***Notes for literature review and conclusion (May 2024)***

* Notes on literature review
  + Mastitis (as relates to dairy cattle housing and farm mgmt. practices)
  + Mastitis epidemiology (generally)
    - **“contagious” vs. “environmental” vs. “host-adapted”/”skin-associated”**
      * ***NAS in particular…***
      * Vanderhaeghen 2015 –
        + *“Mastitis pathogens are also differentiated by their main reservoirs and principal mode of transmission within a herd into contagious, environmental and (teat skin-associated) opportunistic pathogens”*
        + *“The principal source of* ***contagious*** *pathogens is assumed to be the cow or the infected udder, with spread among cows primarily through vectors, such as the milking machine, human hands or flies”*
        + ***“Environmental*** *pathogens are assumed to originate from the cow’s environment, contaminating teats mainly between milkings, especially under suboptimal housing conditions”*
        + *“****Skin-associated opportunists*** *are pathogens normally residing on the skin that only cause disease under conditions favoring colonization of the udder”*
        + Differentiates **ecology** from **epidemiology,** and the terms used around these concepts

Ecology

Habitats, distribution, population structures, movements and interactions of different species and strains of CNS

***“Host-adapted and environmental should only be considered in an ecological framework to refer to the habitat(s) of species or strains of CNS”***

Epidemiology

Considers CNS as pathogens ***in the context of IMI***

***“The terms ‘contagious’ and ‘opportunistic’ should be used when considering the epidemiology of CNS as pathogens causing IMI. Contagious cases of IMI occur in multiple animals on a farm, can be attributed to a single quarter/cow origin and are spread among cows by means of a vector (e.g. milking machine unit liners). Opportunistic cases of IMI can be attributed to a range of different origins and are not spread among animals.”***

* + - * Pyorla and Taponen 2009 –
        + *“Based on current knowledge, it is difficult to determine whether CNS species behave as* ***contagious*** *or* ***environmental*** *pathogens. Control measures against contagious mastitis pathogens, such as post-milking teat disinfection, reduce CNS infections in the herd”*
        + *“CNS have long been regarded as opportunistic skin microbiota that occasionally can cause mastitis (Devriese and Dekeyser, 1980). Control measures against contagious mastitis pathogens such as post-milking teat disinfection reduce CNS infections in the herd (Hogan et al., 1987). Discontinuation of teat dipping significantly increased prevalence of infections with C. bovis and CNS (Lam et al., 1997b). Some CNS isolated from mastitis may be opportunists from the environment, but in the authors’ opinion it is very likely that at least the main species infecting the bovine mammary gland are specifically adapted to the udder environment. Species of CNS may differ in this respect, but information is lacking.”*
      * De Buck 2021
        + *“…****environmental*** *or* ***host-adapted*** *pathogens. This also relates to their commensal nature and their level of* ***host adaptation*** *to the* ***skin, teat canal and/or udder****”*
        + *“Host adaptation relates to colonization and persistence of isolates as well as the level of inflammation caused. Adaptation can be quite specific, demonstrated by the fact that species and frequency of isolation of NAS differs between teat canal and milk samples”*
        + *“It was clearly demonstrated that some NAS species are more associated with* ***IMI*** *than with* ***environmental*** *(e.g., parlor-associated)* ***niches****”*
        + *“…these data demonstrate likely adaption to* ***niches on the cow*** *which seems to underpin its success as an IMI organism. Similar data have been reported for S. aureus, another* ***host-adapted*** *udder pathogen (106).”*
      * **In general (all mastitis pathogens more broadly)** 
        + Klaas and Zadoks 2017
        + Zadoks 2011
        + Zadoks and Schukken 2006

**How pathogens spread, vs. where they come from, are different questions**

“Transmission dynamics” is a term they use

“how organisms spread, as opposed to where they come from”

Contagious transmission vs. common source exposure

*“…presence of the same strain in multiple animals does not necessarily prove contagious transmission. When multiple animals are infected with the same environmental strain, predominance of one strain is the result. It is easy to prove that infection in multiple animals is not the result of contagious transmission. Detection of different strains in each animal proves that. The opposite, proving that contagious transmission causes the spread of a disease, is much harder to do. Usually, a combination of molecular and epidemiologic data is needed to support the likelihood that infection of multiple animals with the same strain was due to common source exposure or contagious transmission, respectively.”*

Use of strain typing to show that transmission of same organism in an “outbreak” was actually different by state

