EPIDEMIOLOGY INVESTIGATION

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- Thank you for participating in this course covering epidemiology investigation.

- This course will take about 90 minutes to complete, but can be stopped and restarted at any time.

OBJECTIVES:

Upon completion of this course, participants will:

- Become versed in the terminology used in epidemiology investigation
- Acquire basic knowledge of epidemiology investigation
- Understand how to complete an epidemiology investigation

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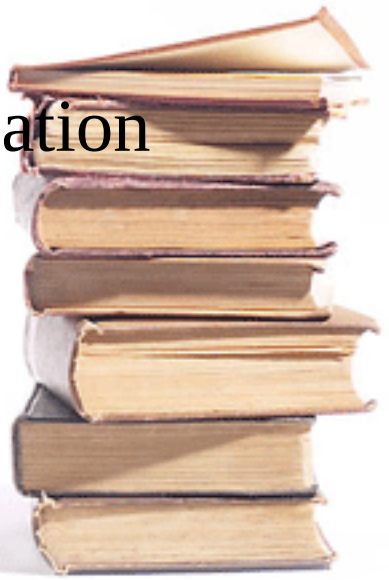
- What is epidemiology?
- History of epidemiology
- Basic knowledge of epidemiology
- The Steps of epidemiology investigation



What is epidemiology

- Epidemiology can be defined as the study of the frequency, distribution and determinants of health and disease in populations.
- *Epidemiology is the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to control of health problems.(Last 1988)*

History of Epidemiology

- The population-level study of death and disease started with the Scientific Revolution of 18th century Europe
- The origins of the observational study of disease occurrence began with Dr. John Snow's analysis of cholera epidemics in London
- From this achievement, epidemiology has become a comprehensive field that combines observational methods with analytic techniques to describe the risk of disease in qualitative and quantitative terms

John Snow 1813-1858

Current applications of epidemiology

- Epidemiology has become an integral component of modern veterinary medicine. In addition to providing a comprehensive perspective of a disease problem at the level of the individual animal, it aids in the design of prevention and control strategies at the international level.
- Practical applications of epidemiology include disease investigation, improvement of productivity, economic assessment, risk analysis and the design of prevention and control strategies.

Fundamental epidemiological terms

- Population
- Disease
- clinical/subclinical
- Carrier
- Immunity
- endemic stability
- Reservoir
- iceberg/pyramid concept
- endemic
- epidemic
- outbreak

population

- A simple definition of a population is a group of individuals.
- To communicate epidemiological information to others, you must define any population you are referring to as clearly as possible.
- Populations can be divided into sub-populations or subgroups based on features of the animals, their management or their environment, etc..

Disease

- **Disease** can be defined as a state in which an animal is not in good health.
- \This includes contagious and non-contagious illnesses. The Oxford dictionary's definition of disease is:
  - an unhealthy condition of the body (or a part of it) or the mind;
  - illness, sickness.

- The use of the term disease usually relies on the results of a diagnostic test or specific clinical criteria. When an animal is noticeably sick, the disease is said to be **clinical**.
- When an animal is infected or otherwise unhealthy, but appears normal, the disease is said to be **subclinical**.
- Animals that recover from infection but remain infective to other animals are called **carriers**, or ‘persistently infected’.

Immunity

- **Immunity** is the ability of animals to resist infection. Acquired immunity is immunity that an animal develops at some time during its life and can be classified as active or passive.
- **Active immunity** results from an actual infection with the agent, whereas passive immunity is acquired either from the mother or from the administration of antibodies (either anti-serum or immunoglobulin).
- **Innate immunity** (or natural immunity) is usually a genetic resistance to infection that is not dependent on an animal's exposure to an agent either directly or via its mother.

herd immunity

- herd immunity is the ability of a group of animals to resist becoming infected or to minimise the extent of infection (i.e. the number and/or the severity of cases).(Martin et al. 1987)
- Herd immunity can be acquired or innate.

