

A Systematic Approach to Herd Disease Outbreak Investigation

John M. Gay, DVM PhD DACVPM

Associate Professor of Epidemiology, CVM AAHP FDIU

Washington State University, Pullman, WA

When faced with a perplexing, ambiguous problem, a systematic approach helps overcome the barrier of “Now what?”. Haphazard approaches to ambiguous problems are prone to embarrassing mistakes, particularly overlooking what in hindsight was obvious. Because we so easily rationalize our way from cause to effect, being aware of reasoning errors that lead us astray increases our chances for success. Just as a systematic approach to the individual case is best, so is it for herd problems. The following is a general framework for a systematic approach to a herd disease outbreak of an ambiguous nature.

The systematic approach is used to investigate human disease outbreaks (CDC 2004, Gregg 2008, WHO 2008) and is well described in the veterinary literature (Lessard 1988, Waldner 2001, Waldner 2006). Because of the importance of outbreak investigation in the public health sector, Googling “outbreak investigation” hits thousands of on-line resources. These include the free CDC on-line continuing education course SS1000 (<http://www2a.cdc.gov/TCEOnline/>), on-line medical school course materials (e.g., Field Epidemiology <http://sites.google.com/site/medepi/epix>) and websites devoted to field epidemiology training (e.g., FOCUS <http://nccphp.sph.unc.edu/focus/index.htm>). The Center for Food Security & Public Health disease factsheets are good handouts for clients (<http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.htm>) and the site provides information on sanitation, disinfectant use and routes of transmission. Several veterinary academic groups provide goal forms, flow sheets, question sets, data collections forms and other information for working up specific problems, such as calf health, fertility, lameness, and milk quality. Examples include those provided by the University of Wisconsin Food Animal Production Medicine group (<http://www.vetmed.wisc.edu/dms/fapm/index.html>) and the New York State Cattle Health Assurance Program (<http://nyschap.vet.cornell.edu/>). For bovine enteric infectious disease problems, the Johnes risk assessment tools at <http://www.johnesdisease.org/> are useful sources of checklist items. Other checklist sources include those for biosecurity and good management practices (GMP), such as NebGuide G1411 (Buhman et al., 2007) and Biosecurity Checklist (PQAPIus, 2002). Other investigation information sources include reviews, proceedings papers and on-line sources such as Cook (2007) and professional list serves and their archives, such as AABP-L.

Farms are dynamic systems of complex interactions between components. Because of farm diversity, the time passing between the cause and the effect, the biological variability among animals, and the inevitable continuing change (e.g., weather changes, feed changes, personnel changes, flow of the production cycle), sometimes figuring out what happened is a challenge, even with a definitive diagnosis. Certainty about conclusions is rare and acquiring additional information is usually costly. Balance the cost

and delay of acquiring more information against the value of a more timely intervention if successful. The object is to gain sufficient certainty about what is wrong to start fixing it.

Primary Complaint and Problem Type

What is really the primary complaint? Often producers reason from a primary complaint (e.g. low milk production) that caught their attention to what they suspect is the cause (e.g., pneumonia in adult cows) due to a ubiquitous bovine infectious agent (e.g., *Mannheimia hemolytica*) to a key determinant in this causal pathway (e.g. poor barn ventilation). In the actual herd investigation led by Dr. Dale Hancock, the cause of the production loss was a miss-calibrated scale on a grain auger, not poor barn ventilation for which the producer requested assistance (Bradish, 1997). In this case, solving the barn ventilation problem successfully would not have resolved the primary complaint that prompted the producer to act.

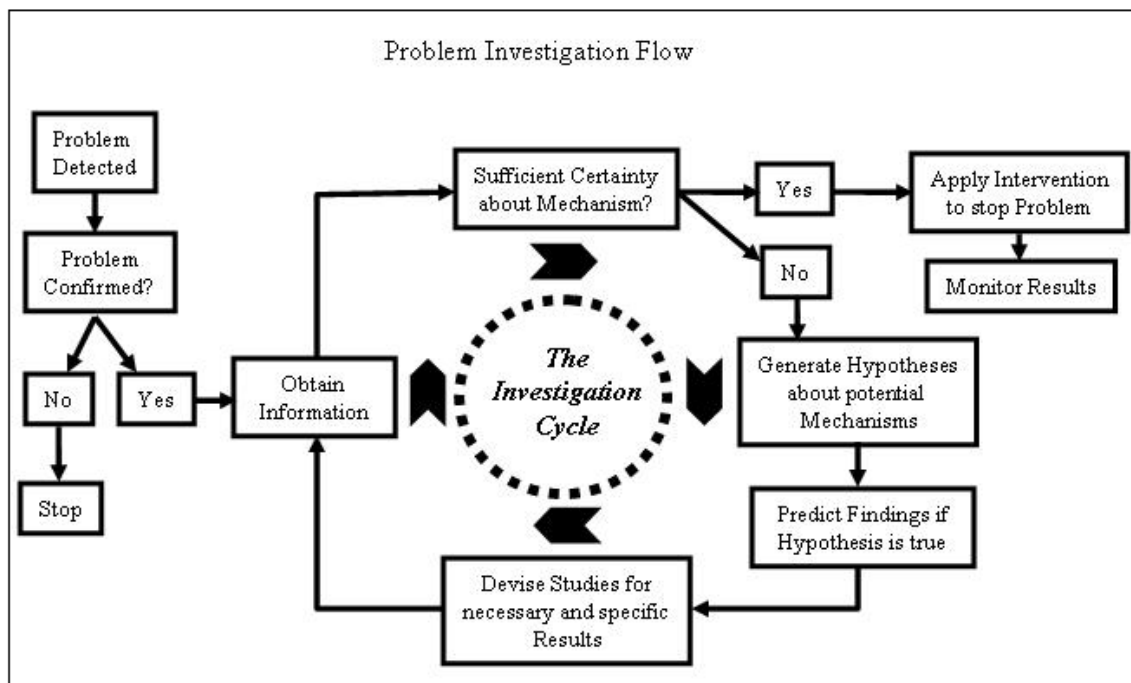
The three herd problem types are:

