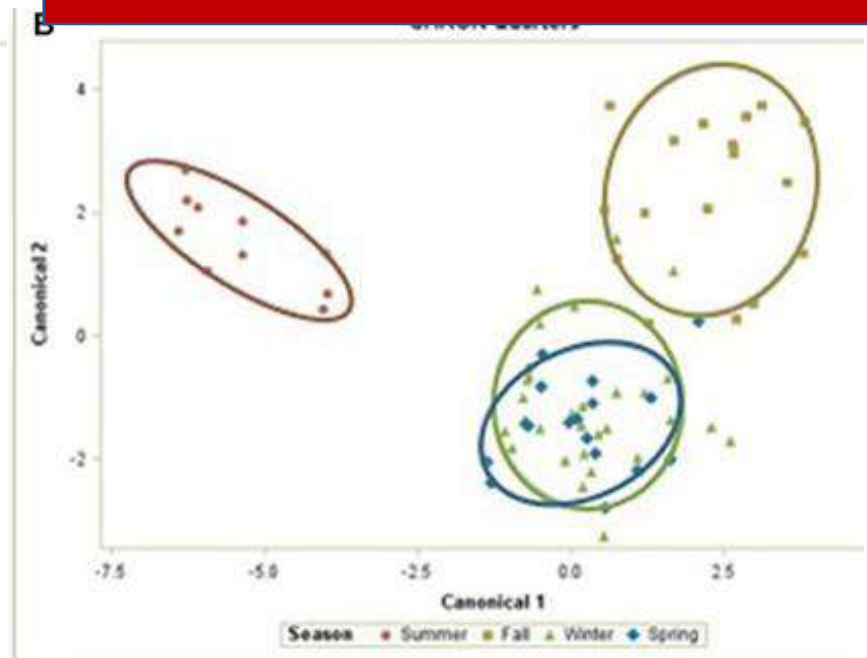
Metataxonomic Sequencing
 OUT- Operational Taxonomic Unit
 ASVs- Amplicon Sequence Variants



With advent of high throughput bacteria identification systems large data on microbiome is now available. Microbiota play important role in local immunity and overall health



When antibiotics and germicidal substances are used these not only kill pathogens but also kill useful microbiota