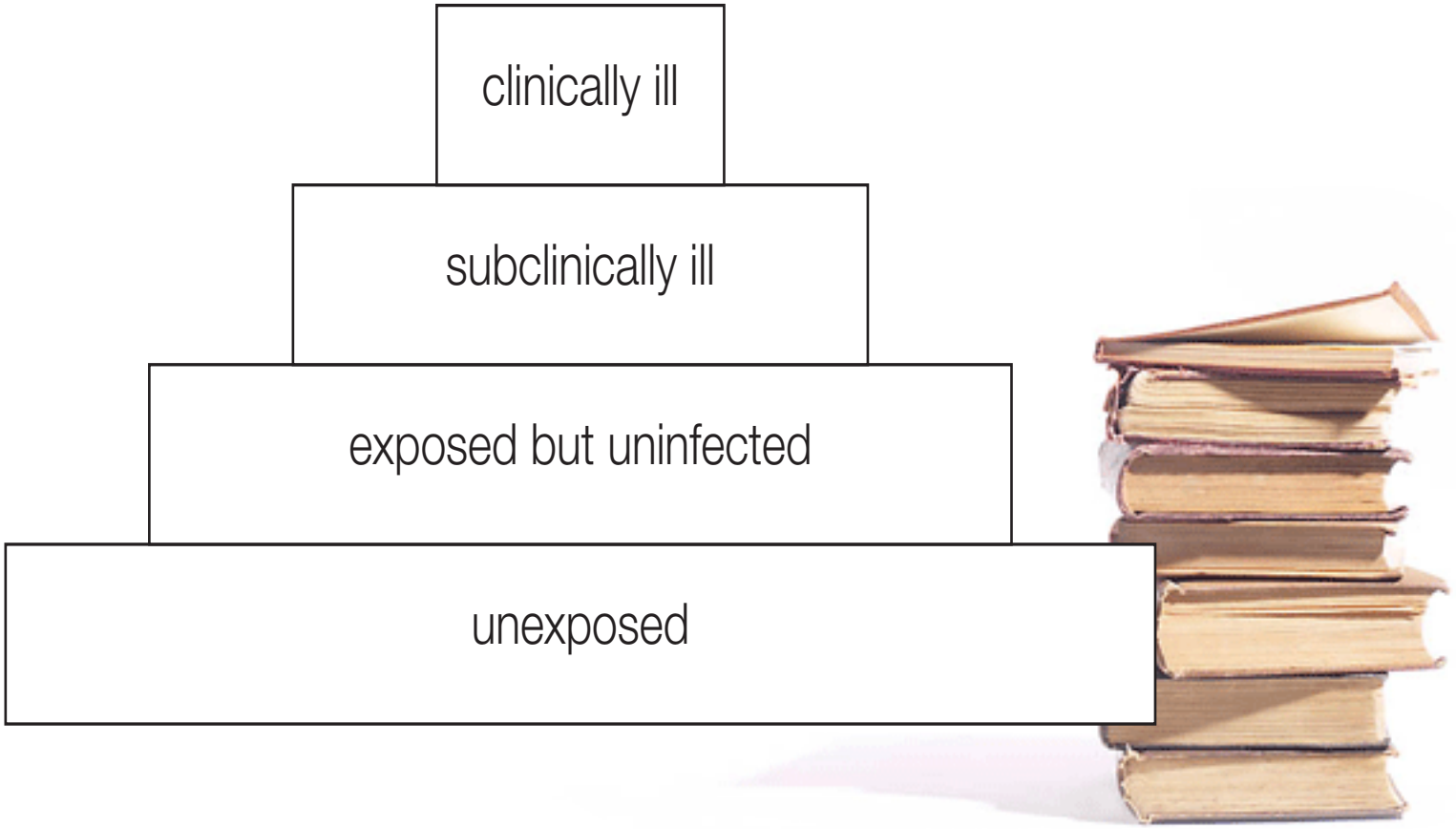
reservoir

- The **reservoir** of disease is the natural host or habitat of the infectious agent.
- A reservoir is often a wildlife species in which infection has become endemically stable.
- Infection is then transmitted from the reservoir to susceptible livestock species.

iceberg

- **the tip of the iceberg that is above sea level and can be seen by passing ships. The much larger part of the iceberg that remains under water**
- **to the diseased (or infected) animals in the population that are clinically ill and can be observed to have disease.**
- **all of the diseased (or infected) animals in the population that are not showing clinical signs (subclinically ill).**
- **iceberg attempts to remind us that the clinically ill animals are usually only a small proportion of all diseased (infected) animals in the population.**

iceberg


clinically ill
subclinically ill
exposed but uninfected
unexposed

endemic

- used to describe disease occurrence with a predictable pattern, either low, medium or high frequency.
- Usually, *Endemic is used in two senses to describe:*
  - *the **usual frequency or occurrence** of a disease in a population;*
  - *the **constant presence** of a disease in a population.*
- *Thus the term implies a stable state; if a disease is well understood, then its endemic level is often **predictable**.*
- Endemic disease can be contrasted with epidemic disease and disease outbreak.

epidemic

- **Epidemic** disease is an unexpected and substantial increase in disease incidence from the normal level.

outbreak

- An **outbreak** is the occurrence of a disease event in one or more animals that is clustered in time and space.
- outbreak and epidemic are often used synonymously.
- outbreaks do not always lead to epidemics.
- However, an outbreak can lead to an epidemic that can, over time, become endemic.

qualitative and quantitative epidemiology

- epidemiology investigation can be divided into two main branches, qualitative and quantitative epidemiology.
- Although ultimately these two branches complement each other and are used together to develop and prioritise livestock disease control, each encompasses its own principles and techniques.
- An epidemiological investigation can be qualitative, quantitative, or both.

