**Historical Perspective:** The concept of disease transmission and contagion was well established

before microorganisms were identified. John Snow was one of the first to apply epidemiologic

methodology to infectious diseases with his classic investigation of the Broad Street cholera

epidemic in 1854.

Ignaz Semmelweiss demonstrated in 1846 the importance of handwashing using

antiseptics in the prevention of puerperal sepsis.

In the 1860’s, John Lister proved the importance of aseptic technique and disinfection in

reducing the incidence of infections following surgery.

In 1890 Robert Koch theorized that certain diseases were caused by particular pathogens

and established postulates for proving the etiologic role of these pathogens. The Henle-Koch

postulates stated that: 1) the bacteria should be identified in the lesions of the infection; 2) the

bacteria could be isolated in pure culture on artificial media; 3) the disease was reproduced when

inoculated into a susceptible animal: and 4) the bacteria was then recoverable from the infected

animal.

These early investigators were among the first to advance the “germ theory” of disease by

recognizing that some infectious diseases were contagious – *i.e.* transmitted by contact, while

others were communicable – transmitted indirectly by water or insects. This was in conflict with

the current theory that diseases were spread by “miasmas” – poisonous vapors.

**Epidemics:** The above descriptions are classic examples of **epidemics.** These are outbreaks of

infections that are in excess of the normal “endemic” incidence of a particular type of infection.

There are 2 types of epidemics. A **Common Source Outbreak** is represented by a sharp curve. It

is a point source outbreak with a single site or agent (*e.g.,* food) causing infection. Eliminate the

source and eliminate the epidemic. (*i.e.,* removing the handle during the Broad Street Pump

epidemic). A **Propagated Epidemic** is when secondary cases are involved such as chicken pox

affecting a large community. A wave of individuals acquires the infection and because of the

presence of susceptible subjects secondary cases occur. This continues until a sufficient amount

of community members develop immunity and are protected from subsequent infection.

**Terminology**

**Pathogen**: A pathogen is any microorganism that is capable of causing disease in a susceptible

host. Pathogens are often described as primary, capable of causing disease in normal hosts, or

opportunists, primarily causing disease in immunocompromised individuals. Some

microorganisms are highly pathogenic, *e.g., Shigella spp*., and a relatively small number are

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capable of causing disease while others, *e.g., Staphylococcus epidermidis*, require special settings

or a relatively high bacterial inoculum.

**Infection:** Infection refers to the ability of microorganisms to invade tissue and find conditions

that are suitable for growth and replication. It should be noted that it is, in general, not in the

interests of the organism to destroy the host; rather it is preferable to find an ecological niche that

will allow tissue colonization with perhaps some replication, but without the risks of invasion. It

is the exception for microorganisms to cause infection rather than the rule (See Lewis Thomas –

Lives of a Cell - Essay “Germs”). Alterations in the site of colonization, the bacterial density or

level of host immunocompetence will alter the likelihood of infection. Infection is also sometimes

a function of the host’s response to microorganisms. Infections may cause either clinical or

subclinical illness *i.e.* apparent versus inapparent illness. Many individuals develop an immune

response to a pathogen without manifesting any signs of illness.

**Intoxication:** Some pathogens can cause disease by the elaboration of a toxin. This can occur

in the absence of viable bacteria. One example of this is certain types of food poisoning.

**Carrier**: An individual with asymptomatic colonization or infection who is capable of

transmitting infection to others. They may or may not be ill themselves (*e.g.*, hepatitis C).

Historically, “Typhoid Mary” a cook was responsible for several outbreaks of *Salmonella typhi*

infections in the Northeast.

See: http://www.history1900s.about.com/homework/history1900s/library/weekly/aa062900a.htm

**Latency**: The pathogen remains viable but is dormant within the host. It however remains

capable of causing disease at a later date (*e.g., Mycobacterium tuberculosis* or herpes viruses).

**The Infectious Disease Cycle:**

Reservoirs: Reservoirs for bacterial pathogens are generally divided into the following: humans

(the most common animate reservoir), animals, soil and water. Knowing the reservoir and the

exposure history of the patient is often helpful in establishing the likely pathogen. For example a

farmer with a puncture wound from a stray nail is more likely to have an infection caused by a

soil pathogen such as clostridia than a pathogen carried by water (*e.g.,* legionella)

Patterns of transmission: Infections can be acquired from within the host (endogenous infection)

or from without (exogenous infection). Endogenous infections usually result from an alteration in

the equilibrium between the host and the pathogen. The host may become immunocompromised,

a commensal may be inoculated into a sterile site, or antibiotics may alter the “normal” or

indigenous microbial flora. Exogenous infections may spread by horizontal transmission *i.e.*

spread to unrelated individuals or by vertical transmission *i.e.* spread from parent to offspring.

