Herd Problem Investigation – Tuesday Morning Seminar

Goal of problem investigation:
- Sufficient understanding of what happened to make changes that prevent future occurrence

Distinction from Individual Problem Investigation:
- A common group of animals with different intrinsic characteristics (e.g., age, gender, breed, immune status) experiencing multiple risk factors at different stages of their growth, reproduction and production cycles
- Provides important basis for comparisons that are not available in individual animal

Comparison:
- Between groups of animals with different problem status (proportion affected, problem severity)
- Across time

Most important parts for clues:
- Classifying individuals efficiently – excellent clinical skills, critical observational skills
- Establishing timelines of problem occurrence with respect to animal flows

Approaches:
- Pattern recognition based on rapid assessment of key indicators
  - Mode typical of experts that develops with experience
  - Dangerous risk of overlooking evidence
- Systematic problem workup – answering who, where and when:
  - The herd is a livestock production system that is composed of dynamic relationships between animal hosts, infectious agents and their environment that change over time
  - Understand the timings and locations of animal flows and events across the production cycle
    - Start with a typical animal at their entry point and follow them through each stage and each event
  - “Starting with history discourages the common and distracting tendency we all have to define a problem not by the system's actual behavior, but by the lack of our favorite solution” (D Meadows)
  - “Starting with the behavior of the system directs one’s thoughts to dynamic, not static analysis; not only to "what's wrong?" but also to "how did we get there?" (D Meadows)

Problem Investigation Flow
**Important Disease Concepts for Understanding Disease in Populations**

http://www.vetmed.wsu.edu/courses-jmgay/EpiMod2.htm

**Status and Spectrum of Disease Severity**

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<tr>
<th>Exposure Status</th>
<th>Unexposed</th>
<th>Exposed</th>
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<tr>
<td>Infection Status</td>
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<tr>
<td>Uninfected</td>
<td>Subclinical (Inapparent)</td>
<td>Clinical Disease (Apparent)</td>
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<td>Recovered</td>
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<table>
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<tr>
<th>Disease Status</th>
<th>Uninfected</th>
<th>Infected</th>
<th>Recovered</th>
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<td>Subclinical</td>
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<td>Clinical</td>
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<td>Morbidity (Sickness)</td>
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<td>Mortality</td>
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<td>Fatal</td>
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- **Iceberg Principle** – For most diseases in large groups for every clinical case there are at least 10 clinical cases.

\[
R_0 ("R Zero") \text{: For infectious diseases, the average number of susceptible animals that are infected by each infected animal. Over the long run, an } R_0 \text{ equal to or greater than one is required for an infectious agent to survive in a group. If it can be lowered to less than 1, eventually the agent will be eradicated from the group.}
\]
Logical Reasoning to Conclusion

“In God we trust, all others bring data” (W. Edwards Deming).

"More mistakes are made from not looking than from not knowing!"

The goal is to identify the key determinants, which are those specific risk factors acting in the causal pathway on that farm that can be modified or eliminated to prevent or reduce the problem. Although their presence is necessary, few infectious agents cause disease solely by themselves but rather operate more as opportunist, exploiting weaknesses in livestock management systems. Focusing exclusively on an agent overlooks the fact that the opportunity is present for other similar opportunistic agents. For example, the risk factors on a given farm for the transmission of calf scour agents are the key determinants rather the presence the agents themselves. Such agents are essentially holoendemic, meaning that they are everywhere and that most all cattle are exposed to them at some point in their lives. In these circumstances the objective is to delay exposure until the animal is older, minimize exposure dose when it occurs and maximize host resistance at that time. In the midst of a scours outbreak, the questions are why is the exposure earlier, the dose higher or the host more susceptible on this particular premises? Rather than biologics or pharmaceuticals, the best long term interventions involve altering facilities or changing human behavior, which is the most difficult, particularly when the current way apparently worked without problems previously.

The three general types of herd problems are:

- **Acute**: Precipitated by recent management or husbandry errors of sufficient magnitude to be cause the problem and evidence of the problem is readily apparent.

- **Additive or Cyclic**: Precipitated by management or husbandry errors and the effects of cyclical factors, such as season or production cycle stages, that in combination precipitated the problem.

- **Chronic**: Precipitated by the long action of a combination of management or husbandry errors that required the passage of time before the consequences became sufficient to be recognized, such as the slow spread of a contagious mastitis agent or of Mycobacterium avium var paratuberculosis.

**Investigation Flow**:

0. Confirm that the problem is real
1. Establish the pathologic and etiologic diagnosis
2. Establish a working case definition
3. Establish the magnitude of the problem with data
4. Description
   a. Elucidate the mechanics and flow of the production system
   b. Establish the timing of the problem (When?)
   c. Establish the demographics of affected vs. non-affected animals (Who?)
   d. Establish the place of the problem (Where?)
5. Assemble, verify and analyze the data
6. Generate hypotheses (differential diagnoses) about key determinants
7. “Test” your hypotheses
8. Design interventions or prospective studies
9. Document findings and recommendations
10. Monitor results

Why did these get it and why did these not? “Who Where When”

- What is common and what is dissimilar between two groups that were affected at different times or places?
- What is common and what is dissimilar between one group that was affected and another that was not at the same times or place?

