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## Infectious Diseases Modules

1. Overview
2. Normal flora & innate immunity
3. Host defences in infection
4. Examples of infectious diseases
5. Bacterial pathogenesis- virulence
6. Bacterial pathogenesis- genetics
7. Bacterial pathogenesis- methods
8. Paradigms of microbe-host relationships
9. Viruses
10. Mycoses and animal parasites
11. Medicine and Infection
12. Future challenges in infectious diseases



## BBS3027 - Infectious Diseases Overview

## Overview of infectious Illness

- What is infectious illness?
- Agents of infection
- How infections occur
  - routes into the body
  - sources of infection
- Establishment of disease
- Course of Infection

## Infection is not the only cause of illness

Illness may be caused by:

**Inborn defects**  
**Metabolic disorders**  
**Developmental changes**  
**Degenerative processes**  
**Malignant growths**  
**Nervous conditions**  
**Poisons**  
**Nutritional disorders**  
**Injuries**



## Disease

Definition: A specific disorder that features a recognizable complex of physical signs, symptoms and effects

All diseases have a cause (known or unknown) that include:

- hereditary
- environment
- new growth (neoplasia)
- diet
- infection

## Infection

Definition

- The process by which organisms capable of causing disease gain entry to the body and establish themselves
- The state of injury or damage to part of the body resulting from this process

## Infection

- Successful invasion of a host by a micro-organism
- Subclinical
- Clinical but self-limiting
- Clinical and associated with morbidity and mortality

## Process of Infection

- The growth/multiplication of a microbe in a host
- Infection does not always result in injury of the host (disease)
- Two main classes - by site
  - Localised
  - Generalised (disseminated, systemic)

## Infectious Diseases

Diseases caused by organisms that can be spread directly from person to person

Common infectious diseases include:

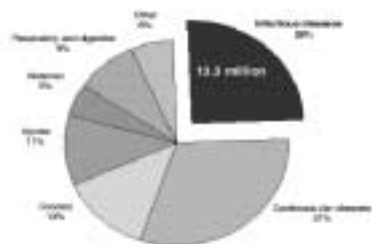
chickenpox	diphtheria	glandular fever
tuberculosis	measles	meningitis
influenza	STD's	gastroenteritis

Diseases requiring a vector (may be excluded)

malaria	leishmaniasis	yellow fever
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## Leading causes of death

53.9 million from all causes, worldwide, 1990

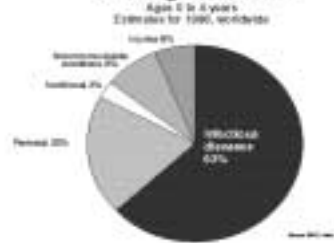


Note: Cancer, cardiovascular and respiratory/digestive deaths are often attributed to infectious disease due to their prevalence in developing countries.

### Top 10 Infections - Mortality

Condition	Frequency (x 1000)

### Main causes of death among children



### Leading infectious killers



### Why study infectious disease?

- Understand pathogenesis
- Aid in early diagnosis
- Develop effective therapeutic measures
- Disease control

### Human Costs of Epidemics

- Loss of life
- Loss of health
- Cost of care
- Costs of lost productivity
- Costs of disability

### Economic Impact of Plague Epidemic India: 1994



>45 000 travellers to India cancelled plans  
20-60% decrease in hotel occupancy



\$66 000 loss by Air India per day  
\$1million loss by Indian Airlines per week



50% decrease in ships docking at Bombay



\$460 million loss in exports  
\$23 million loss in diamond exports alone

Total Loss = >\$1.7 billion

Source: India Today

World Health Organisation



### Economic impact of recent SARS outbreak

SARS virus outbreak Nov 2002-June 2003  
 Focused Beijing, Hong Kong, Canada  
 Eventually cases in 19 countries across 4 continents

Initial SARS related damage to regional GDP in Far East at  
 US\$ 10-15 billion

Hong Kong alone:

Retail sales 50% less since mid-March  
 Tourism arrivals dropped by 80%  
 Entertainment/restaurant 80% less

Travel restrictions lifted mid-June, 2003  
 Most disease contained early July, 2003

### SARS and the economy: impact on global travel, Hong Kong



SARS: 10/2002 and 4/03: © 2003 Lippincott Williams & Wilkins, 47 June 2003

### Agents of Infection

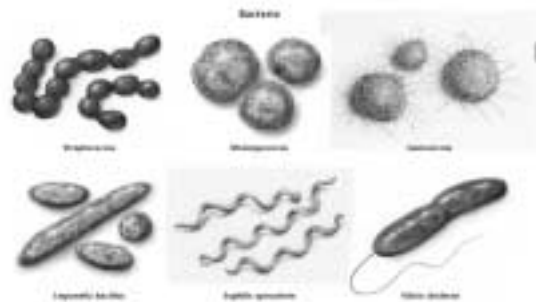
**Infectious illness occurs when certain microorganisms  
 gain access or colonize the body**