Examples of horizontal transmission include sexual or water-borne.

There are several means of microbial transmission including person-person (respiratory

secretions, fecal-oral contamination), vector-borne (mosquitoes, ticks), animals (dogs, cats) or

environmental (food, water).

Portals of Entry: There are numerous means of inoculation, including through breaks in the skin,

inhalation, ingestion, *etc*. Each organ system has its own unique host defense mechanisms that

must be bypassed in order for an infection to be established.

**Response to infection:** There is a varied response to infection ranging from subclinical illness to

full-blown, life-threatening disease. As clinicians we are most familiar with the extreme

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presentations of illness – witness the first presentations of AIDS, West Nile virus or

Legionnaire’s Disease. Most infections are, however, subclinical and are detected only when

serologic or other sensitive assays become available for recognition of past exposure. This

concept is often referred to as the “Iceberg Model of Infection.” There are exceptions such as

Rabies and HIV infection which cause overt disease in virtually everyone infected.

**The Nature of Infections**

Infectious disease syndromes: It is important to keep in mind that many different bacterial

species may cause the same syndrome. For example both Gram positive and negative bacteria can

cause the sepsis syndrome characterized by fever, disorientation and shock. In addition, the same

bacterial species is capable of causing multiple different syndromes. For example *Streptococcus*

*pyogenes* causes impetigo as well as toxic shock.

Pathogenesis of host damage: Pathogens cause damage in a number of different ways. They may:

1) directly cause tissue damage by the elaboration of proteolytic enzymes that destroy or damage

tissue; 2) induce an excessive immune response resulting in damage *e.g., endotoxin* induction of

cytokines; 3) cause a hypersensitivity reaction as may be seen in endocarditis with immune

complex glomerulonephritis ; or 4) may cause malignant transformation of host cells as is seen in

hepatitis B or with helicobacter.

Host susceptibility to infection: There are a number of host factors that increase susceptibility to

infection such as the extremes of age, malnutrition, congenital or acquired defects in immunity

and various forms of medical treatment.

**Sequence of Steps Necessary for Infection**

Adherence and colonization: adherence may be the result of specific (adhesin-receptor) or

nonspecific (e.g. hydrophobic) interactions.

Evasion of host defense: Bacteria utilize a variety of mechanisms to evade the host immune

response. One example is the presence of a bacterial capsule that helps prevent phagocytosis by

polymorphonuclear leukocytes. Other examples include the capacity of bacterial pathogens such

as salmonella, listeria and *M. tuberculosis* for prolonged intracellular survival. Bacteria can also

express surface molecules mimicking host molecules – e.g. staphylococci express protein A, an

Fc receptor.

Invasion: the ability to invade tissue or cells. There are different pathways of invasion. Some

bacteria may spread as the result of the elaboration of proteolytic enzymes. Other spread by

surviving intracellularly and spreading with host cells to other tissue sites. Invasion sometimes

involves the subversion of host enzymes or pathways to facilitate survival and spread.

Interference with the host response: some pathogens mimic or co-opt host defense mechanisms

and utilize them to invade tissue.

Host tissue damage: much of the damage resulting from infection is the result of the host immune

response rather than the pathogen itself. One example of this is bacterial meningitis.

**Virulence:** Virulence (from the Latin virulentus – full of poison) refers to the ability of an

organism to cause disease. This is often dependent on the possession of factors such as surface

adhesins that enable the microorganism to colonize host tissue, toxins that can cause cellular

damage or capsules that interfere with phagocytosis. These virulence determinants may be found

on the chromosome, on a plasmid or on a bacteriophage. They are transmissible from strain to

MID 4 strain or species to species and the genes for different virulence factors may be genetically linked.

Some investigators would include antimicrobial resistance as virulence determinants.

Falkow described criteria to demonstrate that a particular bacterial component functioned as a

virulence determinant. He called this the molecular equivalent of Koch’s postulates for

pathogenicity. They include the following: 1) the property under study should be found in the

pathogenic members of the species; 2) inactivation of the gene is associated with decreased

virulence; and 3) reversion of the gene restores the pathogen’s virulence. Pili found on *E. coli* are

examples of virulence genes that confer the ability to certain strains to cause urinary tract

infections because of their ability to adhere to uroepithelial cells.