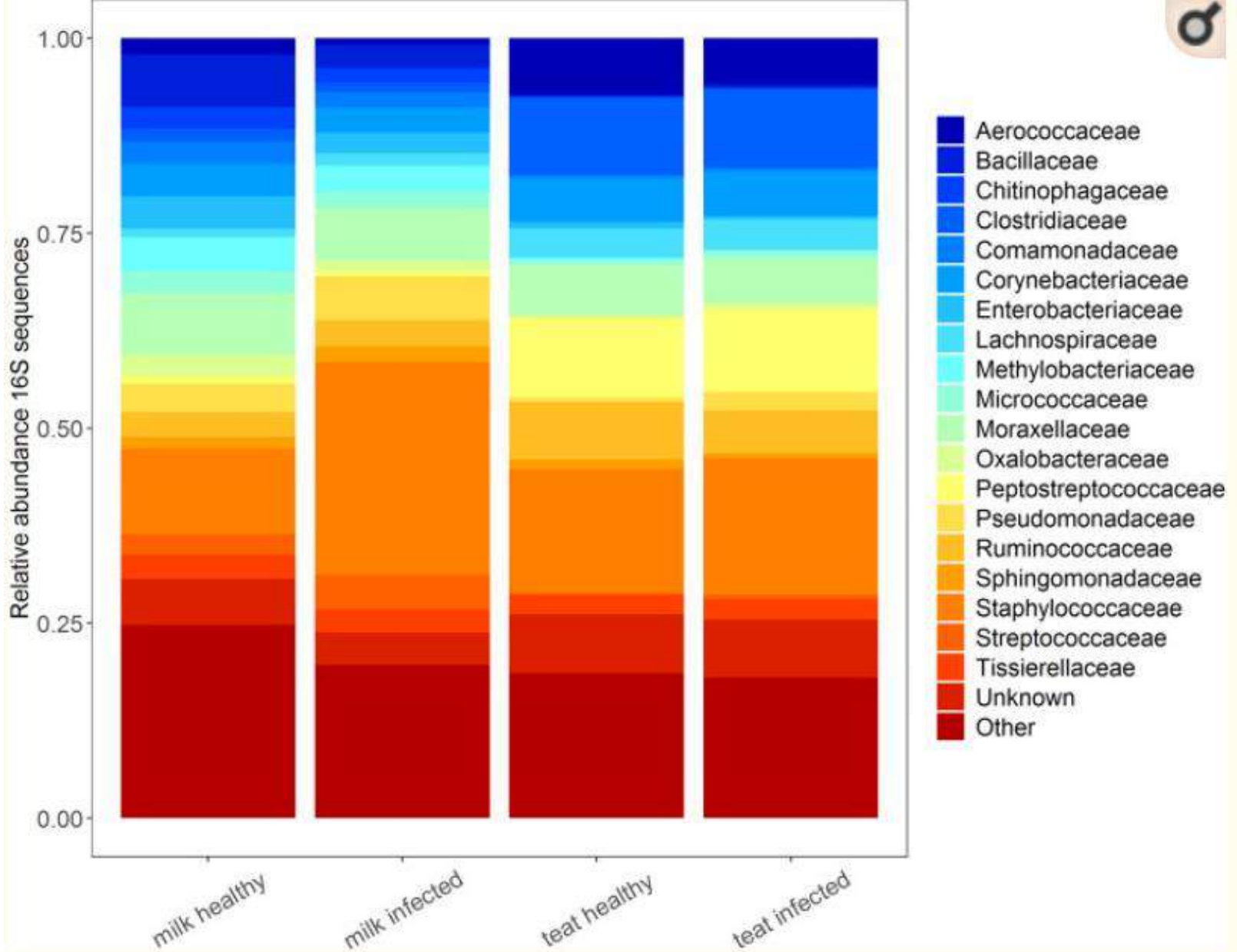


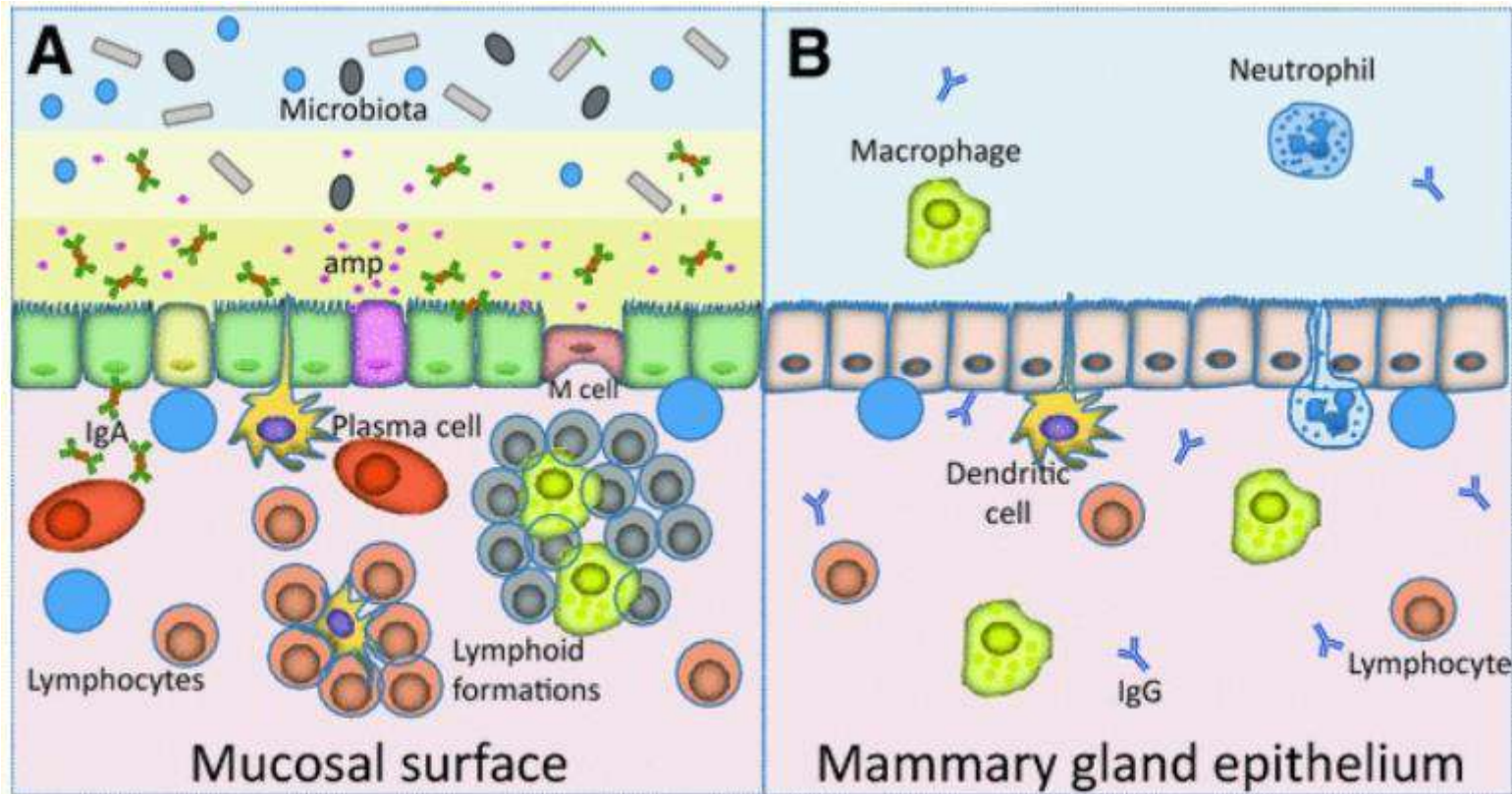
Fig 5

Twenty most relatively abundant categories of 16S rRNA gene sequence OTUs as arranged by bacterial family in each habitat state.