Qualitative epidemiology investigation

- A qualitative evaluation of disease events investigates the characteristics and distribution of a disease as well as the relevant transmission dynamics.
- This is done by collecting data on potential factors of disease from affected populations, such as species, breed, location, age, and so on.

Quantitative epidemiology investigation

- An important role of veterinary epidemiology is to quantify disease occurrence in a population.
- It is often useful to know how extensive an animal health problem is:
- how many animals are affected, or how many farms, for example.
- This information helps farmers, private veterinarians and regional or national authorities to determine the best approach to take for diagnosis and control.
- Livestock production levels are also quantified to evaluate productivity and search for problems.
- Productivity might be measured with parameters such as milk yield, live-weight gain or lambing rate.
- Data on several characteristics of the livestock or farms may be collected at the same time as production data, and factors that might limit or otherwise affect productivity can be identified.

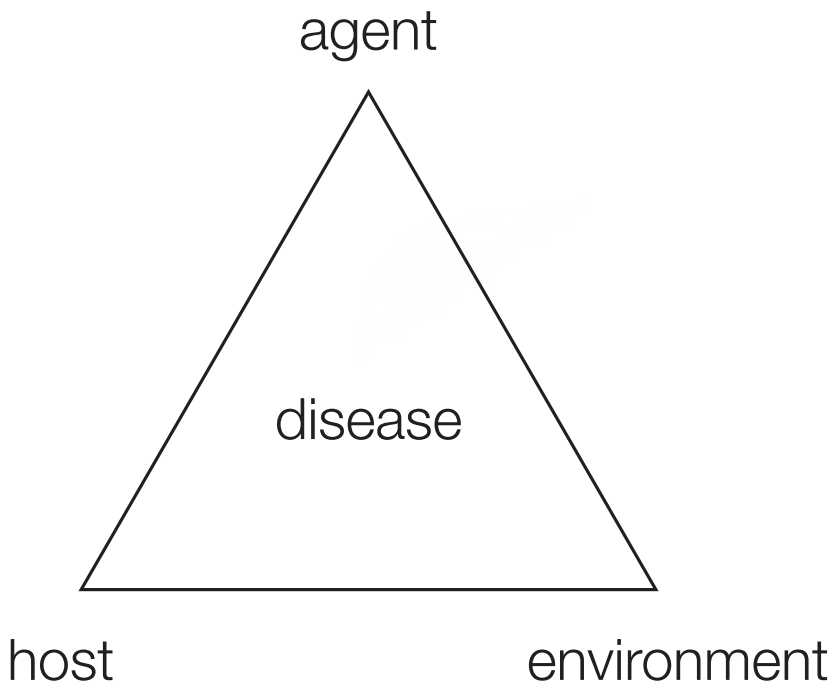
Factors of disease

- Whether or not an animal becomes diseased depends on the interaction of many factors. These can be loosely grouped into agent factors, host factors, transmission factors and environmental factors.
- This itemisation of causal and protective factors helps us to identify areas for intervention to prevent and control disease.

The epidemiological triad

- Traditionally, these factors have been categorised as host factors, agent factors or environmental factors. The three factors were used to construct the epidemiological triad

The epidemiological triad



Agent factors

- The agent is the organism responsible for causing disease. In some diseases several agents act together to cause disease, for example ‘shipping fever’ in feedlot calves, which involves several viruses and bacteria. However, most diseases are caused by a single agent.
- Agent factors are characteristics of the agent that affect transmission and disease presentation in the host animal. The main agent factors are virulence, infectivity and stability.

Host factors

- Characteristics of the host (the affected animal) can make it either more or less susceptible to disease.
- Basic characteristics such as age, breed, immune status or production status are often important factors of disease.
- For example, lactation is a key factor in mastitis; absence of pigmentation is a key factor in squamous cell carcinomas of cattle. These are features specific to each individual host.

- The host factors that most frequently influence disease occurrence include:
  - species
  - breed
  - genotype
  - age
  - sex
  - physical characteristics (such as size and conformation).