Symptoms of illness arise from their effects on the body  
 AND  
 from the body's attempts to cope with them

The agents involved are usually single celled rather  
 than multicellular and are mostly bacteria or viruses

Agents of infection:  
 bacteria & their toxins  
 viruses  
 parasites  
 fungi

### Agents of infection: bacteria



### Agents of Infection: bacteria

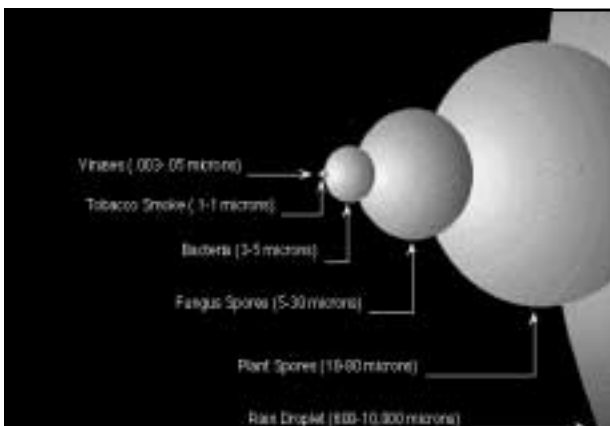
A form of tiny (3-5µm thick) single celled organism  
 Consist simply of outer cell wall, inside mostly  
 protoplasm and DNA

Most are capable of limited movement- flagella

Almost all divide simply into 2- binary fission (rapid)

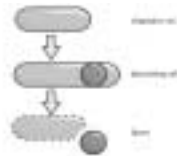
Many form spores, seed like inactive state....enables survival

Preferred conditions vary:  
 temperatures not too hot or too cold  
 and moisture not too acidic



## Endospores

- Resistant to heat, drying, etc.
- Survival, not procreation-
- *Bacillus* and *Clostridium*



## Agents of Infection: bacteria

Bacteria occur commonly in vast numbers in almost every corner of life including  
ON & IN the human body

Most bacteria are harmless to humans

Bacteria play a vital role in the body  
....aid digestion, manufacture vitamins  
& destruct dangerous substances

All life depends on bacteria in the air and in the soil  
without which dead matter would not decay  
and return into the cycle of existence

"Microbes make the difference between a living planet  
and a dead one".....Salyers and Whitt.

## Prokaryotes

- Absence of nucleus
- Singular circular chromosome
- Additional DNA in plasmids
- Transcription/Translation is simultaneous
- Thick protective cell wall
  - Gram-Positive = Peptidoglycan
  - Gram-Negative = PG + LipopolySaccharide



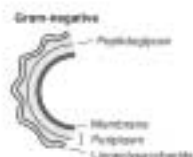
## Gram Stain

Step	Gram-positive organisms	Gram-negative organisms
1. Unstained	Clear	Clear
2. Crystal violet	Violet	Violet
3. Iodine	Violet	Violet
4. Decolourisation (alcohol, acetone)	Violet	Clear
5. Carbol fuschin	Purple	Red