1. **Acute:** Recent husbandry errors precipitated the problem, what went wrong is apparent, and the evidence needed to fix it is readily available.
2. **Additive or Cyclic:** A combination of husbandry errors and cyclical factors, such as season or production cycle stages, precipitated the problem. Risk factor strength often varies with season. Because of seasonal breeding effects, problems related to animal density, such as the seasonal appearance of excessive numbers of DA's, are cyclical and reappear annually. Because of the lag, the relationships are ambiguous.
3. **Chronic:** A combination of husbandry errors required the passage of time before the consequences became sufficient to be recognized, such as the slow spread of an infectious agent. For example, the recognition of a slowly spreading *Staph aureus* mastitis problem in which the major factor is the change to a less efficacious teat dipping procedure a year previously. Because of the long time between cause onset and effect recognition, these problems are difficult to untangle, particularly because the change appears successful for some time and details have faded.

Establishing problem type at the outset is important because if you mistake a chronic problem for an acute one, results of comparisons between current and recent history may be misleading. Sometimes the precipitating event is dramatic, such as the sudden appearance of deaths or a dramatic production decline, but more often the effects of a chronic problem that has been occurring for some time are finally recognized. The earlier problems are detected, the more successful the investigation and resolution. Once a problem with an infectious agent reaches clinical outbreak levels, more animals are carriers, the environmental load is higher and control has to be more effective to stop transmission. Because the ratio of subclinical infection to clinical disease is 10 to 1 or more for many infectious agents, they often spread for some time before being detected, whether BVD, *Mycobacterium avium* subsp. *paratuberculosis* or *Tritrichomonas foetus*. Herd production medicine is geared toward establishing systems for the early detection if not the outright prevention of common problems, hence the development of herd scoring

systems, such as for body condition and lameness, routine monitoring, such as BTSCC and DMI, beef herd calving strategies and metaphylaxis for BRD (Brand 1997, Chenoweth 2005, Radostits 2001). Remember, *"He who detects the problem is often called on to solve it"* (Fetrow).

The goal is to identify the key determinants for the primary complaint on that premises. Key determinants are those risk factors in the causal pathway on that farm that within their control. Because few infectious agents cause disease solely by themselves but rather function more as opportunists exploiting weaknesses in livestock management systems, they are usually not key determinants. Focusing exclusively on an agent overlooks the fact that the opportunity is present for similar opportunists. For example, the risk factors 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. Many scour outbreaks involve multiple agents and a significant proportion of the calves are infected with multiple pathogens. In such 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 premise? Rather than biologics or pharmaceuticals, the most effective long term interventions involve permanently modifying facilities and changing human behavior. These changes are often the most the most difficult, particularly when the current methods apparently worked without this problem previously. Hence the response "But we've been doing it this way for years!"



Problem investigation is the thorough, systematic search for and comparison of clues. In contrast to individual animal investigation, the opportunity for solid comparisons is the power of herd investigation. Comparisons between affected animals, both clinical and subclinical, and their unaffected herdmates and between affected and unaffected groups, in both cross-sections (at one point in time) and over time identify the differences and the similarities between the animals themselves, the groups and the factors affecting them. Although the component list is linear, investigation flow is "multithreaded", meaning that steps occur more or less in parallel, and "recursive", meaning that new information causes previous steps to be revisited. What is relevant changes as the workup proceeds and differentials (hypotheses) are ruled in or out. Too little information leads to errors of omission, too much to overload and excess cost.

The Systematic Approach Framework

The 10 basic components of the systematic approach framework are:

0. Confirm that the problem exists
1. Establish the pathologic and etiologic diagnosis
2. Establish a working case definition
3. Use data to establish the problem magnitude
4. Problem description
 - a. Establish 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

Start the process by developing a preliminary synopsis of the problem over the phone. Obtain a herd history by asking questions on the herd demographics, the signs of the problem, the number of animals in the group and the number affected and their demographics, treatments that have been tried and the response, risk factors they have observed, recent changes they have made and other basic husbandry questions. Preliminary differentials from this information provide guidance for refreshing one's memory on the potential problems, for contacting diagnostic labs for advice on any special sample acquisition, preservation and handling that might be needed, and for planning the on-farm investigation. To shorten the process, ask the client to begin assembling information needed for the on-farm investigation, such as

counting up the number affected and the locations and dates they were affected, assembling working map of the premises with group sizes, and so on.

0. Confirm that the Problem Exists

With the more vague problems, be careful of "pseudoepidemics" resulting from the producer becoming aware of a chronic problem or resulting from a definition change. Verify that empirical data supports clinical impressions before proceeding far. If a chronic problem is misclassified as acute, the wrong time frame will be searched for clues and the wrong comparisons made. For example, a producer alleged that this was his first experience of low weaning weights but his weaning data showed that a downward trend had been underway for at least three years. In an abortion pseudoepidemic the veterinarian invested \$1,000 in lab fees attempting to establish an etiologic diagnosis. Further investigation revealed that the dairy had switched from a dairy herd records program that required manual entry of abortion events to one that automatically classified any cow returning to heat after a positive pregnancy exam as an abortion event. Obviously, this step is unnecessary if an unusual number of animals are dead or clearly sick or production has dropped sharply.