Mammary Microbiota Essential Defence

- Hub species and Foundation Taxa that are associated with the inflammatory status of the MG and/or future incidences of clinical mastitis.
- Udder homeostasis.
- Commensal microbiota inhabiting teat apex, teat canal, and milk have the potential to govern susceptibility to IMI by mastitis pathogens via several mechanisms.
- For instance, certain non-*aureus* staphylococci (NAS) and *Corynebacterium* species colonizing the teat apices and teat canals of dairy cows have the ability to produce a wide range of bacteriocins.
- Foundation species increase the diversity of the ecosystem and make it more resilient against invasion by exogenous species
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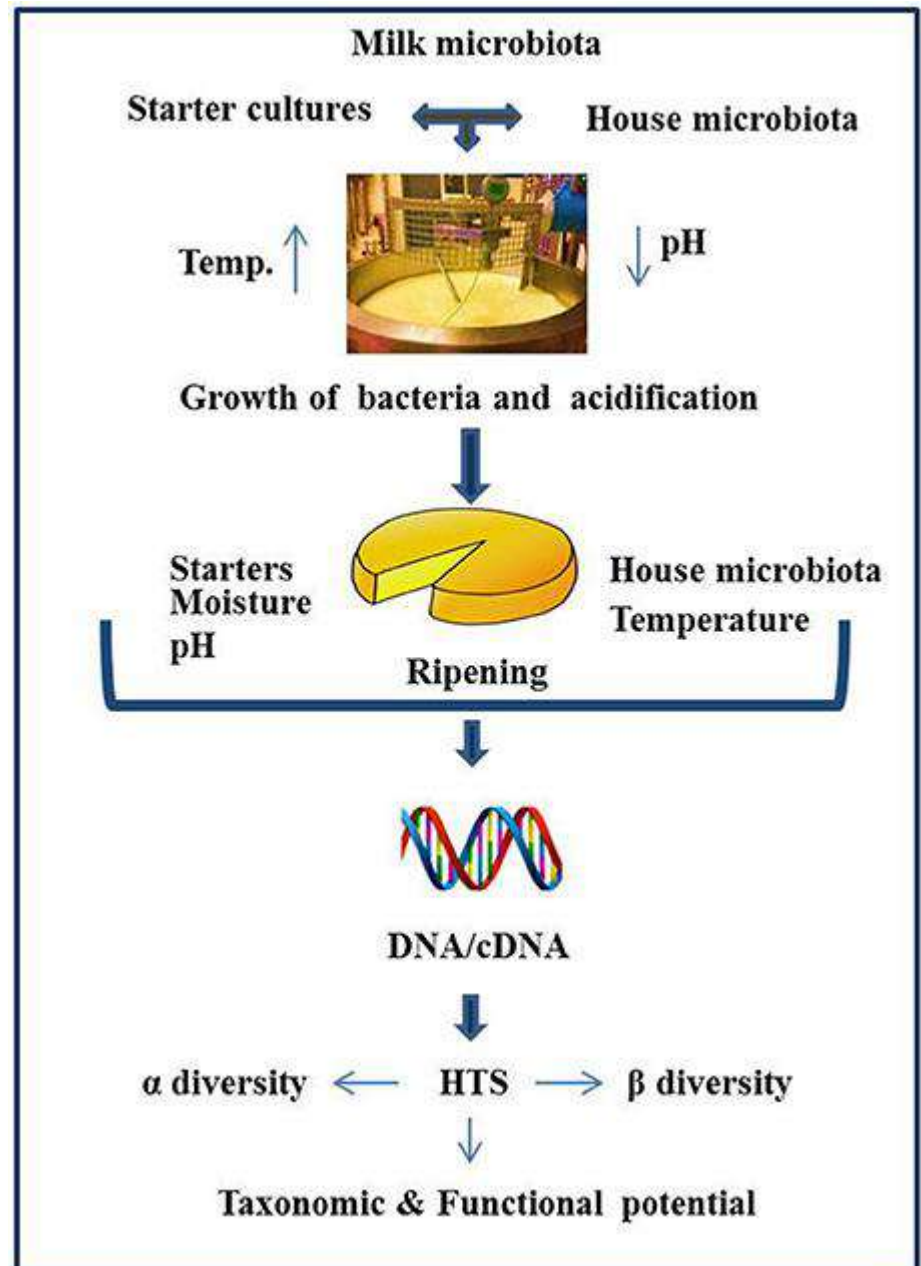
Upheaval in Traditional Veterinary Clinicians



Cheese ripening, shelf-life and Taste depends on the house microbiome

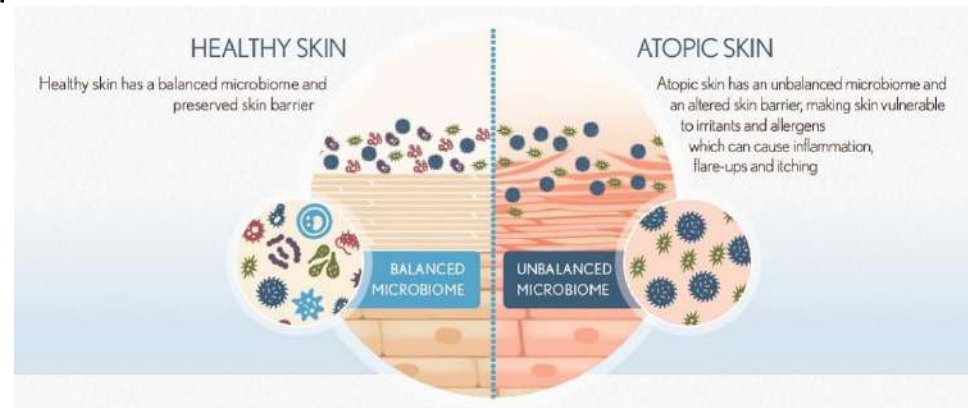
Teat canal / teat sphincter and teat skin microbes have been found to be part of the milk and cheese

Certain Taxa of these decide the good character of cheese
Dahi / Shrikhand / Paneer