Factors of transmission--1

- Diseases are transmitted either directly or indirectly.
- Direct transmission of disease occurs from one individual animal to another. This might be through contact between a susceptible animal and an infected animal, resulting in exposure to an agent; for example, two pigs in the same pen can transmit Aujeszky's disease (pseudorabies) by nose-to-nose contact.
- Direct transmission can also occur during mating or from close contact with aerosols emitted from coughing or sneezing. This type of direct transmission is described as horizontal transmission
- vertical transmission (another type of direct transmission) which involves spread of infection from dam to offspring.

Factors of transmission--2

- Indirect transmission of disease occurs when the disease agent is conveyed to a susceptible animal via a vector (an object or insect or a non-susceptible animal), or airborne over long distances on dust particles or in large droplets.
- For examples:
  - mastitis, which is transmitted between cows on milking equipment;
  - foot and mouth disease virus, which can reach susceptible animals by becoming airborne.
- Transmission factors essentially comprise aspects of the mode of transmission (direct or indirect) and the vector, if indirect.

Interaction of factors

- The factors described above act together to influence whether or not a susceptible animal becomes diseased
- these factors might also interact with each other to make disease occurrence either more likely or less likely than expected from consideration of the factors individually.
- to identify all the possible components of a livestock disease thereby determine all feasible interventions that might be considered

Patterns in disease occurrence

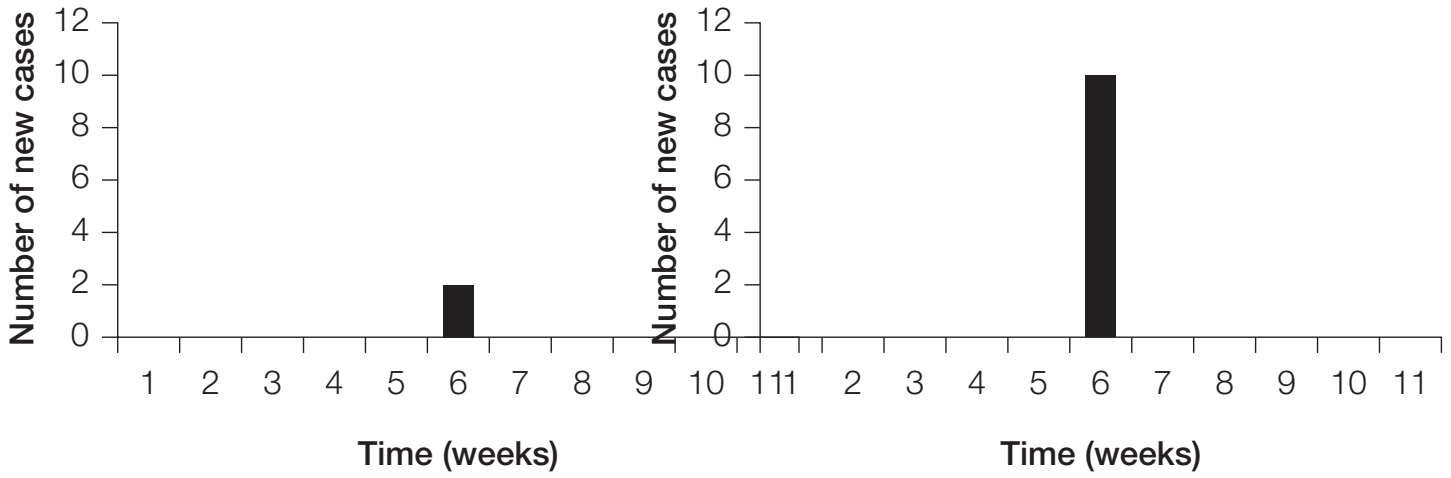
- patterns in disease occurrence can implicate potential factors of disease.
- Patterns can be seen when you step back and take a population view of a disease situation.
- By noting the characteristics of all animals affected and any common factors in their environment, you might discover for instance that most of the affected animals are of a specific age or production status, or most of them share the same water or feed source.
- If a pattern is detected, it might indicate an underlying disease factor that could be targeted to control or prevent further disease.

Patterns in animals

- Animal-associated patterns of disease occurrence can be seen as higher incidences in certain species, breeds, ages, or production types.

Patterns in time

- Temporal patterns can tell a great deal about disease transmission and cause.
- In some instances disease cases are observed to be clustered in time and these clusters can occur at either regular or irregular intervals.
- Diseases occurring at regular intervals might have a seasonal pattern Or they may occur at times linked with specific management events, such cattle being turned out to pasture.
- Diseases occurring at irregular intervals might be related to owner-controlled events (holidays, agricultural shows, trips to market, etc.) or natural events (unusually heavy rainfall, or uncommon droughts).