1. Establish the Pathological and Etiological Diagnosis

If the diagnosis is not definitive but needed, collect samples to obtain a definitive pathologic and etiologic diagnosis. Do not accept a provisional etiologic diagnosis as definitive without clear evidence. Doing so may lead to overlooking important contrary clues and thus seriously mislead the investigation, which can have serious consequences for the producer and for the clinician's credibility. The previously cultured mastitis cases may have been *S. aureus* but this outbreak may be due to *M. bovis*. On the other hand, recognize that only establishing a definitive pathological and etiologic diagnosis does not solve the producer's problem; that something has to be changed but what? Realize that the key determinants for many emerging agents were identified long before the agents themselves were identified (e.g., HIV, Enzootic Bovine Abortion).

If dead or dying animals are involved, have complete field necropsies been performed on a sufficient number of representative animals? Selecting a few of the worst rather than enough of the representative is a serious mistake. In one herd, none of the owner-selected animals with clinical signs were shedding the infectious agent infecting a significant proportion of their herdmates subclinically.

A common diagnostic lab complaint is that practitioners fail to submit a full set of properly handled and preserved tissue and fluid samples from complete necropsies, rather submitting only those samples that would confirm their diagnosis. To counter this, some labs structure their fees to encourage the submission of a complete set. In a major morbidity problem in a large dairy herd, the underlying problem was believed to be a severe respiratory condition but laboratory findings on the lung samples from partial necropsies of several thoraxes were inconclusive, frustrating both the practitioner and the diagnostic lab. Complete gross necropsies performed later on several euthanized moribund cases revealed a severe uterine condition subsequent to an improper but widely applied uterine infusion. The pathologists

indicated that the uterine lesions were the most severe they had ever seen. Balance the potential "regret" cost of missing a major gross or laboratory diagnosis against the marginal cost of doing complete necropsies compared to partials. .

When taking samples, consider the regret factor vs. current cost of obtaining samples. For example, when working up a reproductive problem in a grazed beef herd, taking and holding blood samples from palpated animals only to discard them later is less expensive than finding such samples are needed when new hypotheses emerge and that to obtain them the herd must be rounded up and corralled again. Take and preserve sample of perishable items that may be involved, such as feeds. A quick check with your diagnostic laboratory to verify what samples they recommend taking, how much to take, how to preserve it, and how to ship them if needed is time well spent and will keep you in their good graces. As few labs run low demand, special diagnostic assays, if you need such a test you likely need to contact the lab running it for guidance on taking representative samples, sample handling and interpreting results. Getting representative samples from heterogeneous materials such as potentially contaminated feedstuffs requires special procedures.

2. Establish a Working Case Definition

Establish a working case definition, as precise as reasonable. A case definition is that set of criteria an animal has to meet to be classified as a case of the problem, such as particular clinical signs or test results. As one works through a problem, this definition may change. Consider the expected number of endemic background problems, the "red herrings", ongoing in any group of livestock and exclude these if possible. For example, in a group of pregnant cattle approximately 10% of all pregnancies diagnosed prior to 45 days of gestation are lost and approximately 20% of these losses are observed. Including cases that are due to other problems weakens the comparisons between affected and unaffected, impeding problem solving. For example, if death is a component of the problem, was an individual's death likely due to the problem or better explained by another condition? If animals experiencing the problem are culled, was an individual's culling likely due to the problem or better explained by something else?

<i>Exposure Status</i>	Unexposed	Exposed				
<i>Infection Status</i>		Uninfected	Infected			Recovered
<i>Disease Status</i>			Subclinical (Inapparent)	Clinical Disease (Apparent)		
			Morbidity (Sickness)		Mortality	
	Mild	Severe	Fatal			

Spectrum of Disease

Remember the iceberg principle, that for most conditions subclinical cases outnumber clinical cases at least several fold, and the spectrum of disease, that animals can be incubating, clinical and recovered. Even in general herd problems (e.g. low milk production), some individuals are affected more severely than others, the more severely affected animals usually having experienced higher levels of a risk factor or a greater combination of risk factors than lesser affected animals. If necessary, establish degrees of certainty (i.e., certainly affected, uncertain, certainly unaffected). Overlooking these concepts can lead to comparing clinically-affected animals with subclinically-affected and recovered animals instead comparing definitely affected to definitely unaffected. Excellent individual animal exam skills are often an asset in such circumstances. If many animals fall into the uncertain category, applying case-control comparison methods may be necessary using animals classified with more certainty through lab testing.

3. Use Data to establish the Problem Magnitude

Remember the principle "*In God we trust, all others bring data*" (W. Edwards Deming). Use objective data to establish the problem magnitude. Do not rely only on the recall or perception of farm personnel as their impressions may be well off the mark because of biased recall. Compare the observed number of cases to the expected number to determine whether or not the frequency is excessive and if it has changed. Avoid comparing "dangling numerators", which is comparing the number of cases without considering the number of animals at risk of becoming a case during that time period. Even when the underlying risk remains constant an increase or decrease in the number of animals susceptible to a condition causes a corresponding change in the number of cases of that condition. Because of seasonal effects, few herds maintain a constant number of animals passing through a risk period year around.

