

CHS 2413
Pathology and Physiopathology

Assoc.Prof.Dr. Thavatchai Kamoltham
MSc.MD.FICS.FRCST.Dr.PH

Infectious Disease

General Consideration

Synopsis

- Infectious disease (Terminology, communicable disease) is:
 - ① A clinical medicine
 - ② A part of internal medicine
 - ③ To study the regularity of the occurrence and development of infectious disease in human body
 - ④ To study etiology, pathogenesis, pathology, clinical manifestation and the methods of diagnosis, treatment and prevention for infectious disease.
 - ⑤ In order to control spread of infectious disease in population
 - ⑥ Infectious disease is related to biology, immunology, parasitological, epidemiology, pediatrics

Synopsis

- **Infectious disease is:**
 - ① A group of common disease
 - ② Caused by different pathogens
 - ③ To possessing infectivity
 - ④ To form epidemic
 - ⑤ Infectious disease is a threat to the health of people
 - ⑥ The pathogens causing infectious diseases are:
virus, Chlamydia, rickettsia, mycoplasma, spirochete,
bacteria, fungus, protozoa and helminthes

<https://youtu.be/TDoGrbpJJ14>

Epidemic **process** and epidemic **factors** of infectious disease

- **Source of infection (basic conditions)**

Patients (acute , chronic) ,Covert infection , Carrier ,Infected animal

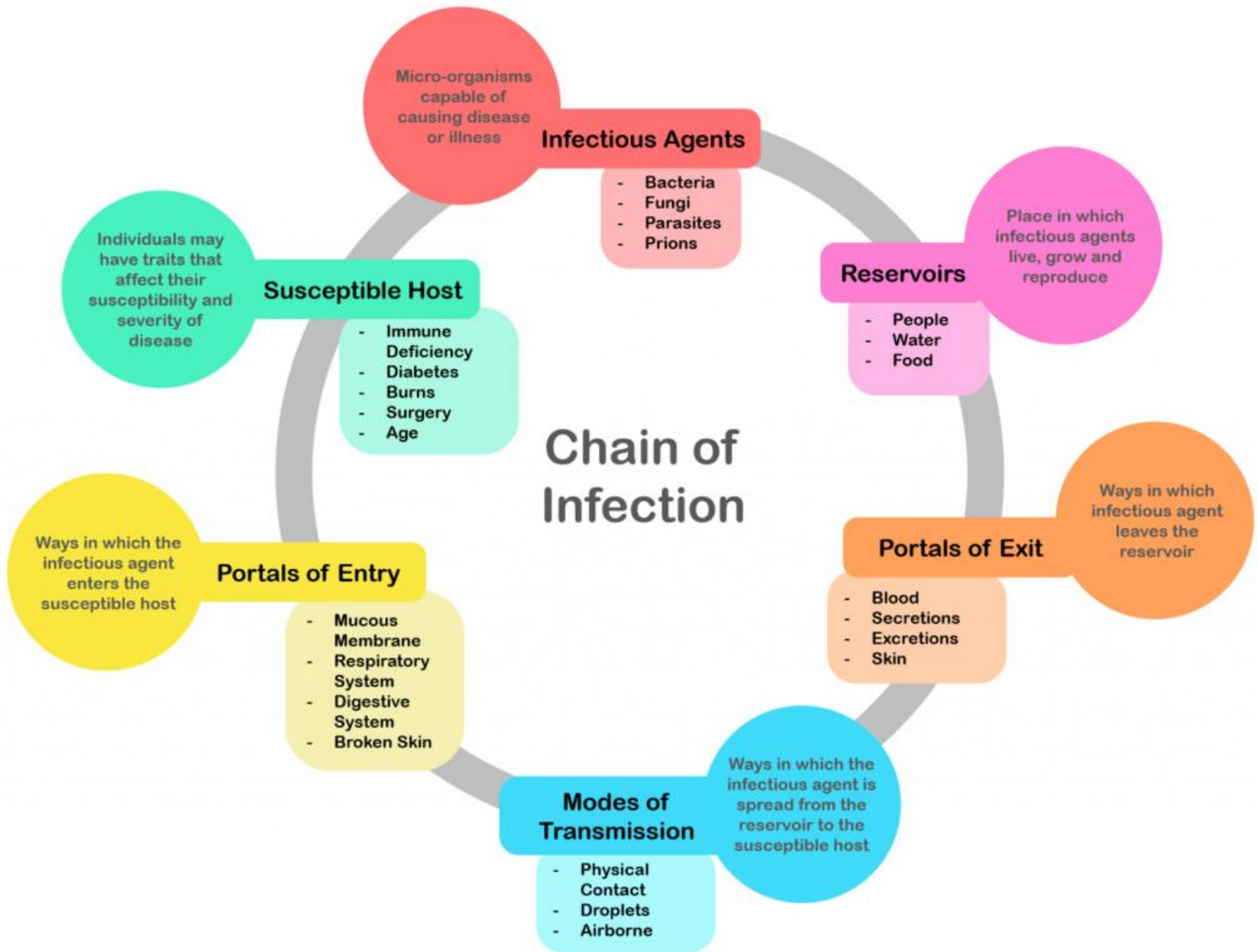
- **Route of transmission**

Contact transmission (direct and indirect) , Air-borne , Food water fly borne, Insects borne, Blood borne ,Soil borne

- **Susceptibility of population**

- **Factors of influencing epidemic process**

nature factors ,social factors



Features of infectious disease

- Basic features

Pathogen

9 kinds of pathogen

Infectivity

Epidemiological features

Quality : exotic , local , endemicity

Quantity : sporadic occurrence, epidemic, pandemic,
outbreak, endemicity, seasonal

Post infection immunity

Viral infection: life-long immunity

Bacteria infection: shorter immunity

Helminthes infection: no protective immunity

Protozoa infection: shorter immunity

Features of infectious disease

- Clinical features

Regularity in the development of course

Incubation period : diagnosis , quarantine period

Prodromal period

Period of apparent manifestation

Convalescent period

Relapse

Recrudescence

Common symptoms and signs

- Fever:

Three stages : effervescence

fastigium

deffervescence

Five kinds of fever: sustained fever,

remittent fever,

intermittent fever,