Number of new cases
0
2
4
6
8
10
12
1 2 3 4 5 6 7 8 9 10 11
Time (weeks)

Number of new cases
0
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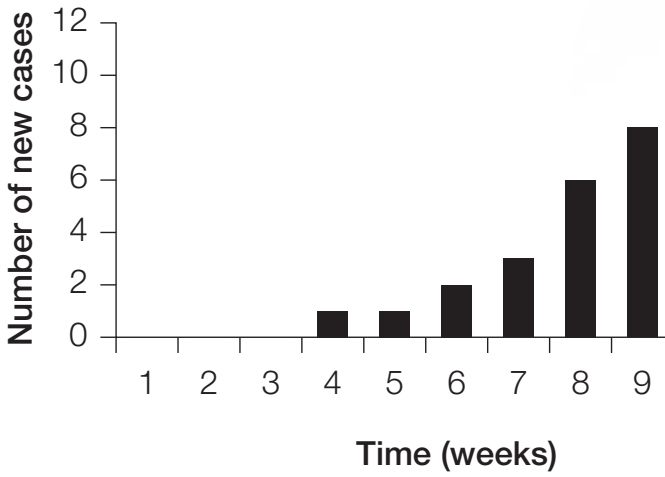
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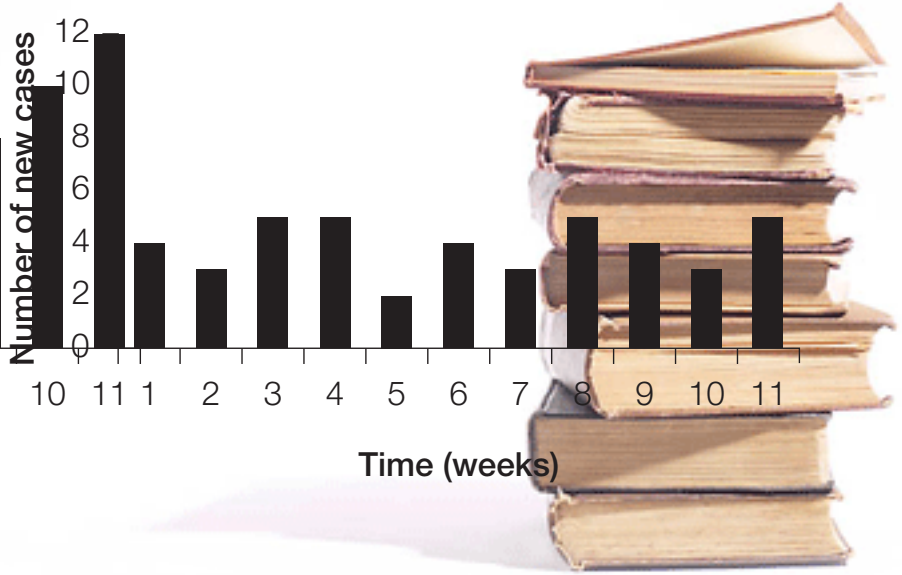
Time (weeks)


Number of new cases
0
2
4
6
8
10
12
1 2 3 4 5 6 7 8 9 10 11
Time (weeks)

Spatial patterns

- When diseases are clustered by location, they are referred to as having a spatial pattern. An infectious disease that affects a population tends to cause a contiguous spatial pattern.
- This is in contrast to sporadic non-infectious diseases that tend to be distributed randomly over a region.
- However, this is not always the case and some infectious diseases can appear to have random spatial patterns, such as those spread by breeding techniques (artificial insemination or stud animals) or by feed.
- A major advance in this area is the availability of computer software that allows epidemiologists to analyse statistically the spatial distribution of animal disease.

Determination of causation

- An underlying aim when investigating livestock health problems is to establish the cause of disease in order to treat the animal, control the disease and prevent recurrence.
- For many diseases, the primary causal agent is known, but new diseases continue to appear (BSE, for example) for which causes must be determined. Also, many diseases have several causal factors and elucidating previously undetermined factors might provide helpful information for disease prevention and control.

- Finding an association between a disease and a potentially causal factor does not mean that the factor is the cause of the disease.
- Often disease is the result of several causal factors acting together. When an association between a disease and a factor is detected, it might simply be coincidence, or the factor could even be a result of the disease.

Some key terms in disease causation

- risk factor
  - is a factor that increases or decreases the risk of disease; for example, poor ventilation is a risk factor for respiratory disease in chickens.
- **causal factor**
  - is more directly responsible for causing disease; in the same context, buying infected chickens and placing them in contact with a susceptible flock will cause the susceptible flock to develop infection.
- necessary/sufficient cause
  - is an actual agent of disease, such as the HPAI virus that causes infectious HPAI of poultry.