In a registered dairy, one-third of the retained heifer calves were dying due to salmonellosis. However, the producer did not recognize these losses because the calves were dying acutely one by one and were picked up by the rendering service running a daily route. Only by comparing the current youngstock inventory with the calving events and calf gender recorded on a calendar did the producer recognize the loss magnitude. In another large dairy, the manager knew that 10% of the cows calving during a two week period were clinically affected by a problem. However, when the records of their calving cohort, which is all of the cows that calved during this period, were reviewed, much to his surprise all had been culled in the intervening two months. In both situations the problem was considerably larger than the producer recognized, which provided additional motivation to adopt recommendations. The lesson is to construct a list of all the animals that entered a risk period or were exposed during the time period of interest, which is the cohort, and not basing the investigation on the remaining animals.

Be careful of what a producer accepts as "normal" (endemic) occurrence. In a small high producing herd the producer believed that 3rd or higher parity Holsteins going down with milk fever was a "normal" occurrence. Thus, he accepted most of his older cows going down with milk fever, did not recognize that as an abnormal situation that could be corrected and neither his veterinarian nor his nutritionist were aware of the high incidence. Be careful of missing relevant events that the producer omits, assuming that

they are not related to the problem. Asking the question “Has anything else happened to any of the animals in this group?” may help bring these other events to light.

If death is a significant component of an ongoing problem, arrange for necropsy of dead animals to reduce misclassification problems. In a year study of a large dairy herd, without necropsy over 50% of the deaths were misattributed (McConnel et al., 2009). If circumstances warrant, use resources such as the CSU Integrated Livestock Management’s Dairy Cattle Necropsy Manual (Severidt et al., 2002) to train farm personnel to perform necropsies and acquire samples.

Above all, remember "*More mistakes are made from not looking than from not knowing!*" (Sir William Jenner)

4. Problem Description

1. Establish the Mechanics of the production system

A systems analysis expert states: "*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?' . . . And finally, 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.*" (Meadows) For ambiguous problems first develop a complete understanding of how the system actually works before trying to fix it. Map out the layout of the premises, label the animal locations (e.g. pens, lots, pastures, barns, hospital pens) with the names or numbers that the producer uses, the animal numbers that are typically in each and the typical routes between these. Include water sources, feed storage and processing areas, animal processing facilities and waste flows. Large farms often have such maps. If not, check Google Earth for a high resolution satellite image of the premises. Establish the flow of animals through the production cycle including locations, the timing and criteria for the moves and the associated management practices, such as ration steps, and processing, such as vaccinations and, and any recent changes in these.

Interview the manager or herdsman to establish the timing of the events in an appropriate animal's life as it moves through the production cycle including the criteria or triggers for the steps and who is responsible for each. Generally, starting at entry or birth is easiest for a producer. If the problem involves potential carryover from the previous production cycle, such as postparturient or neonatal problems, start far enough back to cover the relevant events. Use questions such as "Now what happens?" and ask "Did I miss anything?" at each step. Ask if there have been any changes in these procedures and events and “When did you start doing it this way?” for the important ones. The goals are to define process and policy details and to jog the recall of events they might otherwise overlook. Similarly, ask what happens to the exceptions, such as how the sick and the poor doers are identified and handled. Where are they moved, how are they treated and what happens after recovery? Ask if any unusual or extreme events impacted the affected animals compared to the others. Don’t assume that they are following your vaccination

recommendations or other SOP's as you laid them out. Ask about cleaning, animal waste and excess feed handling practices and policies.

Estimate the deviation from intended policy, which inevitably occurs. Asking questions in terms of numbers yields better answers than asking for percents. For example, ask "Of the last 30 cows calving, how many didn't calve in (the location prior to where they are supposed to calve)?" and "Of the last 30 cows that calved, how many calved after less than (the number of days they are intended to spend) days in the (location they are intended to be prior to calving)?" Ask if these deviations were unusual for the affected group. When the opportunity arises, verify these flows, event timings, policies and deviations with the employee doing that work. On larger operations, the discrepancy between what the management intends and what actually happens are sometimes amazing.

What are the infectious agents of concern to the operation and what biosecurity practices are in place against these? For operations involving livestock confinement and feed storage facilities, what are the details of the vermin (flies, rodents, birds) control practices?

If a confinement facility is involved, after interviewing the manager walk through the pathway of the animals from their start through the point of the problem, verifying the information. Consider documenting with a digital camera. Check feed storage areas, feed handling equipment and feedbunks, including measuring adequacy in critical areas. Check for evidence of significant vermin infestations, such as vermin fecal contamination of feed and water sources, nesting areas, and rodent runways. Check water sources, including cleanliness, amounts and access. Observe waste effluent flows and opportunity for contact between groups. Check the storage and handling of the relevant supplies, such as biologics and pharmaceuticals. If animals are regularly passing through a step involving these, a supply is likely on hand and their waste in evidence. Check refrigerators, shelves, and waste bins for this evidence and observe out dates. If no evidence is there, why not, and if substantial amounts of something unmentioned or illegal is there, why? When possible, observe the relevant processes. If a mixed material is involved, such as a feed or diluted working solution, observe the process and verify that the stock volume purchased over time matches the amount that should have been used over time. In an intractable adult dairy cow diarrhea problem in which a feed toxin was initially suspected, the veterinarian finally observed the producer putting far too much MgO in the mixer wagon. The producer had mistaken the unit of measure.