*“Using RAPD typing, the origin of perceived epidemics of Corynebacterium pseudotuberculosis, which mostly affected horses, was shown to differ between states. All isolates from Utah belonged to one RAPD type of Corynebacterium pseudotuberculosis, consistent with a clonally expanding epidemic in that state. In contrast, the increased number of infections in Colorado, Kentucky, and California was caused by multiple strains of Corynebacterium pseudotuberculosis that were not derived from a common source. Possible causes for the perceived increase in Corynebacterium pseudotuberculosis incidence include reporting bias due to increased awareness of the disease, environmental factors facilitating infection, or host factors facilitating infection, such as greater herd susceptibility”*

* + - **Subclinical vs. clinical**
    - **Acute vs. chronic**
  + Epidemiology and ecology of NASM (specifically)
    - Pyorla and Taponen 2009 –
      * *“For CNS mastitis, as for all other types of mastitis, prevention is the key to combating the problem. However, more knowledge and experience is needed to find the most effective strategies for prevention of CNS mastitis”*
  + Molecular epidemiology, strain-typing methods
  + In-silico data to identify AMR, virulence
  + Comparing prevalence estimates for NASM between studies, and potential issues with this (like DeBuck review article)
    - How study designs differ and how might influence results – what kind of prevalence estimates are reported; how do you compare prevalence between studies
    - E.g. pamela’s paper some sp. higher in first lactation animals, prevalence in diff species as animals age tails off – distribution changes with lactation number and stage of lactation
    - CNS epi (species distribution and prevalence) will differ with both stage of lactation and parity
      * Pena mosca – all periparturient animals, all fresh
      * Pyorla and Taponen 2009 *–*
        + *“The prevalence of CNS mastitis is higher in primiparous cows than in older cows (Matthews et al., 1992; Poelarends et al., 2001; Tenhagen et al., 2006). CNS can colonize the mammary gland of pregnant heifers (White et al., 1989; Myllys, 1995), and CNS were isolated from the mammary gland and teat apices of heifers as young as 10 months old (Boddie et al., 1987; De Vliegher et al., 2003). In intensive management systems, the prevalence of quarters of precalving heifers infected with CNS can exceed 50% (Trinidad et al., 1990b; Oliveira et al., 2006). In pasture-based grazing systems a lower prevalence (16%) has been reported (Parker et al., 2007). Even under grazing conditions, CNS were the predominant isolates in pre-calving heifers (77% of the bacteriologically positive quarters)”*
        + *“CNS are important pathogens in cattle of all ages, but the* ***predominant CNS species causing infection seems to differ between age groups****.* ***S. chromogenes*** *was the major CNS species in* ***pre-calving heifers and primiparous cows*** *(Trinidad et al., 1990b; Rajala-Schultz et al., 2006; Taponen et al., 2006), whereas* ***S. simulans was mostly isolated from cows in later lactations*** *(Taponen et al., 2006). Multiparous cows generally become infected with CNS during later lactation whereas primiparous cows usually already have the infection at the beginning of lactation (Gro¨hn et al., 2004; Taponen et al., 2007)”*
      * De Buck 2021
        + *“Prevalence of IMI with NAS is especially high in virgin and first lactation heifers (18–24). … NAS are very prevalent in bovine IMI, especially in dairy heifers (38, 39)”*
    - Limitation of our study – seasonal
      * Pyorla and Taponen 2009 *–*
        + *“Seasonal differences in occurrence of CNS mastitis have been reported. In Finland, the prevalence of CNS and S. aureus mastitis was highest during winter and spring, i.e. during the indoor season (Koivula et al., 2007). In Norway, too, the highest prevalence of CNS mastitis was found during the late indoor season (Østera˚ s et al., 2006)”*
    - Comparing model results from SCC\_DIM paper to Condas 2017 output
    - Even just **definition of a CNS IMI** makes it difficult to compare between studies
      * Series of Dohoo papers
        + *“Diagnosing intramammary infections: …”*
      * Pyorla and Taponen 2009 *–*
        + *“It is difficult to compare results from different countries because the number of colony forming units (CFU) per ml that is used as cut-off to categorize samples as CNS-positive varies between studies”*
* Pick one novel thing that not really covered in the literature, stick to JDS guidelines
  + NASM epi on organic dairy farms
  + Really only have Pena-Mosca to compare to
  + *prepared according to JDS Style and Form, contain no more than* ***30 double-spaced pages*** *and* ***75 references***
* Mastitis on organic dairy farms … NASM mastitis on organic dairy farms?
  + How different mgmt. factors affect species diversity and prevalence of NASM factors, generally
    - Potential for difference between conventional and organic farms
    - How ARE organic and conventional farms different, with respect to mgmt. factors, mastitis mgmt.
      * Stiglbauer paper
  + Does relative species distribution of pathogens causing mastitis differ between conventional and organic farms
    - Prevalence of different pathogen groups causing mastitis (strep, staph, gram neg, etc.)
    - Species diversity same between different mgmt. types?
  + Does species diversity of **NASM** differ between organic and conventional farms
  + Does prevalence (by species) of **NASM** differ between organic and conventional farms
  + AMR on organic vs. conventional farms
    - Tikosfky, Ruegg; European papers (found no difference; difference in organic rules between US and Europe)
* First chapter sets tone for rest of chapters; kind of introduces these
  + Ends with: given these foundation of knowledge, here are the gaps
* Intros and discussions in chapters expand on these themes