Criteria for determining causation

- In the 1800s, Henle formulated the first set of criteria for establishing a link between micro-organisms and disease.
- In 1877, Robert Koch (a scientist who discovered the causal bacteria of tuberculosis and cholera) developed these into the Henle-Koch postulates, revising them in 1882.
- These postulates state that to be considered the cause of a disease, an organism must:
  1. be present in every case of disease (a ‘necessary’ cause)
  2. not be present in other diseases (a ‘specific’ cause)
  3. be isolated and grown in pure culture
  4. be capable of inducing disease in susceptible animals (a ‘sufficient’ cause).

In 1976, this Criteria was modified by Evans and referred to as the ‘unified concept of causation’.

1. The proportion of individuals with the disease should be significantly higher in those exposed to the putative cause than in those not exposed.
2. The exposure to the putative cause should be more common in cases than in those without the disease.
3. Exposure should precede the disease.
4. There should be a measurable biological spectrum of host responses, from mild to severe, following exposure.
5 The disease should be reproducible experimentally.
6 Preventing or modifying the host response should decrease or eliminate the expression of disease.
7 Elimination of the putative cause should result in a lower incidence of the disease.

outbreak investigation

1. Prepare for field work
2. Establish the existence of an outbreak
3. Verify the diagnosis
4. Define and identify cases
5. Perform descriptive epidemiology
6. When necessary, reconsider/redefine hypotheses and execute additional studies
7. Communicate findings

1. Prepare for field work

- Investigation
  - Assemble appropriate supplies and personal protective equipment (PPE), if needed.
  - Familiarize yourself with the suspect disease
  - Assemble useful references and investigation forms which may be created for the outbreak
  - Know who you will be interviewing and where they will be
- Consultation
  - Know your expected role in the field
  - Know who if anyone to report to when you arrive at your destination
  - Know who to call if you have questions

2a. Establish the existence of an outbreak

How Department of Animal Health staff would be notified of a possible outbreak

- Regular analysis of surveillance data
- More commonly, calls from health care providers or citizens about "cases"
- Confidential Morbidity Reports
- Laboratory Reporting

2b. More on establishing the existence of an outbreak…

- Determine if the observed number of cases is greater than the expected number of cases
  - Compare with the number of cases from the previous few weeks or months or from a comparable period during the previous few years

2c. Is the excess really an outbreak?

- Excess may not necessarily indicate an outbreak
  - What else can contribute to an increased number of reported cases?
    - Reporting procedure changes
    - Changes in case definition
    - Improvements in diagnostic procedures
    - Increased interest because of media awareness
      - Increased awareness of health practitioners often leads to increased reporting

3. Verify the diagnosis

- **Confirm that the problem has been properly diagnosed**
  - Rule out laboratory error as basis for increase in diagnosed cases
- **Review clinical findings**
- **Summarize clinical findings with frequency distributions**

4a. **Define** and identify cases

- **Establish a case definition**
  - Case definition is a standard set of criteria for deciding whether an individual should be classified as having the health condition of interest
  - Case classifications
    - **Confirmed case:** A case that is classified as confirmed for reporting purposes. May also be epidemiologically linked case or laboratory-confirmed as a case
    - **Probable case:** A case that is classified as probable for reporting purposes. There may be supportive laboratory results or inconclusive laboratory results
    - **Suspected case:** A case that is classified as suspected for reporting purposes. Some diseases require laboratory confirmation for diagnosis regardless of clinical symptoms, others are diagnosed based on epidemiologic data
      - Suspect cases may be dropped when case definition is tightened over the course of the investigation

4b. Define and **identify** cases

- Identify and count cases
  - "Cast the net wide"
    - Use as many sources as you can
    - Enhanced passive surveillance
    - Active surveillance
    - Conduct a survey if outbreak is in a restricted population