## Bacterial cell wall-Gram stain

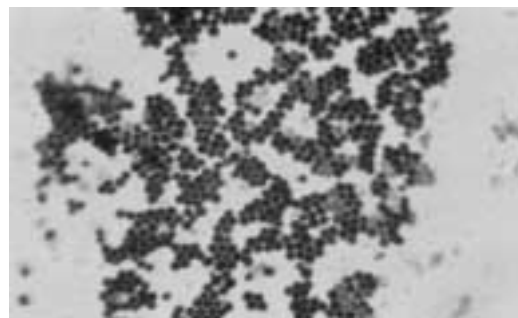


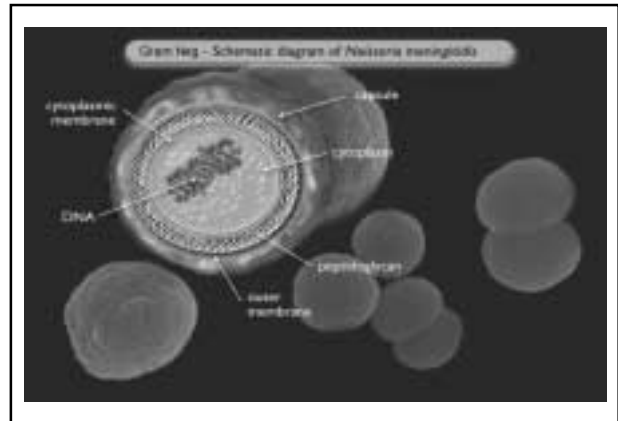
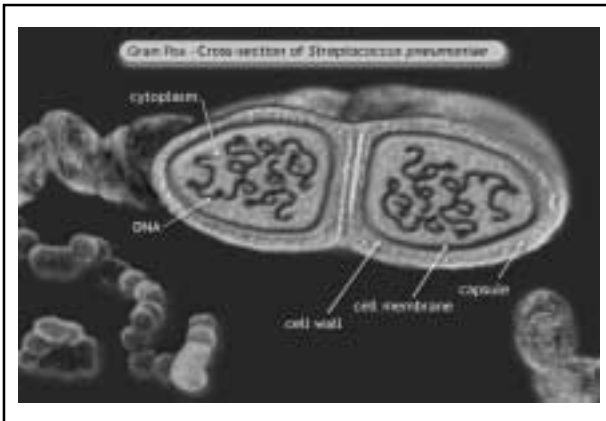
40-80 % PG  
Teichoic acids  
Polyol pphosphate polymers  
Inner cell membrane



No teichoic acids  
One layer PG (5% CWW)  
Inner & outer membrane  
LPS in OM  
-Protects against C' lysis  
-Stimulates cytokine release

## Gram Stain





### Microbial Growth

<p><b>Physical requirements</b></p> <ul style="list-style-type: none"> <li>• Temperature</li> <li>• pH</li> <li>• Osmotic pressure</li> </ul>	<p><b>Chemical Requirements</b></p> <ul style="list-style-type: none"> <li>• Carbon</li> <li>• Nitrogen</li> <li>• Sulfur</li> <li>• Phosphorus</li> <li>• Trace elements</li> <li>• Oxygen               <ul style="list-style-type: none"> <li>- Aerobic = requires O<sub>2</sub></li> <li>- Facultative anaerobic = use O<sub>2</sub> when present</li> <li>- Obligate anaerobic = unable to use O<sub>2</sub> as final electron acceptor</li> <li>- Microaerophiles = [O<sub>2</sub>] &lt; 20% i.e. surface of water</li> </ul> </li> </ul>
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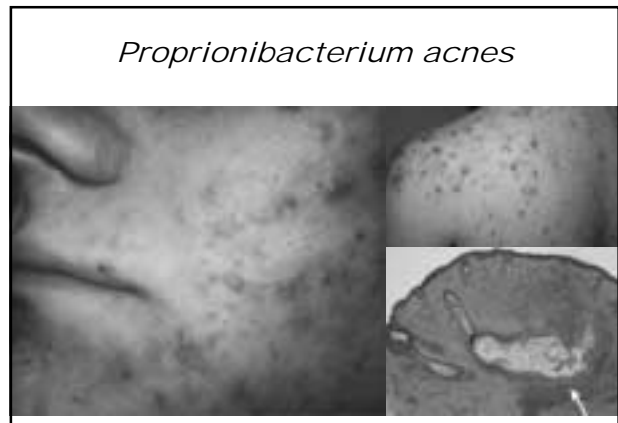
### Bacteria

- Normal flora
  - Colonize the body and usually do not cause disease
- Opportunistic pathogens
  - Normally do not cause disease, but may under certain circumstances
- Frank pathogens
  - Always cause disease
- Other
  - Caused mostly by the ingestion of preformed toxins or when toxins are produced from bacteria during infection

### Illness from bacteria arise in two ways

1. ENDOGENOUS: bacteria that normally exist in the body.... get into the wrong part.

<p>Acne Pimples Boils</p>	<p>normal skin flora gain entrance to sebaceous gland skin wound</p>
<p>UTI</p>	<p>bacteria (<i>E.coli</i>) from anal area gain entry to UT (mainly in females)</p>



2. EXOGENOUS: bacteria that are always harmful gain access to the body

Examples of illness carried by one specific organism

scarlet fever	<i>Streptococcus</i>
tuberculosis	<i>Mycobacterium tuberculosis</i>
syphilis	<i>Treponema pallidum</i>
typhoid	<i>Salmonella typhi</i>
gonorrhoea	<i>Neisseria gonorrhoea</i>
diphtheria	<i>Corynebacterium diphtheriae</i>

### Illnesses that can be caused by a range of bacteria

Tonsillitis  
 Dysentery/diarrhoea  
 Pneumonia  
 Food poisoning

### Bacteria of Medical Importance

#### Gram-positive

- Gram-positive cocci
  - Staphylococci
  - Streptococci
- Gram-positive bacilli
  - The genus Bacillus
  - Clostridia
  - Other Gram-positive bacilli