relapsing fever,

saddle type fever.

And irregular fever

Common symptoms and signs

- **Rash eruption**

Date of eruption

1st: chickenpox	2nd: scarlet fever
3rd: smallpox	4th: measles
5th: typhus	6th: typhoid fever

Location of eruption

Form of rash

- Exanthema :maculo-papular rash
- Petechia
- Vesiculo-pustular rash
- Urticaria

Enanthema

Common **symptoms and signs**

- **Toxemic symptoms**
- **Mononuclear phagocyte system reactions**
 - Hepato-splenomegale
 - Lymphonodus enlarged
- **Clinical types**
 - acute, subacute, mild, common, severe, fulminant, typical, atypical, abortive, ambulatory

Diagnosis of infectious diseases

- Epidemiological dates

- Clinical features

Symptoms and signs

- Laboratory findings

Routine examination of blood, urine, feces

Bio-chemical examinations

Etiological examinations

Direct exam

Isolation of pathogen

Molecular biological examinations

Immunological examinations

Endoscope examinations

Image examinations

Treatment of infectious disease

- General and supporting therapy
 - Isolation of patients, rest, diet, nursing
- Pathogen or specific therapy
- Symptomatic therapy
- Rehabilitation
 - Physiotherapy acupuncture
- Chinese herbs or tradition medicine

Prevention of infectious disease

- Management of source of infection
 - 35 kinds of notifiable infectious disease divided into 3 class
 - First class:** 2 kinds. Reported 6h in city, 12h in country.
 - Second class:** 24 kinds. reported 12h in city and country
 - Third class:** 9 kind
- Cut off of route
 - Personal hygiene, public hygiene, insecticide, disinfection
- Protect susceptible population
 - Active immunization
 - Passive immunization

35 kinds of infectious diseases

class one: plague, cholera

class two: viral hepatitis, bacillary dysentery and intestinal amebiasis, typhoid fever and paratyphoid fever, AIDS, gonorrhoea, avariosis, poliomyelitis, measles, pertussis, diphtheria, epidemic cerebrospinal meningitis, scarlet fever, epidemic hemorrhagic fever, rabies, leptospirosis, brucellosis, anthrax, typhus, kala-azar, epidemic encephalitis B, malaria, dengue fever, lung tuberculosis, fetal tetanus

class three: schistosomiasis, filariasis, hydatid disease, leprosy, influenza, mumps, rubella, infectious dysentery, acute hemorrhagic conjunctivitis

Infectious agents:

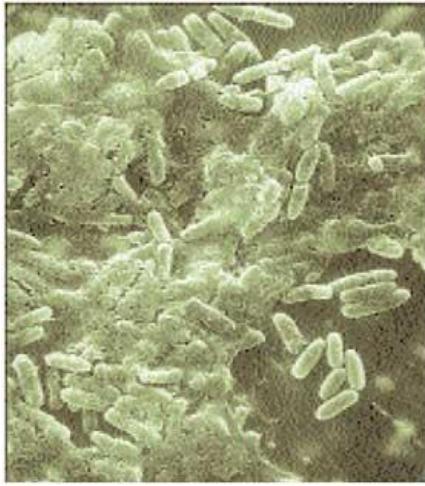
Infectious agents belong to a wide range of classes, they include;

- 1- **Prions**: which are modified host proteins lacking genetic molecules.
- 2- **Viruses**: obligate intracellular parasites which only replicate intracellularly.
- 3- **Bacteria**: prokaryotes lacking nucleic acid and endoplasmic reticulum.
- 4- **Mycoplasma, rickettsiae, Chlamydia.**
- 5- **Fungi**: non-motile filamentous, branching strands of connected cells.
- 6- **Protozoa**: single cell organisms with a well defined nucleus.
- 7- **Helminthes**: multicellular parasites with complicated life cycles often involving several hosts.

INFECTION AND INFECTIOUS PROCESS

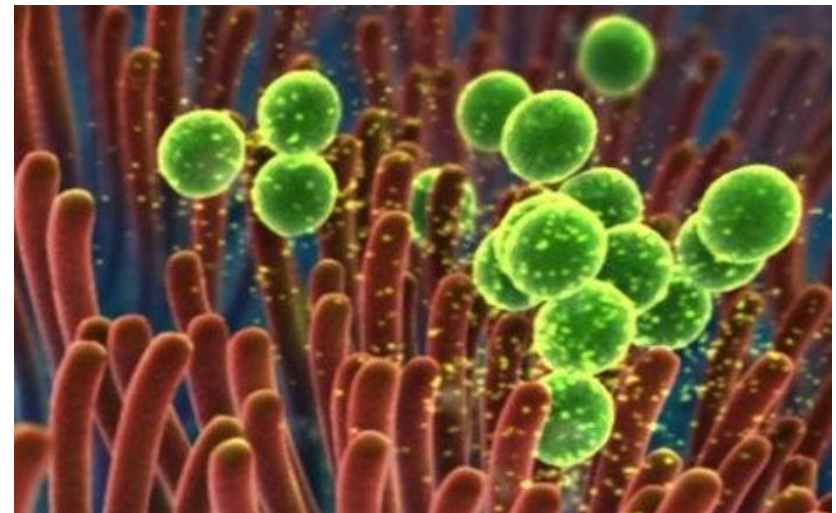
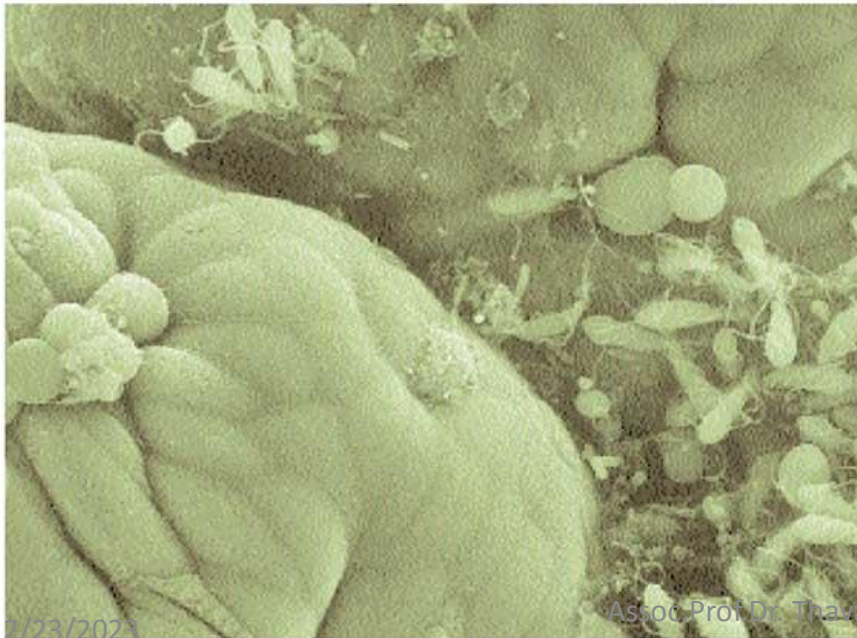
1. Classification of infections
2. Sources of infection in Man
3. Methods of transmission of infection
4. Factors predisposing to microbial pathogenicity
5. Types of infectious diseases





▲ *Biofilms of the different types of bacteria*

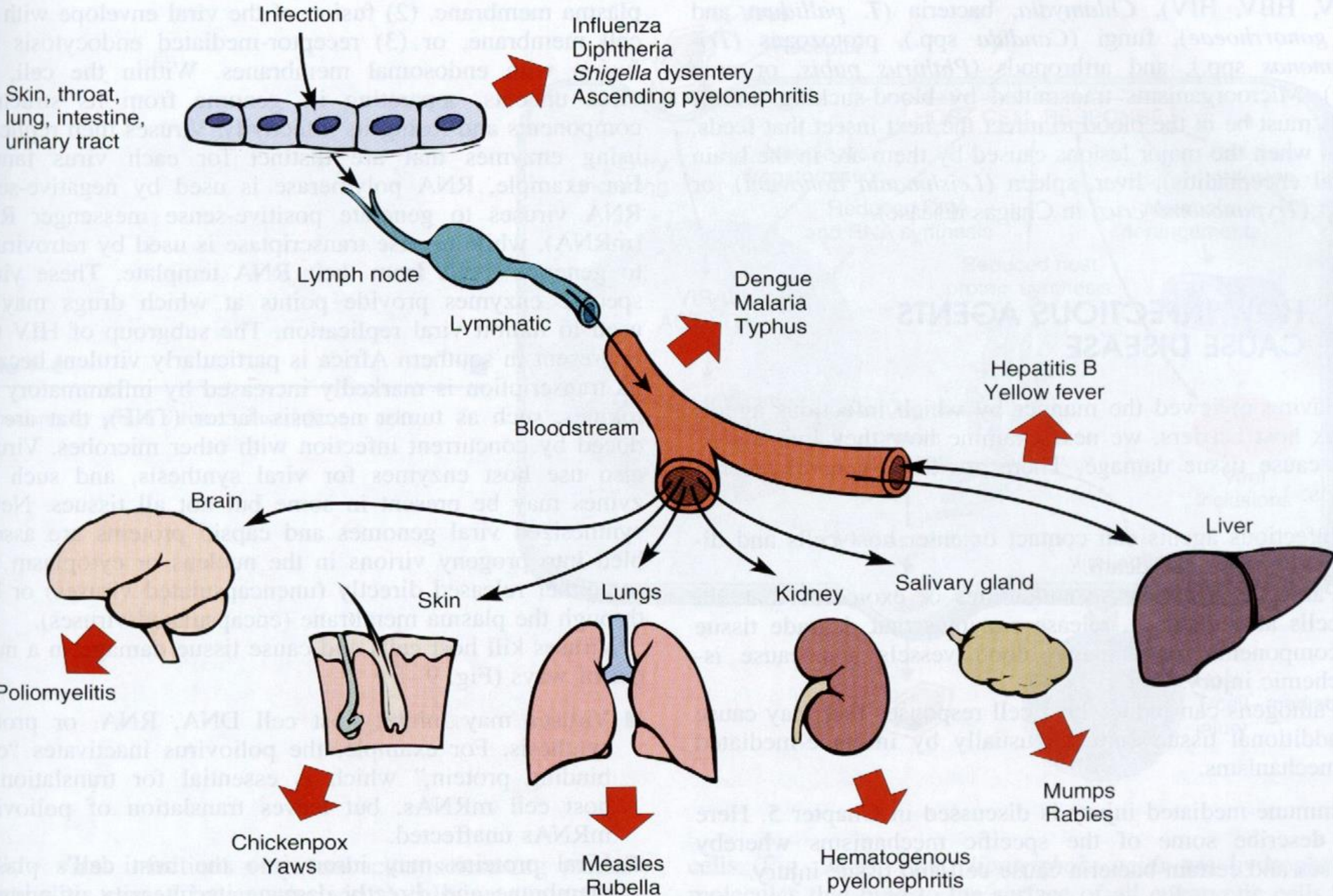
Infection is the lodgement and multiplication of organism in the tissue of host



The transmission can be:

- 1- Direct from person to person by aerosols, direct contact as in **chicken pox, measles**, (contagious).
- 2- It may need prolonged intimate or mucosal contact e.g sexually transmitted diseases
Chlamydia , syphilis.
- 3- Some respiratory bacteria and fungi are transmitted only when the lesion is opened to the airways e.g in **T.B.**
- 4- Other may take the **feco-oral route** for transmission (ingestion of stool contaminated food or water) as in **cholera , rotavirus.**
- 5- Other microbes need a reservoir host and transmitted from **animal** to human.
- 6- Others may be transmitted by human agency as in **HBV**, HIV that can be transmitted by sharing needles by addicts or viral contaminated blood transfusion.
7. **By blood sucking arthropods** (malaria, leishmania).
8. By **kissing, talking**, spitting (mumps).