4c. Types of information collected on potential cases

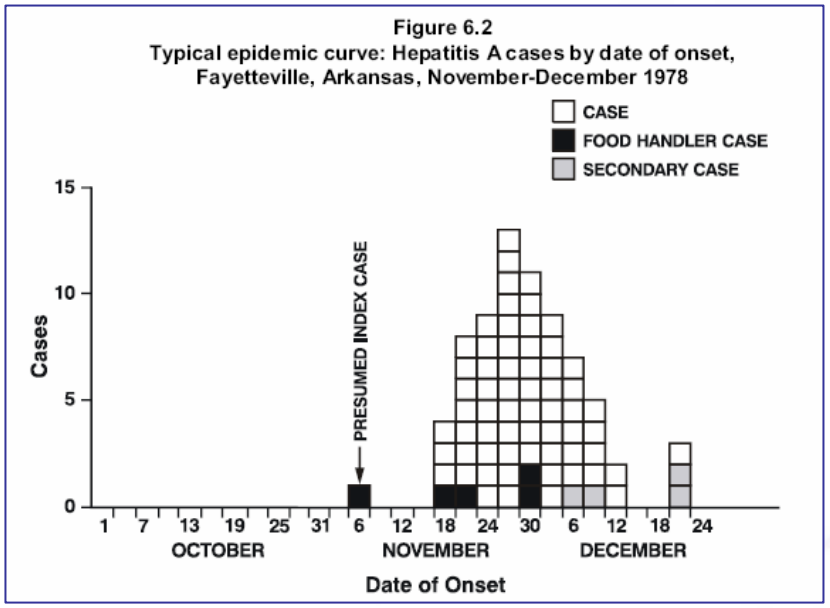
- Standard case reporting forms should be used for data collection.
- Consult with Disease Control for the appropriate communicable disease investigation form to use for the specific disease being investigated
  - Information collected includes
    - Identifying
    - Demographics
    - Clinical
    - Risk Factor
    - Reporter

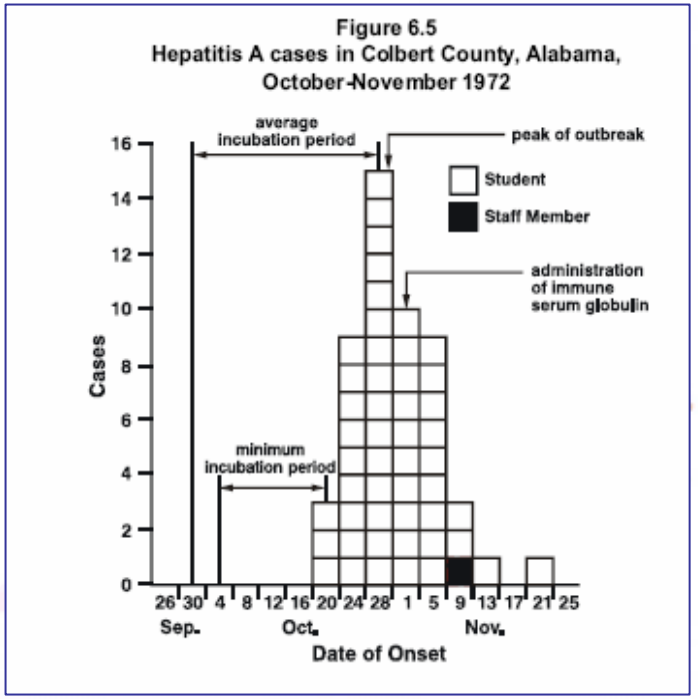
5a. Descriptive Epidemiology

- The following 3 slides demonstrate what is done with information that you have collected in the field
- These analyses are typically done by County epidemiologists back in the office
- In the case of a multi-jurisdictional outbreak the analysis may be done by another county or CDHS

5b. Time

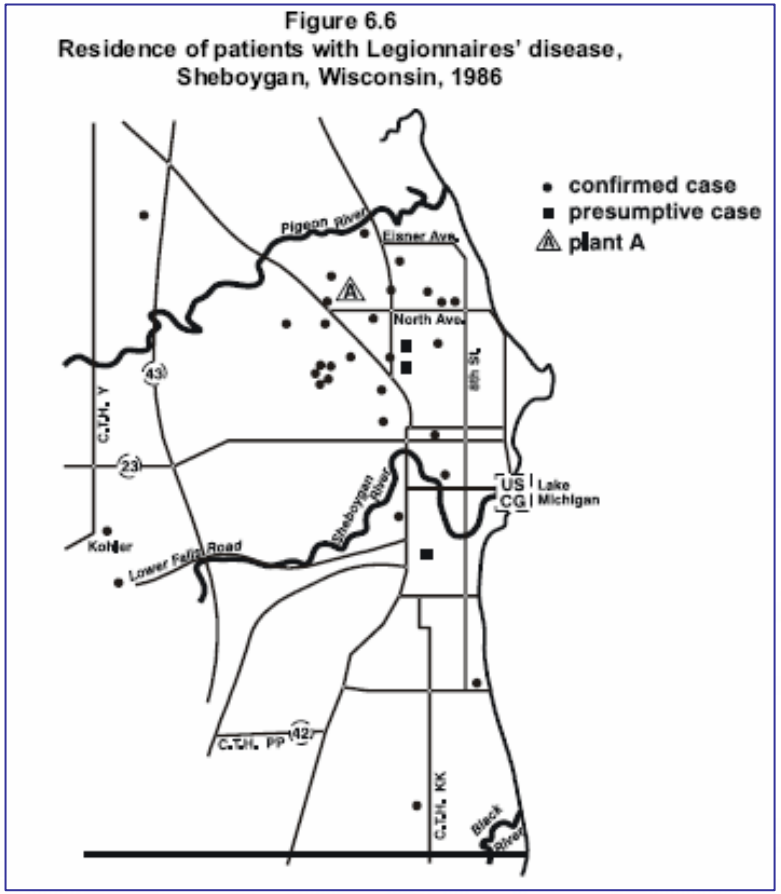
- Epidemic curve
  - Depicts time course of the outbreak by drawing a histogram of number of cases by their date of onset