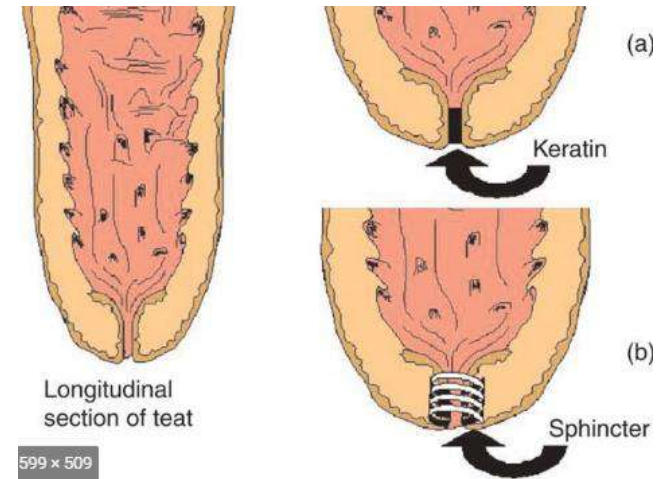
When microbiota become pathogen?

- When these get dislocated from natural predilection site
- When ratio between good and bad bacteria is tilted towards bad
- Teat skin bacteria – teat canal
- Teat canal bacteria – Teat cistern and alveoli
- Skin bacteria entering in vagina and cervix
- Vaginal bacteria – uterus
- Upper respiratory bacteria entering lungs



Novel Technologies: Prevent Invasion of Pathogens

- Teat Sphincter- First line of defence to pathogens
- Post-milking sphincter relaxation – If animals do not feed after milking
- Dry Period - one week after drying off and two weeks before calving
- Lung-Uterus-Udder route of bacterial metastasis

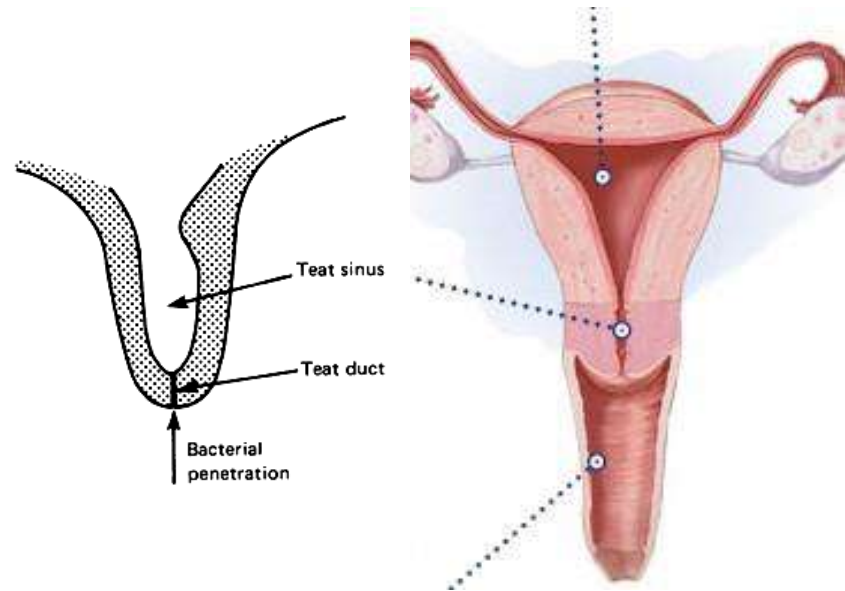


Novel Barrier Technology

- **Antibiotics, antibacterial and chemicals alter microbiota with long term consequences**
- **Intramammary formulations**
- **Teat Dip**
- **Dry Cow Therapy**
- **Intra-uterine / Intravaginal**
- **What is the solution?**
- **Since infection occurs when bacteria enter the body through natural orifices a better option will be:**
- **Put a chemical barrier to entry of bacteria without changing the micro-environment**

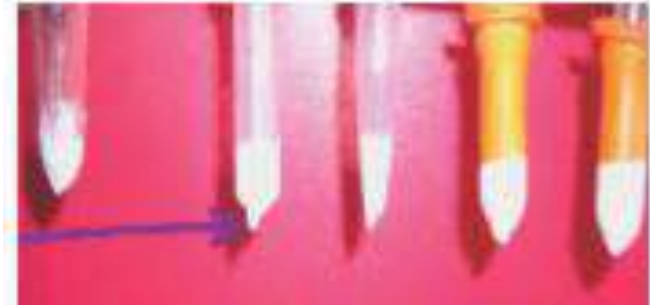
What is Barrier Technology?

