Epidemiology Session
Principles of epidemiology and surveillance and their application to aquaculture

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FAO/ASTF Project: GCP/RAF/510/MUL:
Enhancing capacity/risk reduction of emerging Tilapia Lake Virus (TiLV) to African tilapia aquaculture: Intensive Training Course on TiLV
4-13 December 2018. Kisumu, Kenya
in cooperation with Kenya Marine Fisheries Research Institute (KMFRI) and Kenya Fisheries Service (KeFS)
Available resources & useful references
Overview

• What is epidemiology
• The epidemiological approach
• Investigating disease outbreaks
• Causality
  • Patterns of disease
• Measuring disease frequency
Social & environmental determinants

Primordial prevention
Actions and measures that inhibit the emergence of risk factors (environmental, social, economic, cultural, behavioral, etc.)

Primary prevention
Actions taken prior to the onset of TiLV, which removes the possibility that the TiLV will ever occur

Secondary prevention
Actions which halt the progress of TiLV and its incipient stage and prevents complications (early diagnosis and adequate treatment)

Tertiary prevention
All the measures available to prevent new TiLV outbreaks and further deterioration through tilapia monitoring and recovery

Best management practices for Tilapia health
What is aquatic epidemiology?

• The study of disease in fish populations and of factors that determine its occurrence; the **keyword** being **fish populations**

• Additionally includes investigation and assessment of other health-related events, notably productivity

• All of these investigations involve observing fish populations and making inferences from the observations

• An integrating science with close links to clinical and laboratory medicine as well as biostatistics and health economics
Diseases in fish populations

Fig. 1.1. Representation of the relationship between the traditional perspective of investigating disease and a population perspective.
Diseases in fish populations

• Most diseases do not occur at random in a fish population – they follow distinct patterns according to exposure of individuals in the population to various factors associated with the host, agent and environment.
Web of causation for fish diseases

Objectives of epidemiology

• Detecting the existence of a disease or other production problem
• Identifying the causes of disease
• Estimating the risk of becoming diseased
• Obtaining information on the ecology and natural history of the disease
• Defining and quantifying the impact and extent of the problem
• Planning and evaluating possible disease control strategies and biosecurity measures
• Monitoring and surveillance to prevent further disease episodes
• Assessing the economic impact of disease and control programs
The Role of Epidemiology in Policy Development


• Effective animal health policy development requires:
  • a sound scientific basis
  • clear understanding of social and political context in which policy is being made.

• Successful interventions need to be:
  • Politically, socially and economically acceptable
The Veterinarian’s Role in Food Animal Practice Changing Over Time

- 1900
- 1950
- 1990
- 2000

Focus on Single Animals
Controlling Epidemics, Treating Diseases
Eradicating Pathogens, Increasing Herd Health & Production
Focus on Herd
Standardization and Certification of Herd Health, Food Safety, and Food Quality

Consumer Concerns with Food Safety and Food Quality
High

Low
Components in epidemiology

• The first stage in any investigation is the collection of **relevant data**
• Investigations can be either **qualitative** or **quantitative** or a **combination** of these two approaches

• **Qualitative investigations**
  • The natural history of disease
  • Causal hypothesis testing

• **Quantitative investigations**
  • Surveys
  • Monitoring and surveillance
  • Epidemiological studies
  • Modeling
  • Risk assessments
  • Disease control
Components in epidemiology

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Natural history of disease

• Is the progression of a disease process in an individual over time, in the absence of treatment.

• The ecology of diseases, including the distribution, mode of transmission and maintenance of infectious diseases, is investigated by field observation.
Natural history of TiLV
(do we have drawn this?)

- Exposure
- Pathologic Changes
- Onset of Symptoms
  - Usual time of diagnosis

| Stage of Susceptibility | Stage of Subclinical Disease | Stage of Clinical Disease | Stage of Recovery, Disability or Death |

May vary from fish to fish and are influenced by preventive and therapeutic measures
Causal hypothesis testing

- If field observations suggest that certain factors may be causally associated with a disease, then the association must be assessed by formulating a causal hypothesis.

- Causality (the relating of causes to effects) is described later

- Qualitative investigations were the mainstay of epidemiologists before the Second World War.
Components in epidemiology

- The first stage in any investigation is the collection of relevant data
- Investigations can be either qualitative or quantitative or a combination of these two approaches
- Qualitative investigations
  - The natural history of disease
  - Causal hypothesis testing
- Quantitative investigations
  - Surveys
  - Monitoring and surveillance
  - Epidemiological studies
  - Modeling
  - Risk assessments
  - Disease control
Surveys

• A survey is an examination of an aggregate of units (e.g., a group of fish)
• The examination usually involves counting members of the aggregate and characteristics of the members
• In epidemiological surveys, characteristics might include the presence of particular diseases, or production parameters such as harvest yield.
• Surveys can be undertaken on a sample of the population. Less commonly, a census, which examines the total fish population.
Monitoring

• Monitoring is the making of routine observations on health, productivity and environmental factors and the recording and transmission of these observations.

• Thus, the regular recording of harvest yields is monitoring, as is the routine recording of tilapia fillets inspection findings at processing plants.

• The identity of individual diseased fish usually is not recorded.
Surveillance

• Surveillance is a more intensive form of data recording than monitoring.

• Includes all types of disease - *infectious and noninfectious* - and involves the collation and interpretation of data collected during monitoring programs, usually with the recording of the identity of diseased fish or farms, with a view to detecting changes in a fish population's health.

• It is normally part of control programs for specific diseases.
Types of Epidemiological Studies

- **Observational studies**
  - Descriptive
    - Sampling independent of exposure and disease status
  - Cross-sectional
  - Case-control
  - Cohort

- **Intervention studies**
  - Randomized assignment to intervention and control groups but little control of disease challenge and environment

- **Theoretical studies**
  - Mathematical modelling

**Fig. 1.3.** Classification of quantitative epidemiological study types.
Epidemiological approach

• The key to any successful epidemiological investigation is to use a structured approach, being as systematic as possible and always ensuring that the current working hypothesis is that which is most consistent with available data and information.

• Use of a clear, objective and well-structured approach will ensure that your conclusions and recommendations are easily understood, and that the process of arriving at these conclusions is transparent.
Epidemiological approach

- Evaluate Patterns in fish populations!
- Describe
  - Current status (ill, not ill, recovered, dead, etc)
  - Changes over time
- Make comparisons
  - Between groups
  - Changes over time
- Establish cause
  - Initiate preventive or corrective measures
Epidemiological approach

• The Five W’s
  • Who ?
  • Where ?
  • When ?
  • What ?
  • Why ?
• Determining “Why” is the ultimate goal!
Epidemiological approach: first step

• To define clearly the problem and the scope, context and expected outcomes of the investigation.
• This might include determining if there is a disease problem and, if there is, to:
  • determine the extent and impact of the problem;
  • identify possible and probable cause(s) and source(s) of the problem;
  • identify likely risk factors for the disease; and
  • make recommendations for control and/or treatment and for future prevention.
SMART Objectives

• *Specific;*
• *Measurable;*
• *Achievable;*
• *Relevant;* and
• *Time-limited.*
Operational Issues

- Make sure that the terms of reference are clear and specific and understood.
- Are the project milestones and deadlines clearly defined and reasonable?
- If there are multiple people or organizations involved ensure that it is clear who is responsible for what, and particularly what your responsibilities are. For example, if you are expecting your client to provide data or assistance in some form be sure that this is clearly stated in your agreement with them, otherwise they might regard it as your responsibility to obtain the data.
- If there are costs associated with obtaining data, are these included in the budget?
- What resources will be available and who will provide them?
- Who will direct the project – who is in charge and what is the chain of command?
- How will data be shared and who will do the analysis?
- Who is responsible for project management (physical and financial), communication, collaboration, etc.?
- Who is responsible for collection, filing and collating of material?
- Who is responsible for writing the final report and in what format is it required?
- What other project outputs are required?
- Are the budget and payment schedule clear and appropriate?
Overview

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• Causality
• Patterns of disease
• Measuring disease frequency
Causes of disease?

- Any “Exposure” that leads to new cases of disease
- Therefore, remove exposure and prevent some cases of disease
Causes of disease

• Examples:
  • Agent?
  • Host?
  • Environment?
Agent Factors

- Infectivity
- Pathogenicity
- Virulence
- Immunogenicity

- Host Range
- Life Cycle
- Reservoir
- Genetic Stability
Host Factors (exposures)

Intrinsic Factors

• Immunity
• Development stage or age
• Sex
• Strain
Host Factors (exposures)

Extrinsic Factors

- Use/occupation
- Nutritional
- Transportation
- Behavior
Host Factors (exposures)

Population Interactions

- Immunity $\leftrightarrow$ most important factor
- Development stage or age
- Sex
- Strain
- Use / occupation
- Nutritional
- Behavior
Herd Immunity

Resistance of a group of fish to the invasion and spread of an infectious agent, because of the collective immunity of the group due to vaccination or prior exposure

Herd Immunity = \frac{\text{No. resistant fish}}{\text{Total number in farm}}
Herd Immunity

Underlying principle: transmission of infectious disease within a farm is primarily affected by

- Proportion of resistant/susceptible fish
- Effective contact rate between fish
Herd Immunity

- Equally Susceptible
- Immune
- Infected

- Individuals can have equal “biological” susceptibility but differ in likelihood of exposure
Environmental Factors (exposures)

- Climate
- Landscape and geography
- Flora and fauna
- Geology
- Hygiene

- Housing
- Noise
- Water (temperature, salinity, oxygen, etc.)
- Currents
- Vector exposure
Infectious Disease Concepts

• Exposed
• Contaminated
• Colonized
• Infested
• Infected
• Infectious
• Infectivity
• Contagious
• Pathogenicity
• Virulence
Infectious Disease Concepts

• **Pathogenicity**
  • the ability to produce clinical disease
  • refers to the proportion of infections that result in disease, and does not take into account the severity of the disease

\[
\text{Pathogenicity} = (\text{mild signs} + \text{mod. signs} + \text{severe signs} + \text{deaths})
\]

All infected fish
Infectious Disease Concepts

Virulence

severity of a disease
the ability of the agent to produce severe disease

\[ = (\text{severe signs} + \text{deaths}) \]
all infected fish
Infectious Disease Concepts

- Phenotype/Genotype
- Antigen
- Antigenic
- Incubation period
- Subclinical disease
- Clinical disease
- Carrier
- Persistent infection
- Latency
- Persistence in environment
Natural history of TiLV
Spectrum of disease

Stage of Susceptibility | Stage of Subclinical Disease | Stage of Clinical Disease | Stage of Recovery, Disability or Death

Exposure → Pathologic Changes → Onset of Symptoms

Usual time of diagnosis

May vary from fish to fish and are influenced by preventive and therapeutic measures
Infectious Disease Concepts

- Clinical disease as the tip of the iceberg

Bacterial Kidney Disease (BKD) in salmonids

- Asymptomatic: 20,000
- Mild: 3,000
- Severe: 150
Infectious Disease Concepts

- Contact & Transmission
  - Direct
  - Indirect
  - Fomites or vehicles
  - Vectors
Infectious Disease Concepts

• Evidence of Exposure
  • Direct: Identification of agents (antigen)
    • Culture (incl. biochemical reactions)
    • Polymerase chain reaction (and sequencing of products)
    • Other antigen detection methods e.g. ELISA
  • Indirect: Biological response to agents
    • Pathology on tissues from animal
    • Serum antibody
      • Seronegative vs seropositive (-/+)
      • Seroconversion (change from negative to positive)
      • “Concentration” or a “score” for tests such as ELISA
Forces Influencing Infectious Disease Occurrence

- Agent characteristics
  - Pathogenicity, virulence, infectivity, survival, life cycle, etc.
- Likelihood of exposure
- Host’s ability to mount an immune response against the agent
Environmental Factors

• Micro-environment
  • Proximity or local environment

• Macro-environment
  • General or regional environment

• Social factors
  • Social and political influences
Multiple Causes

- Bovine Respiratory Disease
- Classic veterinary example of multifactorial disease
Risk of Disease Is Not Equal:

Host

- Age affects risk
  - Fresh calves vs. yearlings
- Immunity
  - Exposure
  - Vaccination
- Stress
  - Weaning
  - Transport
  - Processing
  - Mixing
Risk of Disease Is Not Equal:
Agent

- Variability in agents
  - *Manheimia hemolytica* biotypes
  - *Haemophilus somnus*
  - Virus strains (Bovine herpes virus (BHV), bovine respiratory syncytial virus (BRSV), and bovine viral diarrhea (BVD))

- Different agents
  - Bacterial
    - *Pasteurella, Haemophilus, Actinobacillus*
  - Viral
    - BHV, BRSV, Parainfluenza, Coronavirus, BVD?
Risk of Disease Is Not Equal: Environment

- Season
- Transport
- Pasture vs. Background vs. Feedlot
Multiple Levels of Causation

- *e.g.*, Vector borne-diseases
  - Virus or bacteria
  - Mosquitoes, ticks
  - Environment

Remove Exposure ➔ Prevent Disease
Why Worry about Causation?

• We can only prevent disease by removing exposure to causal factors
Causal Factors?

- Two basic philosophies about causation of infectious diseases
  - Presence of an agent $\rightarrow$ disease
  - Agent alone is not sufficient to produce disease
Henle-Koch Postulates

• First recognized criteria for establishing cause:
  • The organism is found in all disease cases.
  • The organism is not found in other individuals as a non-pathogenic parasite.
  • It must be possible to produce a pure, sustainable culture of the organism.
  • It must be possible to experimentally reproduce the same disease in a susceptible host.

One Agent ➔ One Disease
Problems with Koch’s Postulates

• Doesn’t directly relate to non-infectious diseases
• Not every exposed individual becomes infected.
• Not all infected individuals develop disease.
• Not possible to recovery of infectious agents from all infected individuals or even all disease cases.
• Did Koch identify THE cause?
Multiple Causes - Models

- Agent, host, and environment all contribute to the occurrence of disease
- Causal relationships are not always simple
- Models assist with in understanding and describing complex causal relationships
  - Necessary, sufficient, and component causes
  - Web of causation
  - Path models
  - Venn Diagrams
Necessary and Sufficient Causes

• Component cause
  • Any causal factor (Host, Agent, Env.)

• Sufficient cause
  • Set of component causes that is capable of causing disease
  • Once all of the sufficient causes are present, disease **WILL** occur

• Necessary cause
  • Component cause that is **REQUIRED** for disease to occur
Modern concepts of disease
Bradford–Hill criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength of association</td>
<td>Strong associations with higher risk ratios are more likely to be causal than a weak association</td>
</tr>
<tr>
<td>Consistency</td>
<td>Consistently finding an association between a putative cause and a disease outcome in multiple studies by different investigators</td>
</tr>
<tr>
<td>Specificity</td>
<td>If a factor is only associated with a specific disease it was said to be specific and considered more likely to be causal</td>
</tr>
<tr>
<td>Temporality</td>
<td>The causal factor should precede the outcome it is proposed to be causing</td>
</tr>
<tr>
<td>Biological gradient</td>
<td>A dose-response association is supportive of a causal relationship</td>
</tr>
<tr>
<td>Plausibility</td>
<td>Is the association biologically plausible?</td>
</tr>
<tr>
<td>Coherence</td>
<td>The proposed causal association should not contradict current scientific knowledge</td>
</tr>
<tr>
<td>Experiment</td>
<td>A causal association is more likely if it is supported by results from controlled, randomized trials</td>
</tr>
<tr>
<td>Analogy</td>
<td>A causal association may be more likely if there are other examples of causal associations for analogous exposures and outcomes</td>
</tr>
</tbody>
</table>
Necessary and Sufficient Causes

- 10 Component Causes (A, B, C, D, E, ..., J)
- 3 Sufficient Causes (1, 2, 3)
- 1 Necessary Cause (A)
Total factors = 10
5 sufficient causes to disease
One necessary factor
Fig. 4.1. Use of pie charts to demonstrate three separate sufficient causal mechanisms, each made up of multiple component causes identified by letters. There is one candidate necessary cause (E) that is the only component cause found in every sufficient causal mechanism (adapted from Rothman and Greenland, 2005).
How Do Risk Factors Work Together? Mediators, Moderators, and Independent, Overlapping, and Proxy Risk Factors


FIGURE 1. Five Ways Risk Factors A and B Can Work Together to Affect Outcome O

A solid arrow indicates a correlation. A dotted arrow indicates a correlation that weakens or disappears when the other risk factor is considered.

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Left to right positioning indicates temporal order.
Web of Causation

- Mixing
- Previous Exposure
- Stocking Density
- Age
- SRS
- Transport
Path Model: Causal Sequence

- Stocking Density
- Transport
- Mixing
- Age
- Previous Exposure
- BRD
Venn Diagram
Magnitude and Interaction of Causes

Previous Exposure
Age
Mixing
BRD
How Do We Identify Important Risk Factors?

• Summarize disease occurrence in population.
• Compare risk of disease among animals with different exposures.
• Measure associations with disease occurrence.
Why Characterize Populations

• Look for Patterns!
• Describe populations
  • Current status
  • Changes over time
• Make comparisons
  • Between groups
  • Changes over time
  • Establish “cause”
  • Establish preventive measures
Data collection

Source of veterinary data

Qualitative evaluation

The natural history of disease

Ecology
Transmission and maintenance

Casual Factors
Host, agent and environmental

Modelling

Experimental studies
Critical trials; intervention studies

Cross-sectional studies

Longitudinal studies:
Cohort studies
Case-control studies

Causal hypothesis testing

Studies and surveys
Observational studies
Surveys

Cross-sectional surveys
Monitoring Surveillance

Economic evaluation

Disease control
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