5c. Place

- Provides geographic extent of problem
- May demonstrate clusters or patterns that provide important etiologic clues
- Spot map useful for illustrating where cases exist or may have been exposed



6. Develop hypotheses (a hypothesis is a conclusion drawn before all the facts are established and tentatively accepted as a basis for further investigation)

- To be addressed
  - Causative agent
  - Mode(s) of transmission
  - Exposure(s) that caused the disease

7. Evaluate hypotheses

- From the information gathered in an investigation, epidemiologists can run analyses to test whether hypotheses about the source of the outbreak are true
  - We can compare hypotheses with established facts
  - Analytic epidemiology can be used to quantify relationships
    - Cohort studies
      - Relative risk (ratio of attack rates) can be calculated
    - Case-control studies*
      - Odds ratio can be calculated

8. Reconsider/refine hypotheses

- Sometimes analytic studies are unrevealing
  - Consider new modes of transmission
- Execute additional epidemiologic studies
  - Laboratory
  - Environmental

9 Communication

- Written report
  - Should follow scientific format
    - Introduction, background, methods, results, discussion, recommendations
  - Will be used as reference by animal health department for future outbreaks
  - Will Contribute to knowledge base of epidemiology and animal health

Stages of an outbreak investigation

- There are six stages to an outbreak investigation:
  - the diagnostic phase
  - the descriptive phase
  - the investigative phase
  - the analytical phase
  - the intervention phase
  - the monitoring phase.

Outbreak investigation – a worked example

- *History*
- *Preliminary diagnosis*
- *Description of outbreak*
- *Analysis*
- hypothesis
- Options for control

History

- A farmer calls the local veterinarian to investigate a problem with reduced egg production in her 1600-hen, brown-egg-producing flock. During the past two weeks, egg production in some sections of the barns has decreased by between 2% and 30%. The immediate action taken by the vet has include submission of three poorly-looking hens to the local diagnostic laboratory, where the hens tested negative for Newcastle disease, influenza virus and infectious bronchitis. The veterinarian decides to adopt an epidemiological approach for investigating the problem.

Preliminary diagnosis

- General knowledge about reduced egg production in chickens indicates that most flocks have small depressions in egg yield periodically but not usually as profound as 30%. The potential problem could be environmental (temperature, ventilation, etc.), managerial (for example, if an employee inadvertently fed inappropriate feed or administered contaminated water) or infectious (such as Newcastle disease virus, influenza virus, egg drop syndrome virus, or infectious bronchitis).
- In this case, as a first step in the investigation, a diagnosis has to be verified. For this purpose, further unhealthy-looking hens are necropsied and more samples submitted to the diagnostic laboratory. Eggs are also obtained from affected and non-affected sections of the barns and sent to the laboratory. A **case definition** for reduced egg production in a section of the poultry barn is: a reduction in egg output of greater than 15% compared to production for that section in the previous month

Description of outbreak

- 11 out of 16 sections are affected in this flock (68.8%).
- Population at risk: 16 sections (1600 hens).
- Cumulative incidence (CI)

Analysis

- List of potential factors:
  - whether any hens in the section were new to the flock
  - average age of hens in the section
  - stocking density of hens in the section
  - location in the poultry barn.

Working hypothesis

- Firstly, in this particular case, the statistical power was quite low because of the small number of sections (16) available for analysis. Therefore, although most of the suspected factors were not found to be statistically significant, this analysis does not give strong evidence that they are not significant.
- If the risk of reduced production is found to be related to stocking density or section location, this could indicate a management problem. The section location in the poultry barn might be an indicator of inadequate disinfection and cleaning procedures.
- A second hypothesis is an infectious aetiology which might be indicated by the increased risk when new hens are present in a section, and the possible influence of the average age of the hens.
- Therefore, there are two main hypotheses that could be further investigated to come up with a set of suitable preventive measures.

Options for control

- To test the hypothesis of a management problem, the investigator could closely inspect the barn and observe the cleaning and disinfection programme on the farm.

- Thank you!!!