- We have developed polymer-based formulation that after application forms a chemical film that acts as physical barrier to entry of bacteria



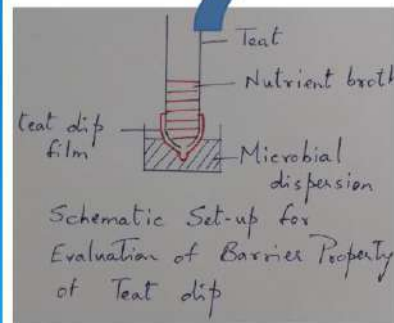
Barrier to entry of bacteria

- Polymer matrix that forms a film pore size is less than 0.2 micron, permit aeration and offer physical barrier to micro-organisms
- We use different classes of polymers – (a) Ion-dependent polymers, (b) temperature-dependent sol-gel (c) pH-dependent polymers and (d) neutral-polymers
- The platform technology can be used to develop numerous formulations
- We use polymers derived from natural sources (no synthetic) that are biodegradable, available in plenty and inexpensive – keep cost low
- Simple formulation technologies- no major or intricate infrastructure is needed to manufacture



Dip the artificial teats
For 24 Hrs at 37^o

After 24 Hrs



Broth in
Nutrient
Agar Plate



Baridip- Teat Dip

- **Baridip** is a novel aqueous product based on ion-dependent polymerization.
- **Germicidal teat dip destroy good bacteria required for cheese flavour and shelf-life**
- Desired features:
 - Forms barrier film instantly
 - The film formed is reinforced film so that it is resilient for breaking
 - Water-soluble constituent but once the film is formed it is hydrophobic hence no effect even when animal sits on wet floor
 - Pore size less than 0.2 micron but allows aeration
 - Easy to come out with little agitation at the time of milking
 - **No antibacterial chemicals added – Green**
 - **No chemical residues, the polymers we use are in fact edible polymers**
 - **Cost effective**

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Dipping Technique: Results

- -ve: negative control
- +ve: positive control
- ACC 1M: Accelerated stability samples, at 1 month time point.
Accelerated conditions: 40°C ± 2°C
75% RH ± 5%RH
- RT 1M: Room temperature stability samples, at 1 month time point.



Results:
No growth was observed in any of the samples.

Green-T-Seal- Barrier-type Dry Cow Therapy

- **Earlier Product:** We have earlier developed a product on sol-gel principle that is in solution form but gels at body temperature
- Antibiotic neomycin has been suspended in such a way that it is released for 45 days at therapeutic concentrations
- **New Product:** New formulation is based on the principle that teat cistern and canal has numerous good bacteria that will also be affected when antibacterial is used.
- Instead, the entry of bacteria through teat orifice can be prevented by a barrier seal.

Green-T-Seal- Radiographic evidence

- Formulation composed of naturally occurring polymers
- Two polymers to reinforce the matrix
- No antibiotic required, in vitro studies show that the seal formed is complete and does not allow entry of bacteria for a period of 45 days under experiment
- The seal remains for as long as it is not removed by stripping
- Cost effective



Leaky Udder

- Before parturition in few cows there is let down and milk starts flowing
- Common in high-yielding cows
- General principle- If milk is there in udder it should be removed
- Nearing calving – terminate pregnancy –Dexamthesaone 40-60 mg, termination 48-72 hours
- Withdraw feeding of concentrate
- Check body Condition Score – should not go beyond 3.75
- Calcium and phosphorous in feed – sphincter patency