#### Gram-negative

- Gram-negative cocci
  - Neisseria sp.
- Gram-negative bacilli
  - Enterobacteriaceae
  - Pseudomonads
  - Curved, Gram-negative rods
  - Other Gram-negative bacilli
- Others
  - Mycobacteria, Spirals

### Bacteria of Medical Importance

- Rickettsia
  - Obligatory intracellular parasite, spread by arthropods (ticks, lice)
- Chlamydia
  - Obligatory intracellular Gram-Negative
- Mycoplasma
  - Lack a cell wall
- Erlichia
  - Obligate intracellular Gram-Negative organism, spread by ticks
- Bartonella
  - Non-contagious, Gram-Negative motile, bacillus-like, spread by sandflies

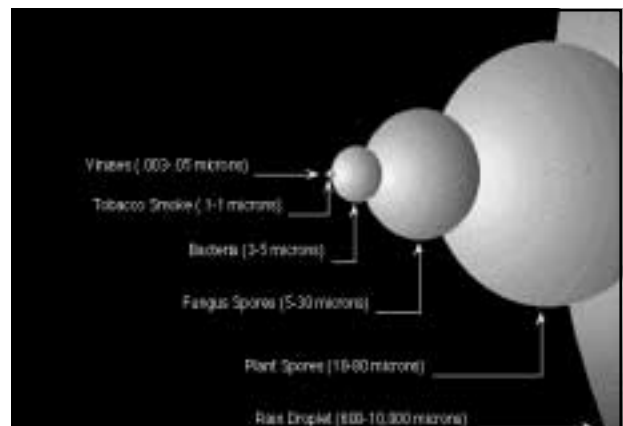
### Agents of Infection: Viruses

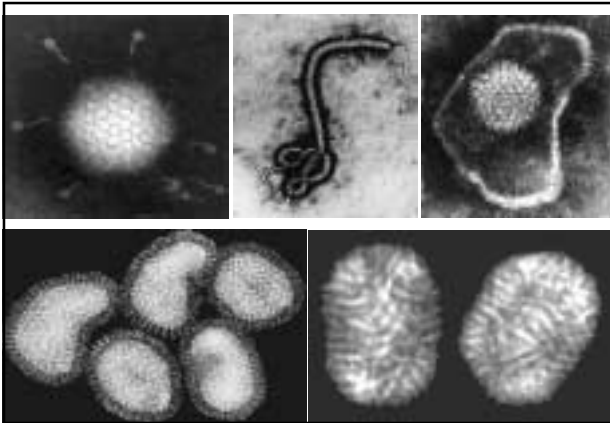
Viruses are most primitive form of life we know- each a minute quantity of nucleic acid wrapped in a protein sheath

Viruses are the ultimate parasites

Exist in most conditions but only active inside a host cell to exploit the cellular enzymes they lack

Virus enters cell  
 Takes over cells chemical processes  
 Uses it to produce hundreds of new virus  
 Cell breaks open.....lyses.....dies  
 Liberates new virus  
 Released virus infects new cells





### Illnesses caused by viruses fall into two groups:

- Attack particular organs

respiratory system.....	influenza, SARS
salivary glands.....	mumps
nervous system.....	poliomyelitis
immune system T cells....	HIV

2. Cause general symptoms with skin rash

measles  
rubella  
chickenpox  
smallpox

### Eukaryotes

- DNA on several chromosomes in a nucleus
- Separate cytoplasm
- Transcription of DNA into mRNA which moves to the cytoplasm
- Cytoplasm is rich with organelles
  - Mitochondria
  - ER
  - Golgi
  - Lysosomes)



### Other agents of infection

Protozoans, single celled organisms and much larger than bacteria cause infection

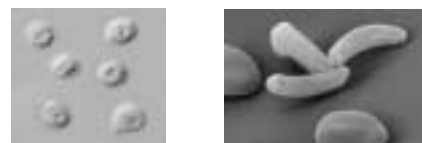
mostly in tropical/sub-tropical parts of the world

often develop into fatal infections

Examples: Amoebic dysentery  
Malaria  
Sleeping sickness

### Protozoans

- Amoebae
  - Move via pseudopods
- Flagellates
  - Move via flagellae
- Sporozoites, merozoites, trophozoites
  - No locomotive organelles

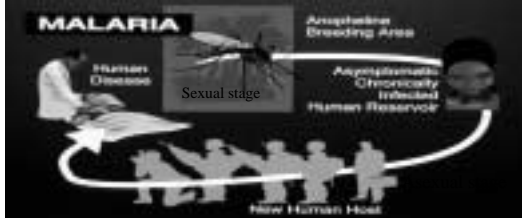




## Parasites

Infectious agents which have developed a life cycle that depends on passing part of their existence in another creature & part in man

Malaria parasite	mosquito and man
Bilharzia parasite	snail and man
toxoplasmosis	cat and man



## Infectious Diseases Top 10 Infections - Frequency

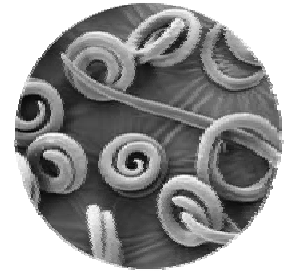
Condition	Frequency (x 1000)

## Macroparasites

- Worms, Arthropods
- Require metabolic nutrients = ingest and digest host cells, tissue fluids, intestinal contents
- Rapid spread through extracellular fluids and over surfaces
- Sheer size renders them unsusceptible to host defences normally used on smaller organisms

## Helminthic Infections

- Roundworms
  - Nematodes
- Flatworms
  - Trematodes
- Tapeworms
  - Cestodes



## Helminthes

Two groups

1. Nematoda
  - Non-segmented roundworm
  - Most are parasites
2. Platyhelminthes
  - Flatworms
  - Trematodes eg. flukes
  - Cestodes eg. tapeworms

## Helminthic Infections - Host Types

1. Definitive host
  - Adult or sexually mature parasite
2. Intermediate host
  - Immature or larvae stages
3. Reservoir host
  - Other animal species act as host for species that are parasites for humans

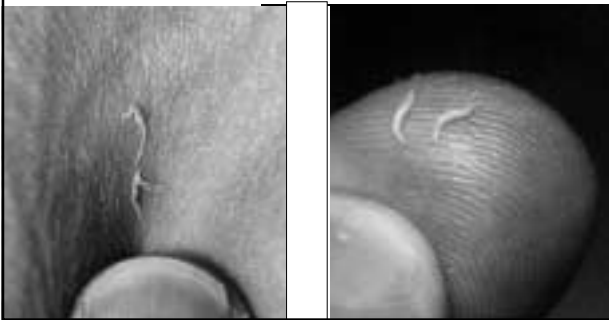
## Infectious Diseases Intestinal Round Worms

- Round worms (nematodes) are extremely common infestations in the Third World
- Most intestinal worms cause little pathology (they don't eat much) except that they may cause obstruction with heavy infestation
  - Hookworms (*Necator americanus*) often cause anemia, depending upon worm load
  - *Strongyloides stercoralis* may proliferate and disseminate in the

## Infectious Diseases Pinworms - *Enterobius vermicularis*

- One of the most common parasitic roundworms in humans
- Found in the colon
- At night, they come through the anus to lay their eggs on the perianal skin
- Common in children who reinfect themselves

## Infectious Diseases Pinworm - Morphology



## Infectious Diseases roundworm-*Ascaris lumbricoides*

- Adult worms are 10-14 inches long
- Larvae hatch in the gut, then migrate through tissue to the lung - are swallowed, then mature in the gut
- Eggs are passed in the faeces, where they may infect another human via faecal-oral contamination

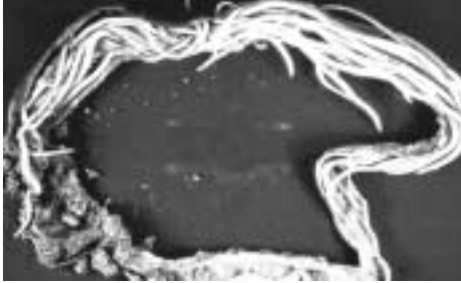
## Infectious Diseases *Ascaris lumbricoides* - Pathology

- Rarely cause obstruction of the colon, appendix, or biliary tree
- Larvae migration may induce an eosinophilic pneumonitis
- Rarely, larval or even adult worms may be expectorated

## Infectious Diseases Appendicitis - *Ascaris*



## Infectious Diseases Colonic Obstruction - Ascaris



## Infectious Diseases Characteristics of Parasitic Flatworms

1. Dorso-ventrally flat
2. Incomplete digestive system with one opening
3. Very simple nervous system

### Two Groups

- Trematodes - Flukes are leaf shaped and non-segmented
- Cestodes - Tapeworms that are ribbon shaped and can be as long as 30 ft with segments called proglottids

## Infectious Diseases Cestodes - Tapeworms

- Live as mature organisms in the intestines of the definitive host
- Hosts include cats, dogs, cows, whales, and humans
- Human infections occur when uncooked, infected meat is eaten, or by ingesting the eggs
- Human infection with the common dog tapeworm is transmitted by the ingestion of infected fleas - most commonly seen in children

## Funghi

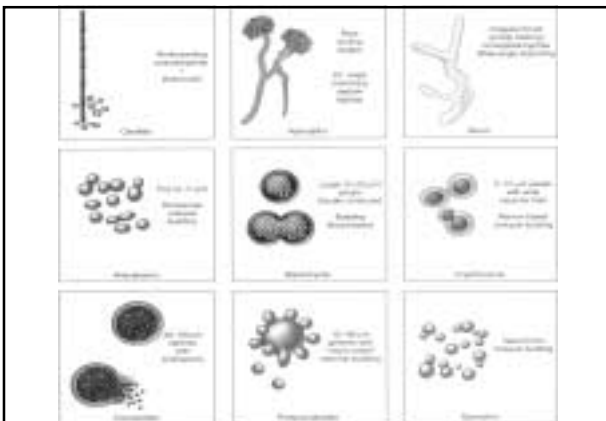
A type of plant that has no chlorophyll and so derive nourishment from Organic matter

Unicellular yeasts  
Filamentous multicellular moulds  
Diphasic (both) forms

Immunocompetent: Infections tend to be limited to the skin epidermis and mucous membranes of the genital tract  
Malnourished & poor living – deeper penetrating infections to feet + other

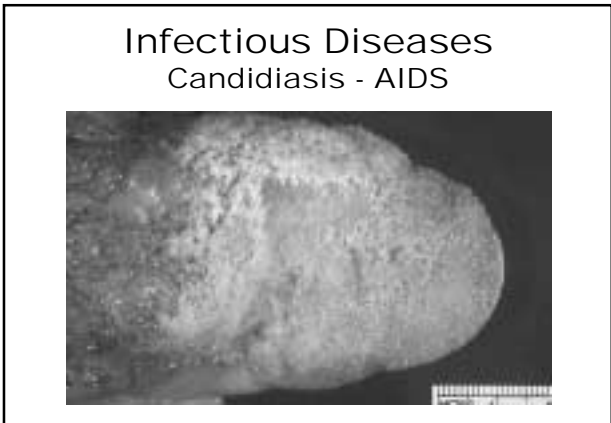
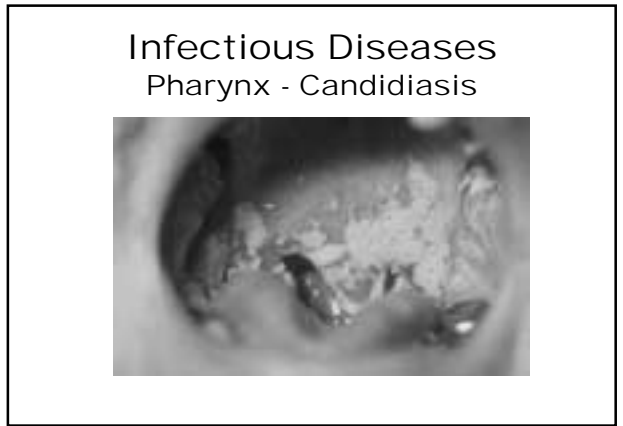
Immune deficiency allows widespread opportunistic fungus infections of all Parts of the body (AIDS, transplants, cancer, diabetes, TB)

Common infections: "ringworm" tinea  
thrush candidiasis (yeast fungus of mouth & vagina)



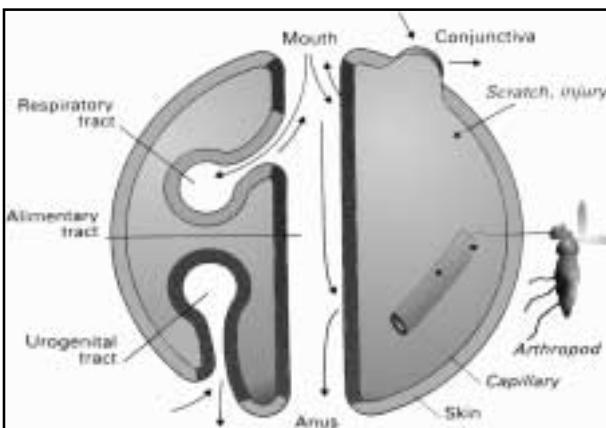
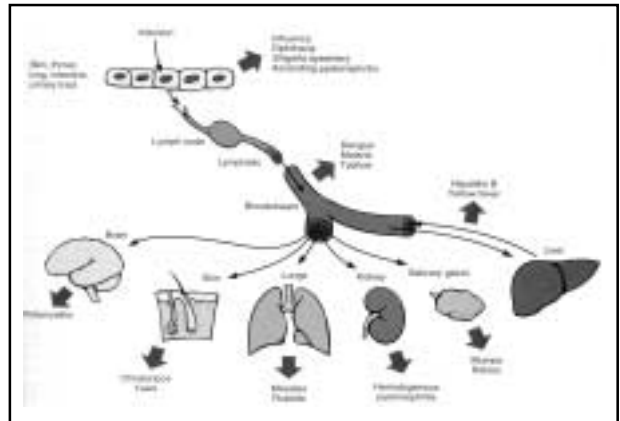
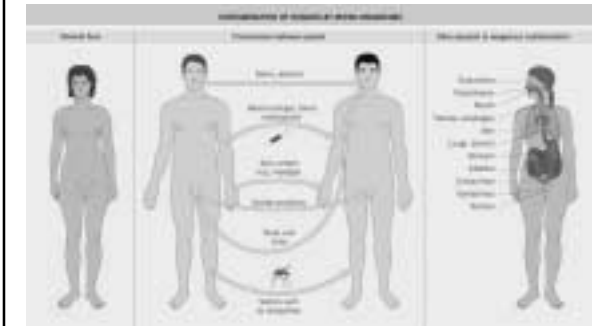
## Fungal Infections

- Opportunistic pathogens - usually systemic infections
- Superficial mycoses - infections limited to outermost/keratinous layers of skin and hair
- Cutaneous mycoses - infections which extend deeper into the epidermis as well as invasive diseases of the hair and nails
- Subcutaneous mycoses - infections involving dermis, subcutaneous tissue and fascia
- Systemic (deep) mycoses - infections



Routes into the body

## Spread of Infection



## Sources of Infection



### Sources of Infection: inhalation

Inhalation-most frequent source of common infections

Breathing, speaking, coughing & sneezing all liberate droplets of saliva, sputum or secretion into the air

- Ordinary breathing > 1m
- Loud speaking > 1.5m
- A sneeze spreads 20000 droplets > 4m

Droplets can be breathed in or ingested with food by others

Inhalation of dried bacterial spores in dusty air eg anthrax


Other sources of infection	
Source of infection	Example
Direct physical contact with infected person	STD's, skin infections
Contact with fomites	colds, hepatitis
Ingesting infected food or drinks	hepatitis, food poisoning
Entry of soil or dust into a wound	tetanus, gas gangrene
Bites of parasitic insects	malaria, bubonic plague
Bites/contact infected animals	rabies, toxoplasmosis
Unsterile medical procedures	hepatitis
Infection carried by mother's bloodstream	rubella, CMV
Self infection-poor hygiene	UTI, staphylococci,

### Congenital Infections

- **T** = toxoplasmosis, treponema (syphilis)
- **O** = other (varicella, Venezuelan equine encephalitis, mumps, coxsackie, parvovirus)
- **R** = rubella
- **C** = cytomegalovirus
- **H** = herpes, HIV, HBV

**Consequences**

- Birth defects (teratogenesis)
- Abortion



### Sources of Infection - Exogenous

- Inhalation common cold, flu, meningitis, Legionnaire's disease, mumps, measles, TB
- Ingestion typhoid fever, tapeworm, cryptosporidium, hepatitis A
- STD gonorrhea, HIV, syphilis
- Wound tetanus, rabies
- Insect Bite malaria, yellow fever, dengue

### Sources of Infection - Endogenous

- Gut *E. coli*
- Skin staphylococcus
- Throat streptococcus
- Blood EBV
- Lungs Candida, CMV, streptococcus


### Pathogen Reservoirs

**Reservoir** - A site where a microorganism can survive and multiply as a source of infection.

**1. Human**

(a) Passive carrier - Show no symptoms of the disease but release microbes eg. Typhoid Mary

(b) Active carrier - Recovery from a disease in the ending stages example of carrier diseases eg. hepatitis (viral), pneumonia (bacterial), *Staphylococcus aureus* poisoning



### Pathogen Reservoirs

**2. Animal**  
Zoonoses - Animals which transmit pathogens to humans  
eg. rabies

**3. Nonliving**

- Soil - Many microbes tolerant to drying ie. spores (bacterial and fungal) eg. *Clostridium tetani*, *Clostridium botulinum*,
- Histoplasmosis (flu- like symptoms), Skin fungi (dermatophyte)

Water - eg. polio virus

Fomite - inanimate objects example spoon, fork and pencils

## Establishment of Disease

## How Microorganisms Cause Disease

1. Contact/Enter host cells and directly kill them
2. Release factors that indirectly kill cells
3. Induce a host response that harms the host as well as the microorganism

