Causation and association

❖ **Learning objectives:**

At the end of the lecture the student will be able to

- Explain basic models of disease causation.
- To understand concepts of cause-effect relation

❖ **Introduction**

Although we use analytic epidemiology to search for causes of disease, this is not a straight forward subject.

1. Not all associations between exposures and disease are causal relations.
2. In addition, the accepted models of disease causation all require the precise interaction of factors and conditions before a disease will occur.
3. The concept of cause itself continues to be debated as a philosophical matter in the scientific literature.

❖ **Definitions:**

- **Cause** of disease: a factor (characteristic, behavior, event, etc.) that influences the occurrence of disease. An increase in the factor leads to an increase in disease. Reduction in the factor leads to a reduction in disease.
- If disease does not develop without the factor being present, then we term the causative factor is "**necessary**."
- If the disease always results from the factor, then we term the causative factor **"sufficient."** Exposure

❖ **Example:** Exposure to ***Mycobacterium tuberculosis*** is necessary for tuberculosis to develop, but it is not sufficient, because not everyone infected develops disease.

❖ General Models of Causation:

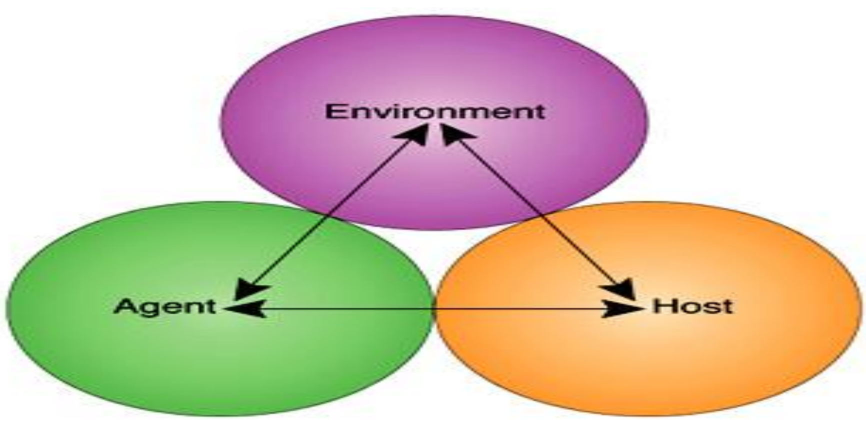
- In epidemiology, there are several models of disease causation that help understand disease process.
- Studying how different factors can lead to ill health is important to generate knowledge to help prevent and control diseases. The most widely applied models are:
  - ☐ The epidemiological triad (*triangle)*,
  - ☐ The *wheel* and the *web*. And others
- The purpose of the model is to facilitate the understanding of nature of causation of disease, which is complex.

❖ The epidemiological triad:

– **It is the traditional model of infectious disease causation**

– **Development of disease is a combination of events:**

- A harmful agent (an external agent)
- A susceptible host
- An appropriate environment



Agent factors

- Infectious agents: agent might be microorganism—virus, bacterium, parasite, or other microbes. e.g. polio, measles, malaria, tuberculosis Generally, these agents must be present for disease to occur.
- Nutritive: excesses or deficiencies (Cholesterol, vitamins, proteins)
- Chemical agents: (carbon monoxide, drugs, medications)
- Generally, these agents must be present for disease to occur. That is, they are necessary but not always sufficient to cause disease

Host factors

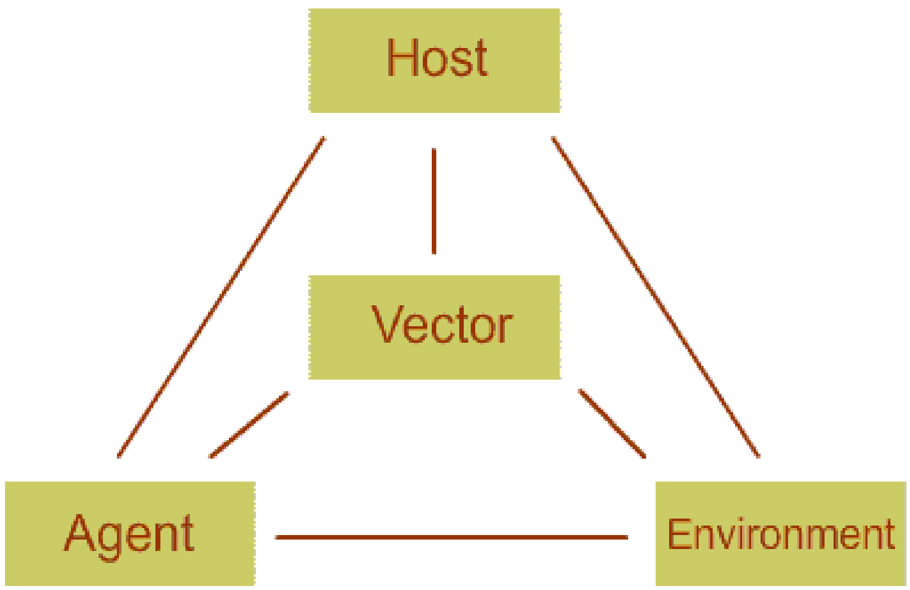
- Host factors are intrinsic factors that influence an individual's exposure, susceptibility, or response to a causative agent.
- Host factors: E.g. Age, race, sex, genetic composition, socioeconomic status, and behaviors (smoking, drug abuse, lifestyle, sexual practices and eating habits) presence of disease or medications, and psychological makeup.

Environmental factors

- Environmental factors are extrinsic factors which affect the agent and the opportunity for exposure.
- Environmental factors include:
    - ☐ Physical factors such as climate; temperature, humidity, ge ology
    - ☐ biologic factors such as insects, snails that transmit an agent; and
    - ☐ Socioeconomic factors such as crowding, sanitation and the availability of health services.
- In this model, the environment influences the agent, the host, and the route of transmission of the agent from a source to the host

– When we search for causal relationships, we must look at all three components and analyze their interactions to find practical and effective prevention and control measures.

The epidemiologic triad Model:



Web of Causation:

There is no single cause

Causes of disease are interacting

<u>Types of causes:</u>

- Sufficient causes:
  - a set of conditions without any one of which the disease would not have occurred
  - not usually a single factor, often several
  - Necessary cause:
  - Must be present for disease to occur, disease never develops in the absence of that factor.

Example

- The tubercle bacillus is required to cause tuberculosis but, alone, does not always cause it,
- So tubercle bacillus is a **necessary**, not a sufficient, cause.

<u>Causation and Association:</u>

- In epidemiology, we determine the *relationship or <u>association</u>* between a given exposure and frequency of disease in populations.
- Association is a statistical relationship between an exposure and disease
- Causation - implies that there is an Association and a true mechanism that leads from exposure to disease

<u>Types of Associations:</u>

- Real (causal)
- Non-causal (Spurious):

Non causal associations depend on bias, chance, failure to control for confounding factors.

Is there an association between an exposure and a disease?"

IF SO….

- Is the association likely to be due to chance?
- If no, is the association likely to be due to bias?
- If no, is the association likely to be due to confounding?
- If no, the association is real(causal)

Epidemiological criteria for causality:

- An association rarely reflects a causal relationship but it may.
- Association implies that exposure <u>might</u> cause disease
- We assume causation based upon the association and several other criteria (Criteria for causality)

<u>Hill's Criteria for Causal Relation:</u>

Temporal sequence
Did exposure precede outcome?

Strength of association
How strong is the effect, measured as relative risk or odds ratio?

Consistency of association
Has effect been seen by others?

Biological gradient (dose-response relation)
Does increased exposure result in more of the outcome?

Specificity of association
Does exposure lead only to outcome?

Biological plausibility
Does the association make sense?

Coherence with existing knowledge
Is the association consistent with available evidence?

Experimental evidence
Has a randomised controlled trial been done?

Analogy
Is the association similar to others?

Temporal sequence (temporality):

- Did the cause precede the effect?
- Temporality refers to the necessity that the cause must precede the disease in time.
- This is the only absolutely essential criterion.
- It is easier to establish temporality in experimental and cohort studies than in case-control and cross-sectional studies.

Strength of association association:

- It refers to the magnitude of the ratio of disease rates for those who have the risk factor and those who do not have it.
- The strength of the association is measured by the relative risk or Odds ratio.

- The bigger the relative risk or odds ratio, the stronger the association and the higher the likelihood of a causal relationship.
- Strong associations are less likely to be caused by chance or bias

Consistency of findings:

- Consistency refers to the repeated observation of an association in different populations under different circumstances by different investigators.
- Causality is more likely when the association is supported by different studies of different designs using different methodology.

Biological gradient (Dose-response relation):

- Does the disease incidence vary with the level of exposure? (dose-response relationship)
- Changes in exposure are related to a trend in relative risk
- A dose-response relationship (if present) can increase the likelihood of a causal association.

Specificity of association:

- It means that an exposure leads to a single or characteristic effect, or affects people with a specific susceptibility
    - easier to support causation when associations are specific, but
        - usually many exposures cause multiple diseases
- This is more feasible in infectious diseases than in non-infectious diseases, which can result from different risk agents.
- Measles virus causes only measles
- But smoking causes lung cancer, coronary heart disease,…

Biological plausibility:

- Does the association make sense biologically

- Is there a logical mechanism by which the supposed cause can induce the effect?
- Findings should not disagree with established understanding of biological processes.

Coherence

- Coherence between epidemiological and laboratory findings
- Coherence implies that a cause-and-effect interpretation for an association does not conflict with what is known of the natural history and biology of the disease

Experimental evidence:

- It refers to evidence from laboratory experiments on animal or to evidence from human experiments (RCTs)
- Causal understanding can be greatly advanced by laboratory and experimental observations.

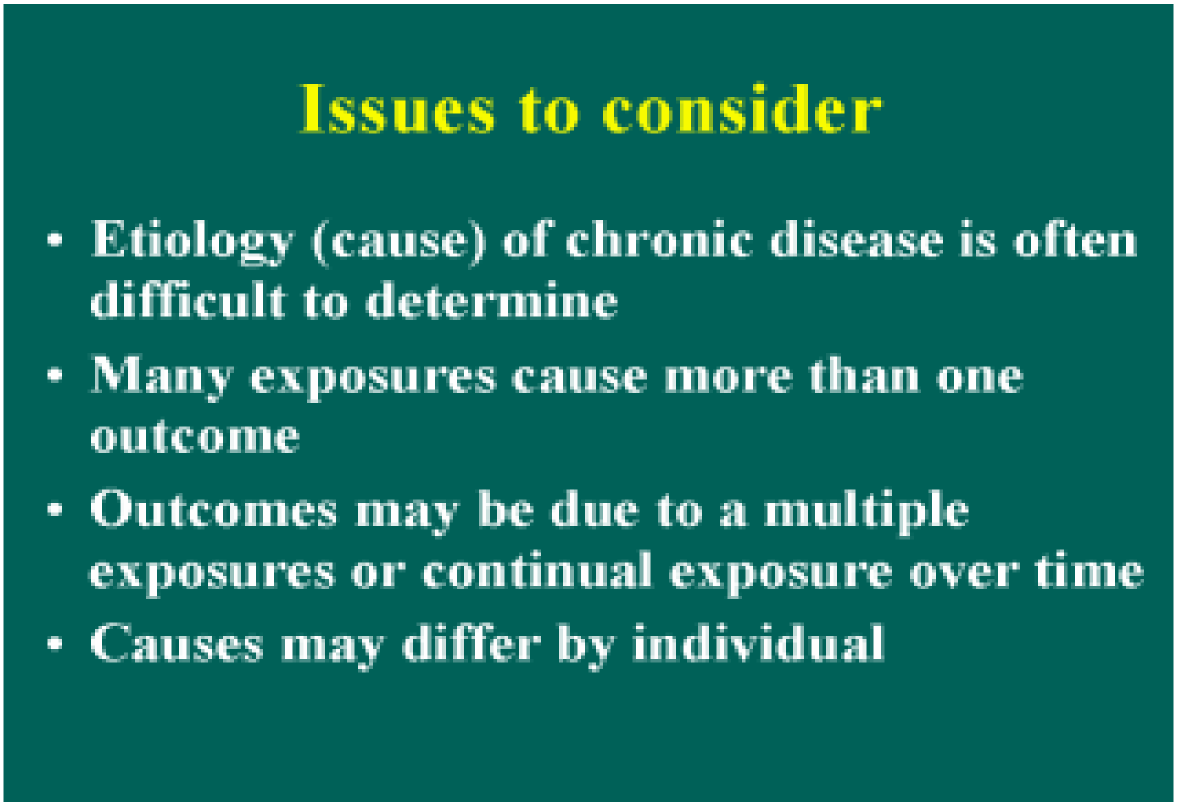
Analogy:

- Analogy:

Consider the effect of similar substances or situations (may be considered).

Judging the causal basis of the association:

- No single study is sufficient for causal inference
- It is always necessary to consider multiple alternate explanations before making conclusions about the causal relationship between any two items under investigation.
- Causal inference is not a simple process
  - consider weight of evidence
  - requires judgment and interpretation



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- **Website http://faculty.ksu.edu.sa/73234/default.aspx**
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