Treatment of Clinical Cases

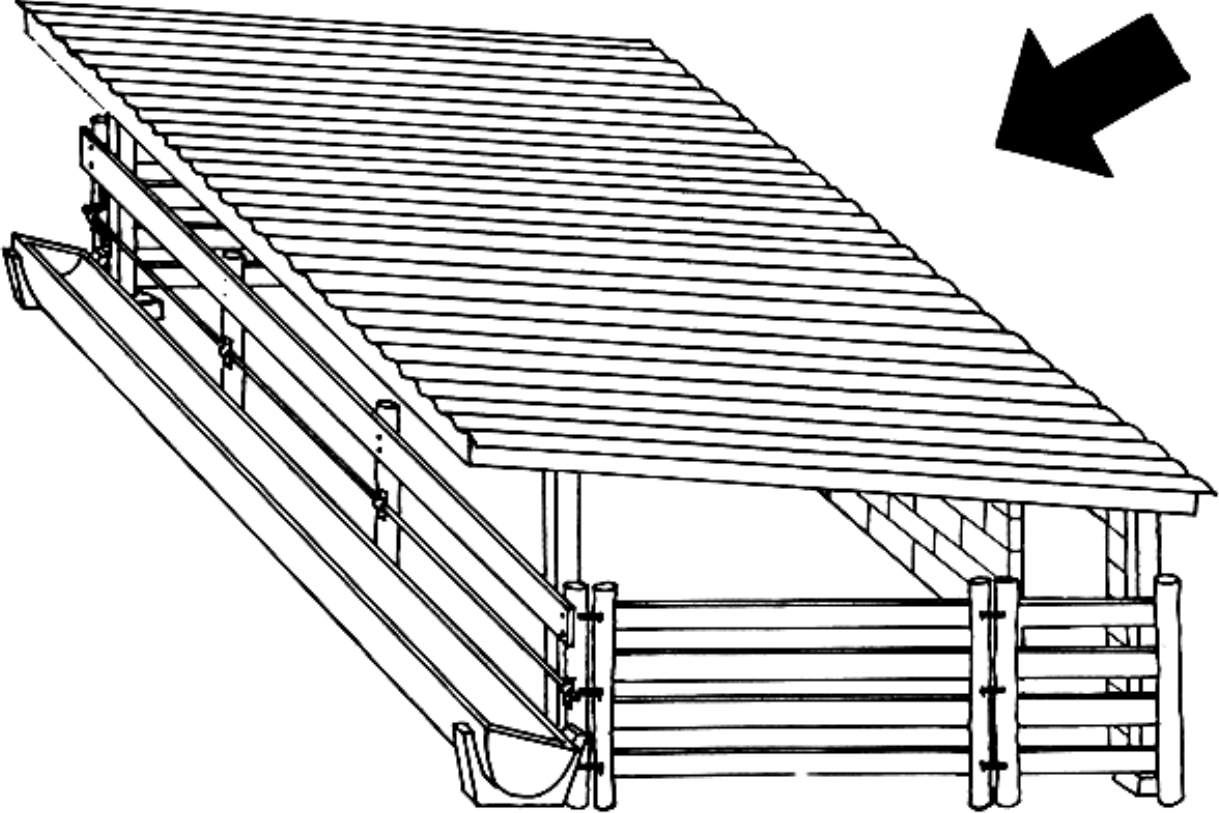
- Do not treat Sub-clinical mastitis cases
- All clinical cases should be promptly treated
- Reliance on antibiotic sensitivity in individual milk samples is questionable.
- It should be used to develop frontline and secondary therapeutic approaches
- Repeated removal of milk, use of oxytocin to empty udder helps a lot
- In acute mastitis cases cold fomentation and anti-inflammatory drugs

Animal Housing – Important to control udder infections

- This is a neglected area of concern in developing and under-developed countries
- Either farmers are forced to invest heavily or nothing is invested
- Cow's needs of housing are different – cow comfort important
- For udder health floor is important-
- Cement-concrete / brick being non-absorbent will not remain dry
- Humidity and liquified dung-breeding ground for bacteria



Correct Housing for High Rainfall Climate









•THANK YOU

**We are looking for partners to
commercialize these technologies
Interested pharmaceutical group can
contact us**

9969371999

drasamad11@gmail.com