## A framework for understanding infectious diseases

- The following steps take place in all infectious diseases:
  - **Encounter:** the pathogen meets the host
  - **Entry:** the pathogen enters the host
  - **Spread:** the pathogen spreads from the site of entry
  - **Multiplication:** the pathogen multiplies in the host
  - **Damage:** the pathogen or the host response or both cause damage
  - **Outcome:** the pathogen or the host win, or they coexist
- The manner in which each pathogen combats host defenses at each step distinguishes one pathogen

## Establishment and Outcome

- **Encounter**
  - time from first encounter
  - exogenous (colonisation)
  - endogenous (normal flora)

## Establishment of Disease

### 2. Entry

- ingress ie. inhalation/ingestion
- mucous membrane
- penetration

## Establishment of disease

### 3. Multiplication and Spread

- physical factors
- microbial nutrition
- anatomic factors
- microbial sanctuary
- microbial virulence

## Establishment of Disease

### 4. Injury

- mechanical
  - cell death
  - microbial product induced
  - host induced
- ie. inflammation, immunity, mediator

## Establishment of Disease

### 5. Course of infection

- mild
- life-threatening
- acute
- subacute
- chronic

## Establishment of Disease

### 6. Outcome of infection

- resolution
- chronic ie. carrier state, latent, reactivation
- death

## Eight Steps in Infection (8 Rs)

1. Reservoir
- Source
2. Route
3. Rupture
- The first line of defense
4. Redeployment
- Spread within the body; the second line of defense
5. Replication
6. Response
- The third line of defense incl. tissue damage
7. Result
- Disease, recovery and health or death
8. Release



## Bacterial Virulence Mechanisms - EAT RICE

- Enzymes eg. streptokinase
- Adherence
- Toxins ie. endotoxin, exotoxins, by-products of growth eg. gas, acid
- Resistance to antibiotics
- Invasion of tissues
- Circulation to other areas of the body
- Evasion of immune response eg. superantigen, capsule, catalase,

## Factors Influencing Infection - Host

### Opportunities for host exposure

- Transmission routes
- Host availability

### Susceptibility factors

- Dosage (quantity) and 'quality' of infectious organisms, including their 'virulence'
- Age
- Social determinants
- Immunity, immunocompetence and health status
- Nutritional status
- Genetics
- Behaviour (personal habits)

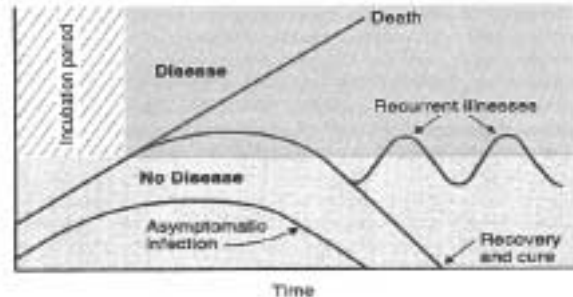


## Factors influencing infection: pathogen

- Virulence of micro-organism
  - Resistance to natural defences
  - Motility and invasiveness
  - Production of toxins (endotoxin or exotoxin)
- Failure of defence system
  - Physical and chemical barriers
  - Cellular or humoral deficiency
  - Immune deficiency states



## Course of Infection



## Stages-course of disease

### • Incubation

Time depends on:

- specific microbe
- number in inoculum
- resistance of host
- distance from portal of entry to target cells

## Stages-course of disease

### 2. Prodromal (early warning signs)

- short period
- early mild symptoms eg. malaise, general aches and pains

## Stages- course of disease

### 3. Invasive

- acute symptoms
- specific/general symptoms
- 2<sup>nd</sup>/3<sup>rd</sup> line of host immune response
- recovery or death

## Stages-course of disease

### 4. Critical

- most intense symptoms
- most intense battle

## Stages-course of disease

### 5. Decline

- signs/symptoms decrease
- secondary infections possible
- 24 hours to several days

## Stages- course of disease

### 6. Convalescence

- microbe birthrate < deathrate
- person regains strength

## Factors contributing to the emergence of infectious diseases

Factor	Circumstance	Example
Ecological changes	Increased forestation	Lyme disease
Human behavior	IV drug use	AIDS
International travel	Transport of mosquitos	"Airport" malaria
Technology	Mass food production	Enterohemorrhagic E. coli
Microbial adaptation	Overuse of antibiotics	Antibiotic resistance
Breakdowns in public health systems	Inadequate water treatment	Cryptosporidium outbreaks

## Goals of the CDC

### Centres for Disease Control and Prevention

1. Surveillance and Response
  - Detect, investigate, monitor
  - Factors influencing emergence
2. Applied Research
  - Integrate lab science and epidemiology
3. Infrastructure and training
  - Strengthen public health surveillance
  - Support the planning, delivery and evaluation of public health activities and practice
4. Prevention and control
  - Prompt implementation and enhance communication