I keep six honest-serving men: (They taught me all I knew) Their names are What and Where and When and How and Why and Who. (Rudyard Kipling)

2. Establish the Timing of the problem (the temporal pattern - *When?*)

When did the index cases occur? When in calendar time did the problem actually begin? When in the production cycle? What is the pattern of performance over time? Don't rely on fallible human recollections alone; verify. When did the numbers of deaths, culls or treatments go up? Did the production per animal suddenly drop or is this actually a long downward trend that was finally recognized? Has such a drop

occurred previously but performance recovered? If the herd is seasonal, how does this season compare to previous seasons? Clearly establishing the timing of the onset from objective data (i.e., herd records, pocket notebooks, receipts) is crucial to determining the relationship between management or input changes, such as feed batches, or other sporadic events and the problem onset. Those changes that occurred after the onset are likely not a key determinant. Be careful comparing aggregate data, such as totals or averages, between groups or times. Distinguish changes in individual animal performance from changes in total output that are due to changes in animal numbers. Medians are more useful than averages for comparing aggregate measures such as days open. Plot an epidemic curve, which is a plot of the number affected within intervals over a time line. The interval width, such as by week month or season, depends on the numbers at hand. Intervals that are too wide or too narrow obscure trends.

3. Establish the Demographics of affected vs. non-affected animals - *Who?*)

The strength of herd-focused investigation compared to individual-focused investigation is comparing affected with unaffected animals, both as individuals and as groups. Establish the characteristics of affected vs. unaffected animals in terms of exposure to potential risk factors, age, production level, stage of production cycle and source. As noted above, because of the spectrum of disease be careful when classifying animals into affected and unaffected groups. A serious error is to overlook the culled or dead animals lost from the cohort of susceptible animals that entered the risk period with the remaining animals but are now missing from the group and maybe even from the records.

4. Establish the Place of the problem (the spatial pattern - *Where?*)

Where were the affected vs. unaffected animals located during the likely exposure period? Because different groups or pens of animals have different levels of exposures (e.g., different amounts of feed ingredients, different water sources, different housing, different pasture, different origins, different stages of the production cycle) and a dose-response relationship exists for many etiologic agents, this may provide an important set of clues. Given the shedding and environment survival characteristics of the infectious agents involved, what are the potential transmission routes between infected and susceptible animals? Are water sources shared? Airspaces? Can nose to nose contact occur at some point? Could vermin have served as mechanical or biological vectors?

5. Assemble, Verify and Analyze the Data

Gathering and analyzing this objective data on a herd problem is an examination process analogous to selecting and interpreting laboratory tests or imaging procedures in individual animal diagnosis. Comparisons based on objective data support or refute clinical impressions of the herd problem, much like the testing or imaging supports or refutes clinical impressions of the clinical case. Concentrate on that data which will support or refute hypotheses (differential diagnoses).

Spreadsheets are convenient for entering, validating and manipulating the relevant individual and group information. To minimize hand entry and its errors, download data from herd record systems and processors when possible. When using data from a production accounting system, evaluate the data

quality by verifying that known relevant events identified by other means are present and correct in the records. In large herds, different employees often use different descriptors to label the same problem. In a large dairy herd experiencing early post-partum deaths, the most complete information was in the pocket book of the employee treating fresh cows rather than the herd record system in the manager's office.

First, screen for outliers and logical inconsistencies by sorting variables into numerical order and looking at the minimums and maximums. Do these make sense? Does the data have a realistic distribution or is someone entering the policy number, such as the target body condition score at dry off, rather than the actual number? For counts, compare groups by calculating odds-ratios in two-by-two tables and for continuous data, such as milk production, compare averages between groups. Calculate risk measures, such as odd-ratios and relative risks, by hand, with freeware such as EpiInfo (<http://www.cdc.gov/EpiInfo/>) or with on-line programs. For guidance in calculating and interpreting these measures, see Dohoo et al. (2009), Noordhuizen et al. (1997), Sanderson (2005), Slenning (2001, 2006) or on-line epidemiology resources, many of which are accessible through "WWWeb Epidemiology & Evidence-based Medicine Sources for Veterinarians" at <http://www.vetmed.wsu.edu/courses-jmgay/EpiLinks.htm>. Spreadsheet charts are useful for comparing risk trend lines between groups and for presenting visual evidence that is easy for clients to understand. Although tests for statistical significance have their place, insufficient sample sizes and the costs of obtaining sufficient numbers limit their utility in herds of moderate size or less. For estimating sample size and sampling procedures for statistical purposes, see Cannon and Roe (1982), the above resources or on-line resources.

Plot production data with a smoothed trend line over time, which enables trends to emerge from the noise of random variation. From count data of the numbers of affected and the numbers of susceptible animals, calculate case morbidity and fatality rates by exposure and relative risks. For the more endemic problems, plot risk over time by cohort groups. Construct cohorts of at risk animals passing through a critical point in the production cycle associated with the problem (e.g., calving, weaning) over a time interval (e.g., day, week, month) that on average have enough animals to reduce the effects of natural variation but doesn't obscure trends over time, wider intervals being needed for smaller herds. Examine the effects of other factors that vary over time (e.g., calving pen density, average of weekly high temperature, sources of animals) on risk of occurrence or production. Weather data from nearby automated weather stations can be downloaded from on-line government sources. If the herd doesn't have a good production accounting system for animal performance information, don't overlook clues in indirect sources of similar information. For example, the delivery dates and weights on feed invoices can provide approximate information on feed batch disappearance and thus approximate information on consumption patterns. On this basis, expected disappearance of feeds can be compared to actual disappearance. Invoices from rendering services may provide information on dates of animal deaths if these have not been recorded. Events such as calvings and breedings are written on walls, calendars or in pocket books. In one herd, the producer only entered the last breeding of the month for a cow into the record system but kept all of them in a card file.