**Sources of hypotheses**:

- In-depth knowledge of medicine, mechanisms of disease, pathophysiology, nutrition and animal husbandry
Logical Principles for Reasoning

Based on knowledge of the natural history of the disease problem and the objective information collected, generate hypotheses about what key determinants are likely involved. Based on each hypothesis, predict what should be found in other animals, such as test results or production effects, and evaluate the predictions. Make predictions of the form "**if this cause is present, then this finding should be present**". Because single causes have multiple effects, finding these multiple effects provides stronger support for the cause than finding only one. As much as possible avoid scattershot sampling and data collecting because doing so without an objective in mind is seldom useful and is expensive in money for the client and in credibility and time for the clinician. What is the simplest set of explanations that covers the most findings?

For counts, comparing groups by calculating odds-ratios or relative risks in two-by-two tables and for continuous data, such as milk production, comparing averages between groups often suffice for evaluation. Spreadsheet charts are useful for comparing risk trend lines between groups and present visual evidence that is easy for clients to understand.

**Mill's Eliminative Methods of Induction** (System of Logic, 1843):

- **Method of Agreement**: "If two or more instances of the phenomenon have only one circumstance in common, the circumstance in which alone all instances agree is the cause or effect of the given phenomenon."
- **Method of Difference**: "If an instance in which the phenomenon under investigation occurs, and an instance in which it does not occur, have every circumstance in common save one, that one occurring in the former, the circumstance in which alone the two instances differ, is the effect, or the cause, or an indispensable part of the cause, of the phenomenon."

**Hill's Criteria for Causation** (Hill 1965):


1. **Strength of Association**: The larger the relative effect, the more likely the causal role of the factor. Although the presence of an association alone is not sufficient to prove causation, at minimum a biologically significant association must be present for cause to be present.
2. **Consistency**: If similar associations are found in different studies in different populations, the more likely the causal role of the factor.
3. **Specificity**: If the effect does not result from other causes, the more likely the factor is causal.
4. **Temporality**: Risk factor exposure must precede the outcome.
5. **Dose-response (biological gradient)**: If the risk increases with increasing dose or longer exposure to the risk factor, the more likely the causal role of the factor.
6. **Biological Plausibility**: Given the state of existing knowledge, the mechanism is biologically plausible in that it does not contravene well-established understanding.
7. **Coherence**: Associations between the risk factor and the outcome is consistent with existing knowledge and does not conflict with the generally known facts of the natural history and biology of the disease.
8. **Intervention (Experiment)**: Reduction or removal of the risk factor reduces the risk of the outcome, the strongest evidence of causation.
9. **Analogy**: That a similar but not identical cause and effect relationship has been observed and established elsewhere as causal provides weak evidence for causality.

**Evan's Postulates** (Evans 1976):

1. Prevalence of the disease should be significantly higher in those exposed to the risk factor than those not.
2. Exposure to the risk factor should be more frequent among those with the disease than those without.
3. In cohort studies, the incidence of the disease should be higher in those exposed to the risk factor than those not.
4. The disease should follow exposure to the risk factor with a normal or log-normal distribution of incubation periods.
5. A spectrum of host responses along a logical biological gradient from mild to severe should follow exposure to the risk factor.

6. A measurable host response should follow exposure to the risk factor in those lacking this response before exposure or should increase in those with this response before exposure. This response should be infrequent in those not exposed to the risk factor.

7. In experiments, the disease should occur more frequently in those exposed to the risk factor than in controls not exposed.

8. Reduction or elimination of the risk factor should reduce the risk of the disease.

9. Modifying or preventing the host response should decrease or eliminate the disease.

10. All findings should make biological and epidemiological sense.

Pitfalls:
- GIGO – Garbage in, Garbage out
- Comparing dangling numerators
- Not accounting for missing animals
- “Hidden” definitions
- Not verifying subjective impressions with solid data; in God we trust; all others must bring data
- Anchoring Bias ("Jumping to Conclusions"): The tendency to fixate on limited information too early in the investigation process.
- Ascertainment Bias: The tendency to allow prior expectations to shape thinking and observation of information, particularly of subtle, vague clues.
- Confirmation Bias: The inclination to look for confirming evidence to support a weak diagnosis or hypothesis rather than looking for refuting evidence, which is logically more definitive. Asking "What would disprove this hypothesis if found?" is more powerful than "What else would support this hypothesis if found?"
- Premature Closure Bias: The tendency to accept a conclusion before it has been sufficiently verified by tests for adequacy, coherence, parsimony and falsification.
- Satisfying Bias: The tendency to stop searching for further information once something is found. The questions to ask are: "Is there anything else to be found?", “Did I look in the right places?” and “Are any clues inconsistent with this conclusion?”

References:
  - Barnyard Epidemiology and Performance Assessment 22(1), 2006
- Essential Field Epidemiology: Outbreak Investigations http://sites.google.com/site/medepi/epix
- Guides for particular problems (see: Herd Problem Investigation Resources for Veterinarians http://www.vetmed.wsu.edu/courses-jmgay/OutBResources.htm ) - examples: