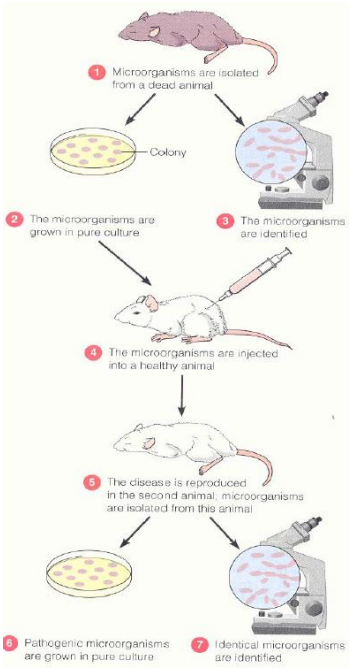
Epidemiology

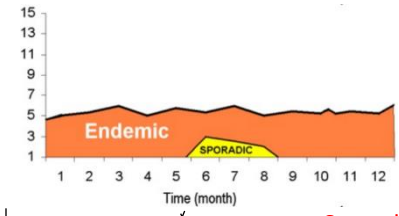
Koch's Postulate



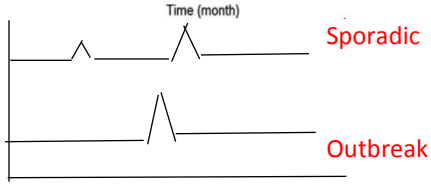
- The same pathogen must:
  - Be **present in every case** of the disease
  - Be **isolated from diseased host** and grown in pure culture
- The pathogen must:
  - **Cause the disease** when inoculated into healthy, susceptible animal
  - Again be **isolated from inoculated animal** and must be the original organism
- Koch's postulate are NOT feasible when:
  - Organisms cannot be isolated in pure culture (Eg. virus)
  - Diseases are so deadly (Eg. ebola), is unethical to use to experiment
  - Appropriate animal models don't exist

Terminology

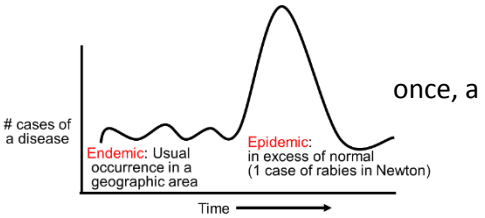
- **Epidemiology**
  - Science that evaluates the occurrence, determinants, distribution and control of health and disease in a defined human population
- **Sporadic disease**
  - Diseases that occur intermittently at random times and intervals. The occurrence is usually occasional and irregular
  - Eg. Salmonella food poisoning



- **Outbreak**
  - The sudden, unexpected occurrence of a disease, in a limited segment of a population
  - Eg. Ebola virus in Africa



- **Endemic disease**
  - A disease maintains a steady, low level frequency at a moderately regular interval within a community
  - Eg. Common cold, malaria, TB
- **Epidemic**
  - An outbreak affecting many people at once, a sudden increase in occurrence of a disease above expected level (baseline)
  - Eg. influenza
  - Occurs when previous antibodies no longer work, or when the organisms evolves to evade immune system attack.

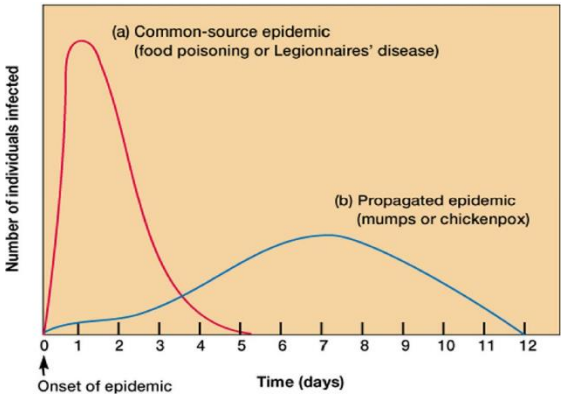


Goals of Epidemiology

- Need to find out:
  - What causes the disease? (infectious agent)
  - Where it came from? (source of transmission)
  - How it got into the population? (what host and environment are involved)
- Control the speed of disease spreading
- Eliminate pathogen from population

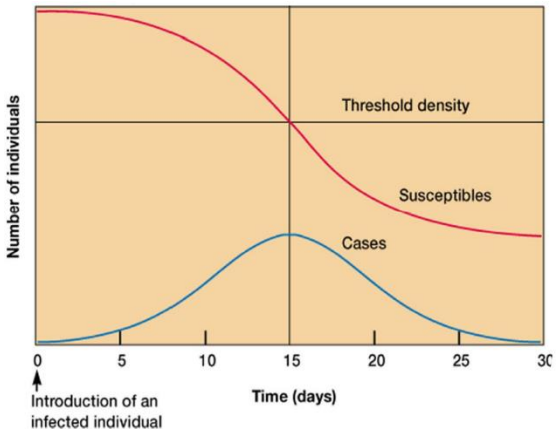
Types of epidemics

- **Common source**
  - Reached a peak level within short period of time, followed by moderately rapid decline in number of infected patients . Results from a single, common contaminated source (Eg. food or water); Eg. food poisoning or Legionaries' disease



- **Propagated source**
  - A relatively low and prolonged rise, followed by a gradual decline in number of infected patients. Results from introduction of a single infected individual into a susceptible population. Infection is propagated gradually and many are infected Eg. strep throat