6. Generate Hypotheses (Differential Diagnoses) about Key Determinants

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. If needed, review the primary literature, review literature (e.g., Dargatz 2002) and current texts (e.g., Radostits 2007) for plausible risk factors and their pathways. Thrusfield (2007) includes an appendix with a long list of risk factor studies and Cornell Consultant (<http://www.vet.cornell.edu/consultant/consult.asp>) lists current clinical literature. These hypotheses are important because they guide further strategic sampling and data analysis instead of scatter-shot sampling and data overload. New hypotheses may lead to revisiting prior steps in this process. Just as in working up individual cases, prioritize the hypotheses by their likelihood and focus efforts on those with the highest priority until these are either sufficiently supported or are refuted. Subjective observations by the producer, employees and other professionals are also sources of hypotheses about risk factors. For your recommendations to be accepted, you may need to support or refute these with objective evidence.

Jumping to this step without first developing the quantitative information (the “who, when, where” counts) beyond vague clinical impressions (e.g., these animals seem to be affected more than those) to support or refute a specific hypothesis is a serious error. Such a jump is analogous to “scattershot” ordering of laboratory tests in working up individual animal cases, hoping something will pop up rather than using the laboratory tests to rule specific differentials in or out, and will likely be as unrewarding. Be wary of jumping to “canned” solutions because the obvious may be missed. Remember, “*There is always a well-known solution to every human problem – neat, plausible and wrong*” (HL Mencken). Be careful communicating a leading hypothesis to a manager or employee before it is substantiated because returning later to a more open mind and more objective recall is difficult for both parties.

7. “Test” Hypotheses

Establishing and executing good “tests” requires ingenuity. 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”. Finding what was predicted supports a hypothesis; not finding what is predicted weakens it. The ingenuity is figuring out what predictions provide good “tests” and are “doable”. 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 is seldom useful and is expensive in money for the client and in credibility and time for the clinician. What is the simplest useful explanation that covers the most findings?

Example predictions are: “If this infectious agent is being transmitted between animals in this manner, then these animals are at risk and some should be infected while those are not and will not be.” “If this risk factor (e.g. overcrowding in the fresh pen) is causing the metabolic disease (e.g., displaced abomasums), then a pattern should appear in the associated data (e.g., higher proportion of cows experiencing DA’s in the cohorts with more crowding in the fresh pen compared to those with less

crowding)" or "If I'm seeing this in the neonates due to this cause, then I should find that in their fresh dams."

8. Design Interventions or Prospective Studies

Generate action items that are compatible with the specific facilities, resources and management ability. Consider how the limitations of the facilities and of management led to the occurrence of the problem in the first place. Judge the number of recommendations that the client can handle and prioritize these. A list of 4 items is much more likely to be successful than a list of 15. Provide sufficient technical detail of what, where and when something is to be done such that an employee can carry out the recommendation successfully. Provide clear evaluation criteria so that performance can be appraised. How quickly do you predict the problem will resolve if the changes are made? How large an improvement is reasonable to expect? When should the problem be revisited if improvement doesn't occur and what are possible next steps? Otherwise, procedural drift will likely occur back to the prior state of affairs, particularly if the personnel doing the work expect results too soon.

If uncertain about the effectiveness of an intervention and the herd situation is appropriate, propose a prospective clinical trial or other follow-up study to evaluate a specific hypotheses or intervention. With your client's consent, another approach is to invite a colleague who has experience working up similar problems in to review your workup and investigation findings.

9. Document Findings and Recommendations

Remember the old aphorisms that "*The faintest pen is stronger than the strongest mind*" and that "*Success has many fathers but failure is an orphan.*" If the recommendations are successful, with the passage of time you will not get credit due unless the recommendations were clearly documented. What isn't written is at risk of being forgotten or, worse, misconstrued. Keep the report short, direct and concise with the action items first followed by the supporting information. Summarize data in brief tables and remember that graphs are worth 1,000 words. If other parties are involved in the problem, such as feed mills, be careful of making statements that you are not willing to defend in court, whether as a party or as an expert witness. In such circumstances, include all the information as appendices that you want in a report should it become part of a lawsuit. Clearly note any human health risks, such as those from zoonotic agents. Do not create overly optimistic expectations.

10. Monitor Intervention Results

How can the producer best determine if the changes are working or if the problem is recurring? For problems with a significant subclinical component, consider proposing a monitoring scheme to provide early warning. What can the producer do to detect or prevent the problem earlier? If the herd doesn't have a good production accounting system to monitor changes in production but one is warranted, propose one. In productivity problems, propose benchmarks of performance if they aren't already in place. Monitoring recommendation results also provides important information about their efficacy. The key is to figure out an economical, easily doable scheme for monitoring the specific herd. For example, for

problems caused by an infectious agent, can pooled samples of effluent or milk or from culls be obtained on a routine basis to effectively but economically monitor for the continuing presence of that agent?

Common Reasoning Errors

When determining cause and effect, we are subject to lapses and biases in reasoning and memory that can lead us astray. We tend to weigh information that is consistent with our current belief heavier and to ignore or discount discordant information, to weight or recall the unusual or more recent heavier than the common or the more distant, and to limit our search for additional information to that which has the potential of confirming rather than refuting our belief (e.g. selective tissue submission to confirm a gross diagnosis). We are programmed by nature to posit explanations from limited, incomplete information without considering the weaknesses in the information or the assumptions being made, which results in the fallacy of misplaced concreteness.

The following are the major reasoning errors and cognitive biases involved in medical decision making (Croskerry 2002, 2003):

- **Aggregate Bias (Ecological Fallacy):** The tendency to substitute the relationship between group averages of two variables for what is happening between these two variables at the individual animal level. Group aggregate data (e.g., bulk tank ship weights, pen intakes) is more readily available than individual data (e.g., individual daily milk weights, individual intakes).
- **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.
- **Availability Bias:** The tendency to judge things as more likely if they readily come to mind, which tend to be the more recent, the more prevalent, the more striking or the more readily available. The lesion in the pathology textbook is likely the most striking one the pathologist has seen.
- **Confirmation Bias:** The strong tendency to look for further confirming evidence to support a weak diagnosis or hypothesis rather than looking for refuting evidence, which is logically more definitive. It is more powerful to ask "What would disprove this hypothesis if found?" than "What else would support this hypothesis if found?"
- **Diagnostic Momentum Bias:** A weak diagnosis may gain momentum without gaining verification, particularly if it is communicated to others without the associated evidence, biasing their reasoning and recall. Don't communicate suspicions or hypotheses.
- **Framing Bias:** Biased thinking or recall that occurs due to the way the problem is stated, the question asked or the information presented. Asking open-ended questions, presenting facts without interpretation, and avoiding value judgments reduces this problem.

- **Fundamental Attribution Bias:** The tendency to take excess credit for our successes and to deflect responsibility for our failures while attributing to others insufficient credit for successes and excess responsibility for failures.
- **Hindsight Bias:** Knowing the outcome profoundly alters our interpretation of the events prior to the outcome, leading to underestimation (illusion of failure) or overestimation (illusion of control) of abilities. In hindsight, events appear to fit together and to be explained better than they did at the time.
- **Multiple Alternatives Bias (Paralysis by Analysis, "Wallpaper phenomenon"):** Multiple options (e.g., multiple differential diagnoses) multiply the conflict and uncertainty compared to fewer, leading to paralysis of action and irrational decision making. Instead of comparing all competing options with each other, compare each with a common benchmark such as the status quo, starting with the more relevant or the more likely. Limit the number of recommendations.
- **Null Feedback Bias:** The failure to regularly obtain feedback, positive or negative, on the outcomes of previous workups and recommendations after the passage of time, instead concluding that they were successful in the absence of evidence. Follow up on how the recommendations turned out.
- **Order Bias:** Information communicated at the beginning and at the end of an exchange is remembered better than the information communicated in the middle. Having a systematic process with question threads worked out in advance and taking notes during interviews rather than relying on recall later reduces this bias. Capture visual observations with a digital camera so they can be reviewed later.
- **Overconfidence Bias:** The tendency to spend too little time gathering and synthesizing information before taking action because of placing too much faith in our opinions and hunches. Ask: "Has information been gathered in a logical, thorough and logical fashion? Does it support my opinion? Have I looked for evidence refuting my opinion?"
- **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?"
- **Support Bias:** The tendency to judge the hypothesis with the more detailed information as being more likely.
- **Sunk Cost Bias:** The greater the investment of funds, time and mental energy in a diagnosis, the greater the reluctance to let it go and consider other alternatives.
- **Vertical Thinking Bias:** The failure to think laterally or "outside of the box", which is reduced by asking the question "What else might explain this?".

Logical Basis of Causal Reasoning

The following, which are the logical basis for reasoning about findings in the presence of uncertainty, provide guidance for constructing comparisons and interpreting the results. For more detail on these general principles and their application, see a veterinary epidemiology text, such as Thrusfield (2007), or a general epidemiology text such as Gregg (2008).

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."

Joint Method of Agreement and Difference (Indirect Method of Difference): The application of both the method of agreement and the method of difference in the same evaluation of cause; ". . . it proceeds by ascertaining how and in what the cases where the phenomenon is present differ from those in which it is absent."

Method of Residues: "Subduct from any phenomenon such part as is known by previous inductions to be the effect of certain antecedents, and the residue of the phenomenon is the effect of the remaining antecedents."

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.

References and Additional Resources:

- Berezowski J (2005). Principles of Disease Outbreak Investigation and their application to potential oilfield toxic events. AB.VMA CE Session Notes, 5/11/05. <http://www.avma.ab.ca/resources/CE-Session-Notes/may11-2005/Principles-of-Disease-Investigations.pdf>
- Bradish SK (1997). A practical approach to the diagnosis of a dairy herd problem: A case report. *Bovine Practitioner* 31.2:111-114.
- Buhman M, Dewell G, Griffin D (2007). Biosecurity basics for cattle operations and good management practices (GMP) for controlling infectious diseases. University of Nebraska Institute of Agriculture and Natural Resources <http://elkhorn.unl.edu/epublic/live/g1411/build/g1411biochecklist.pdf>
- Brand A. et al. (1997). Herd Health and Production Management in Dairy Practice. Wageningen Pers.
- Cannon RM, Roe RT (1982). Livestock Disease Surveys: A Field Manual for Veterinarians. Australian Bureau of Animal Health, Canberra.
- CDC (?). Principles of Epidemiology in Public Health Practice, 3rd ed. (Lesson 6 is outbreak investigation) <http://www.cdc.gov/training/products/ss1000/ss1000-ol.pdf>
- CDC (2004). Steps of an outbreak investigation (EXCITE – Epidemiology in the Classroom) . <http://www.cdc.gov/excite/classroom/outbreak/steps.htm>
- Chenoweth PJ et al. (2005). Beef Practice: Cow-calf Production Medicine. Blackwell.
- Cook NB (2007). A guide to investigating a herd lameness problem. http://www.milkproduction.com/Library/Articles/investigating_a+herd_lameness_problem.htm
Published April 30, 2007, visited 12/15/09.
- Croskerry P (2002). Achieving quality in clinical decision making: cognitive strategies and detection of bias. *Acad Emerg Med* 9:1184-1204.
- Croskerry P (2003). The importance of cognitive errors in diagnosis and strategies to minimize them. *Acad Med* 78:775-780.
- Dargatz DA (2002). Biosecurity of cattle operations. *Vet Clin North Am Food Anim Pract* 18(1).
- Dohoo I, Martin W, Stryhn H (2009). Veterinary Epidemiologic Research, 2nd ed., University of Prince Edward Island.
- Evans AS (1976). Causation and disease: the Henle-Koch postulates revisited. *Yale J Biol Med* 1976;49:175-195. <http://www.ncbi.nlm.nih.gov/pubmed/782050>
- Gay JM. Epidemiology Concepts for Disease in Animal Groups <http://www.vetmed.wsu.edu/courses-jmgay/EpiMod2.htm>
- Gay JM. Herd Problem Investigation Resources for Veterinarians <http://www.vetmed.wsu.edu/courses-jmgay/OutBResources.htm>