In the discussion, I think you may want to add something about the fact that high SCS will not always results in lower milk yield. Therefore: “maybe we still do not need to treat these staph.?”

*Tomazi 2015*

Compared quarters within cow, one infected with NAS and another not infected with NAS

*Goncalves 2020*

Non-aureus staphylococci causing chronic subclinical mastitis had no effect on milk yield (quarter-level)

*Valckenier 2019*

NAS IMI caused only a slight but significant increase in quarter SCC compared with milk from noninfected quarters, whereas no significant difference in daily quarter milk yield was present between NAS-infected and noninfected quarters.

*Valckenier 2020*

In general, NAS should be considered minor pathogens with no adverse effect on daily quarter milk yield in quarters of heifers in early lactation

*Olofsson 2024*

Different NASM species were not found to have an association with quarter milk yield

August 29th 2:30 – 5 L 1 medical center drive Lebanon nh turn onto main rd- follow signs to parking garage; on fifth floor off from parking garage (up 1 floor)

6.25.2024

***Exploratory literature review***

*Searched pubmed:*

(organic) AND (dairy) AND (mastitis)

*Not including articles that:*

* Are about plant-based/holistic therapies (teat dips, teat “sealants”)
* Genetics
* Economic analyses
* Nutrition/supplements
* Calves (feeding mastitic milk)
* Qualitative/social science work about antibiotic treatments
* Welfare (would use mastitis indices if presented)

*Not sure about:*

* Milk production

*Themes I’m seeing:*

* Is udder health better or DIFFERENT on conventional vs. organic farms
  + blue
* Mgmt factors about organic farms, and how they may affect udder health indices … OR what mgmt. factors are different between conventional and organic farms … HOW are organic and conventional farms different?
  + Green
* Virulence or AMR of conventional vs. organic mastitis pathogens
  + Orange
* NASM virulence generally? And some specific to isolates from organic farms
* Maybe just gives estimate of udder health indices for organic farms
  + red

*….is this a weird review, like setting up for people that I’m comparing organic and conventional herds in any of my studies? Bc I’m not… just have a population of entirely organic herds that I can describe what’s going on (no comparison)*

*Counts of different types of abstract:*

* huh? white n=5
* AMR/virulence … orange = 16 (17 with fecal isolate paper)
* Mgmt. factors … green = 20
* Head to head comparisons/udder health … n = 19
* Just description of organic farms milk quality … n = 9
* Overview: how do organic and conventional farms differ in mgmt. practices?
  + Body of work looking at this … AB usage
* Overview: how does milk quality on organic farms stack up compared to conventional farms?
  + Some work will pit them head to head; other papers just give descriptions about udder health metrics for organic farms, and I’ll need to connect the dots
    - Incidence/prevalence clinical mastitis
    - Incidence/prevalence subclinical mastitis
    - BTSCC
    - Pathogen profiles
      * What’s common on conventional farms vs. organic farms?
* Does antimicrobial susceptibility vary between organic and conventional farms?
  + Generally
  + Table
    - Objectives of the study?
    - Methodology
      * **Number of farms in each category**
      * [Number of cows in each category]
      * **Longitudinal or one point in time**
        + **Length of time followed**
      * **In Europe or US**
      * **Quantification of AB usage?**
      * **How long organic farms organic**
      * **Farms matched at all/and by what criteria**
      * Collection of milk samples (does this matter?)
      * **Which AB tested?**
      * **How determine AB sensitivity**
      * Age of animals
      * **Speciation of bacteria (how specific? Esp. for NASM)**
      * **Type of sample (qm from subclinical, fecal sample, BTM)**
    - **Groups of organisms looked at (or species)**
    - **Results**
      * **Susceptibility profiles of different species or groups of species**
      * Some have multiple susceptibility measures or analyses (survival analyses, MIC as a continuous measure, S/IR as categorical/chi-square or fisher)
  + What’s out there for NASM or Staph. specifically?
* AMR in NASM
  + Frey et al., 2013; Fišarová et al., 2019; Fergestad et al., 2021
  + Table in oliver 2011 (by species grp: CNS, SA)
  + (Piessens et al., 2011; Sampimon et al., 2011), Huber et al. (2011
  + Dairy Cows' Udder Pathogens and Occurrence of Virulence Factors in Staphylococci, Zigo 2022
  + In vitro, the transfer of SCCmec was achieved through transformation (incorporation of DNA from the environment) (Morikawa et al., 2012), through plasmids (Ray et al., 2016), conjugation (sexual transfer) (Tsubakishita et al., 2010), and transduction (bacteriophage transfer) (Chlebowicz et al., 2014). All these studies were performed under laboratory conditions. To the best of our knowledge, it remains unclear which mechanism(s) of SCCmec transfer occur in vivo. In conclusion, MR-CoNS could act as a reservoir of resistance genes that may be transferred to MSSA in dairy cows. The role of SCCmec transfer for the development of new MRSA strains needs to be further investigated
  + In China, 73% (82/112) of nonaureus staphylococci carried the mecA gene and MRSA prevalence was 4% (15/96) (Qu et al., 2018). A study from the United States has reported 11 methicillin-resistant coagulase-negative staphylococci (MR-CoNS) in BTM from 288 farms and just 1 single MRSA isolate (Cicconi-Hogan et al., 2014). In contrast, in 3047 mastitis milk samples from Korea, the authors reported 12 MR-CoNS and 13 MRSA isolates (Moon et al., 2007). This would be in line with the lower virulence of the MR-CoNS. The last VetPath study from Europe reported that 7 of 165 CoNS isolates from mastitis milk samples carried the mecA gene (4.2%) and 1.6% (3/192) of S. aureus isolates were classified as MRSA (de Jong et al., 2018). In Finland, two studies reported that 5.2% (17/324) and 1.8% (2/110) of the CoNS isolates were mecA positive and MRSA prevalence among S. aureus isolates was 1.5% (2/135) (Gindonis et al., 2013). A study from Portugal did not find MRSA but 9.3% (19/204) of mastitis milk samples were positive for MR-CoNS (Seixas et al., 2014). In conclusion, MR-CoNS have been detected in MRSA affected dairy herds and the prevalence of methicillin resistance was generally higher than in S. aureus
  + A study from Belgium reported that SCCmec types in bovine MR-CoNS (n = 101) differed from those mostly detected in LA-MRSA CC398 (Vanderhaeghen et al., 2013).
  + In many studies evaluating susceptibility patterns of mastitis pathogens, CNS have been reported to show most resistance against penicillin (Matthews et al., 1992b; Myllys et al., 1998; Gentilini et al., 2002). Also in the current study, CNS exhibited the highest degree of resistance to penicillin, 31.7% of the isolates being resistant. This estimate is between the proportion of CNS resistant to penicillin in Argentina (21.1%) (Gentilini et al., 2002) and in Finland (37.2%) (Myllys et al., 1998). The proportion of CNS isolates that were resistant to at least one antibacterial drug was reported to have increased in Finland from 26.6% in 1988 to 49.7% in 1995 (Myllys et al., 1998). In our study, 43.9% of the CNS isolates were resistant to at least one antibiotic. Todhunter et al. (1993) reported multiple antibiotic resistance in 86% of their CNS isolates
  + Significance of AMR in NASM –
    - Potential for transmission of resistance genes to more contagious/virulent pathogens?
      * “CNS could potentially provide a reservoir of resistance genes”
    - Mechanisms
      * Horizontal gene transfer
    - Any evidence for this?
* Virulence in NASM
  + Molecular studies suggest that CoNS carry fewer virulence genes than S. aureus and are therefore considered less pathogenic (A˚ vallJa¨a¨skela¨inen et al., 2018)