Spread of Epidemic diseases

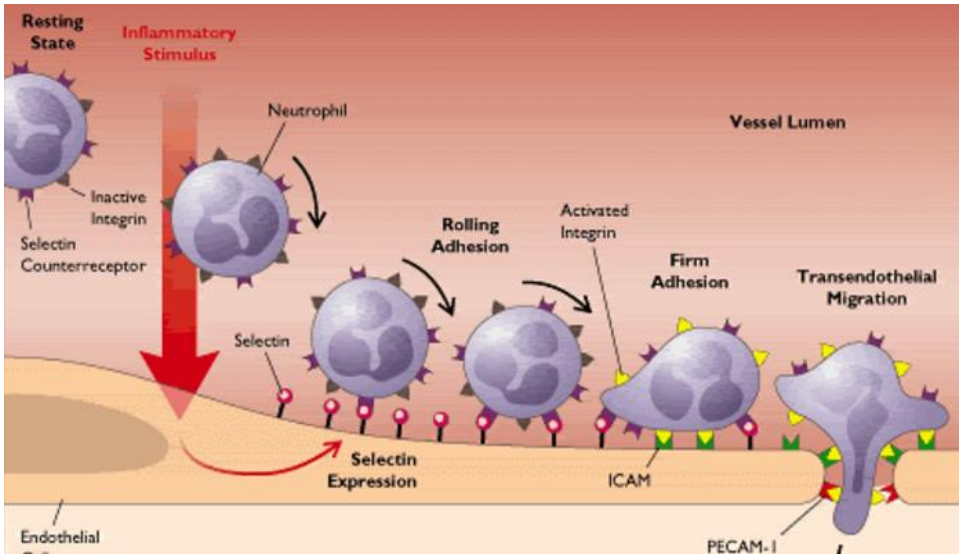


- At time 0, all individuals are susceptible to a disease. Introduction of an infected individual initiates epidemic outbreak (blue curve), and spreads to reach peak by day 15
- As individuals recover from the disease, they become immune and no longer transmit pathogen (red curve)

- The number of susceptible individuals decreases. The decline in number of susceptible individuals to **threshold density** (the minimum no. of individuals necessary to continue propagating the disease) matches the peak of epidemic curve. The incidence of new cases decline as a result.

Leucocyte – endothelium Interaction

1) **Activation**
   - Endothelial activation causes conformational changes of receptors, the PSGL-1 on leucocyte binds to newly expressed L-selectin and P-selectin on endothelial cells
2) **Rolling**
   - Leucocytes roll and slow down, they have a chance to bind to other receptors, L-selectin on leucocyte binds to L-selectin ligands (Eg. CD34) on endothelial cell
3) **Adhesion**
   - Firm adherence mediated by integrins, they are now activated, gaining more affinity and binding to ICAM-1 and VCAM-1 on endothelial cells
4) **Diapedesis**
   - Transmigration mediated by PECAM-1 (CD31), a protein expressed on leucocyte surface, it binds to itself (homotypic interactions), another CD31 that IS expressed on endothelial cell surface. After leucocyte migrate outside, chemotactic factors trigger movement of leucocyte in a gradient



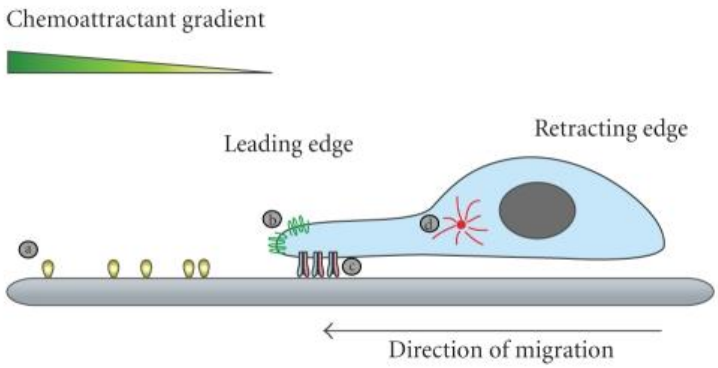
Neutrophils are activated by inflammatory signals. Endothelium surface expresses selectin, when bound to their receptors on neutrophils, initiates rolling and adhesion. Neutrophils activate their integrin after slowing down which binds to ICAMs on endothelial wall, to have a firm, stationary adhesion (arrested), trans-epithelial migration guided by adhesive molecules like PECAM-1 which is expressed at cell junctions

Phagocytosis and degranulation

- Phagocytosis (attach, engulf and kill) done through degranulation and oxidative burst (using reactive species) to destroy engulfed particles
- **Chemotactic factors** include: complement components, arachidonic acid metabolites, soluble bacterial products and chemokines

Neutrophil movement is influenced by:

- **Chemo kinesis**: increased movement in random directions
- **Chemotaxis**: increased movement towards a target and source
- **Tissue accumulation**: increase number of neutrophils in a region
- **Chemoattractant (**chemotaxin or chemotactin):
    - Agent that can induce chemotaxis in target cells. Neutrophils move towards areas with high concentrations of chemoattractant,
    - As they move towards high concentration, the cell is polarised, elongated, with one side pulling towards the source (front of cell is profoundly different from back of the cell)



<u>Chemotactic factors for neutrophils</u>

1. **Direct acting** = act on neutrophils
    - Leukotrienes, interleukin, formylated peptides
    - Formylated peptides are exclusively prokaryotic products
2. **Indirect acting** = act on other cells to induce chemotaxins release
    - Tumour necrosis factor, interleukin-1, lipopolysaccharide (LPS)
    - LPS = endotoxins produced by bacteria