Gay, JM. WWWeb Epidemiology & Evidence-based Medicine Sources for Veterinarians

<http://www.vetmed.wsu.edu/courses-jmgay/EpiLinks.htm>

Gregg M (2008). Field Epidemiology, 3rd ed. Oxford.

Hill AB (1965). The environment and disease: Association or causation? *Proc R Soc Med* 58:295-300.

<http://www.ncbi.nlm.nih.gov/pubmed/14283879>

Iowa State University Center for Food Security & Public Health

<http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.htm>

Lessard P (1988). The characterization of disease outbreaks. *Vet Clin North Am Food Anim Pract* 4:17-32.

Lessard P et al. (1988). Investigation of Disease Outbreaks and Impaired Productivity. *Vet Clin North Am Food Anim Pract* 4(1)

McConnel CS et al. (2009). A necropsy-based descriptive study of dairy cow deaths on a Colorado dairy. *J Dairy Sci* 92:1954-1962.

National Johnes Education Initiative <http://www.johnesdisease.org/>

Handbook for Veterinarians and Beef Producers: A guide for Johnes's disease risk assessments and management plans for beef herds

[http://www.johnesdisease.org/Handbook for Vets & Beef Producers.pdf](http://www.johnesdisease.org/Handbook%20for%20Vets%20&%20Beef%20Producers.pdf)

Handbook for Veterinarians and Dairy Producers: A guide for Johnes's disease risk assessments and management plans for dairy herds

[http://www.johnesdisease.org/Handbook for Vets & Dairy Producers.pdf](http://www.johnesdisease.org/Handbook%20for%20Vets%20&%20Dairy%20Producers.pdf)

How to Do Risk Assessments and Management Plans for Johnes's Disease: A veterinary instructional handbook used for cattle herds in the Voluntary Bovine Johnes's Control Program and to improve biosecurity and reduce pathogens

[http://www.johnesdisease.org/Risk Assessment & Management Plans for Johnes's.pdf](http://www.johnesdisease.org/Risk%20Assessment%20&%20Management%20Plans%20for%20Johnes's.pdf)

New York State Cattle Health Assurance Program <http://nyschap.vet.cornell.edu/>

Noordhuizen JPTM, Frankena K, van der Hoofd CM. (2001). Application of Quantitative Methods in Veterinary Epidemiology. Wageningen Pers.

PQAPlus (2002). Biosecurity Checklist,

<http://www.pork.org/Producers/PQA/BiosecurityChecklist.pdf>

Radostits OM et al. (2001). Herd Health: Food Animal Production Medicine, 3rd ed. W.B Saunders.

Radostits OM et al. (2007). Veterinary Medicine: A textbook of the diseases of cattle, horses, sheep, pigs, and goats. 10th ed. Saunders.

Ruegg PL (2006). Barnyard Epidemiology and Performance Assessment. *Vet Clin North Am Food Anim Pract* 22(1).

- Sanderson MW (2005). Chapter 3: Records and epidemiology for production medicine. Pgs. 29-63 in: Chenoweth, PJ, MW Sanderson. Beef Practice: Cow-calf Production Medicine, Blackwell.
- Severidt JA et al. (2002). Dairy Cattle Necropsy Manual. Integrated Livestock Management, Colorado State University <http://www.cvmb.colostate.edu/ilm/proinfo/necropsy/notes/INDEX.HTML>
- Slenning BD (2001). Chapter 2: Quantitative tools for production-oriented veterinarians. In: Radostits OM et al. (2001). Herd Health: Food Animal Production Medicine, 3rd ed. W.B Saunders.
- Slenning BD (2006). Hood of the truck statistics for food animal practitioners. *Vet Clin North Am Food Anim Pract* 22(1):149-170.
- Thrusfield M (2007). Veterinary Epidemiology, 3rd ed. Wiley-Blackwell.
- University of Wisconsin Food Animal Production Medicine group
<http://www.vetmed.wisc.edu/dms/fapm/index.html>
- Waldner CL (2001). Chapter 5: Investigation of disease outbreaks and suboptimal productivity. In: Radostits OM et al. (2001). Herd Health: Food Animal Production Medicine, 3rd ed. W.B Saunders.
- Waldner CL et al. (2006). Disease outbreak investigation in food animal practice. *Vet Clin North Am Food Anim Pract* 22(1):75-101.
- WHO (2008). Foodborne disease outbreaks: Guidelines for investigation and control. http://www.who.int/foodsafety/publications/foodborne_disease/outbreak_guidelines.pdf (section 4 of this 160 page pdf includes 14 pages on investigation)