Routes of entry, release and dissemination of microorg.



How can the microorganism cause a disease?

Infectious diseases involve interplay between microbial virulence factors and host responses.

The infectious agents damage the tissue in 3 ways:

- 1- Enter the cell and cause **death** or dysfunction directly.
- 2- Injury may be due to local or systemic release of microbial products including **endotoxin, exotoxins** or **superantigens**.
- 3- Induce host cellular responses which may cause additional damage to the surrounding tissues e.g **suppuration**, scarring, hypersensitivity reactions.

Spectrum of Inflammatory Responses to Infection:

*Microbes produce **5 types** of tissue reaction :*

- 1) **Suppurative** (Purulent) Inflammation:*
- 2) **Mononuclear & granulomatous** inflammation:*
- 3) **Cytopathic-cytoproliferative** response:*
- 4) **Necrotizing** inflammation:*
- 5) **Chronic** inflammation and scarring:*

Classification of infections

- 1. *Primary infection:*** Initial infection with organism in host.
- 2. *Reinfection:*** Subsequent infection by same organism in a host (after recovery).
- 3. *Superinfection:*** Infection by same organism in a host before recovery.
- 4. *Secondary infection:*** When in a host whose resistance is lowered by preexisting infectious disease, a new organism may set up in infection.

Classification of infections

- 5. Focal infection:** It is a condition where due to infection at localized sites like appendix and tonsil, general effects are produced.
- 6. Cross infection:** When a patient suffering from a disease and new infection it set up from another host or external source.
- 7. Nosocomial infection:** Cross infection occurring in hospital.
- 8. Subclinical infection:** It is one where clinical affects are not apparent.

Necrotizing infection



Causative agents of infections

- ***Saprophytes:*** They are free living organisms which fail to multiply on living tissue and so are not important in infectious disease.
- ***Parasites:*** They are organisms that can establish themselves and multiply in hosts. They may be pathogens or commensal. Pathogens are those which are capable of producing disease in a host. On the contrary commensal microbes can live in a host without causing any disease.

Sources of infection in Man

Man: Man is himself a common source of infection from a patient or carrier. Healthy carrier is a person harboring pathogenic organism without causing any disease to him. A convalescent carrier is one who has recovered from disease but continues to harbor the pathogen in his body.

Anthroponosis

Sources of infection in Man

Animals: Infectious diseases transmitted from animals to man are called ***zoonosis***. Zoonosis may be bacterial, (e.g. *Plague* from rat), rickettsial, (e.g. *Murine typhus* from rodent), viral, (e.g. *Rabies* from dog), protozoal, (e.g. *Leishmaniasis* from dogs), helminthic, (e.g. Hydatid cyst from dogs) and fungal (zoophilic dermatophytes from cats and dogs).

Sources of infection in Man

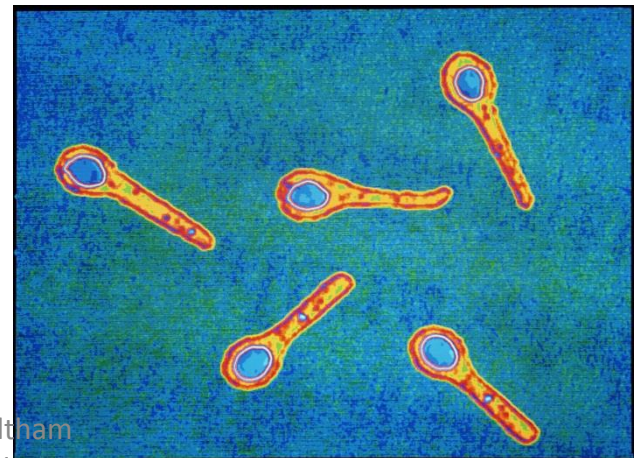
Insects: The diseases caused by insects are called ***arthropod borne disease***. Insects like mosquitoes, fleas, lice that transmit infection are called **vector**. Transmission may be mechanical (transmission of *Dysentery* or *typhoid bacilli* by housefly) and these are called **mechanical vector**. They are called **biological vector** if pathogen multiplies in the body of vector, e.g. *Anopheles mosquito* in *Malaria*.

Sources of infection in Man

Some vectors may act as **reservoir** host, (e.g. ticks in *Relapsing fever* and *Spotted fever*).

Soil: Spores of tetanus bacilli, Gas-gangrene infection remain viable in soil for a long time.

Clostridium tetani



Sources of infection in Man

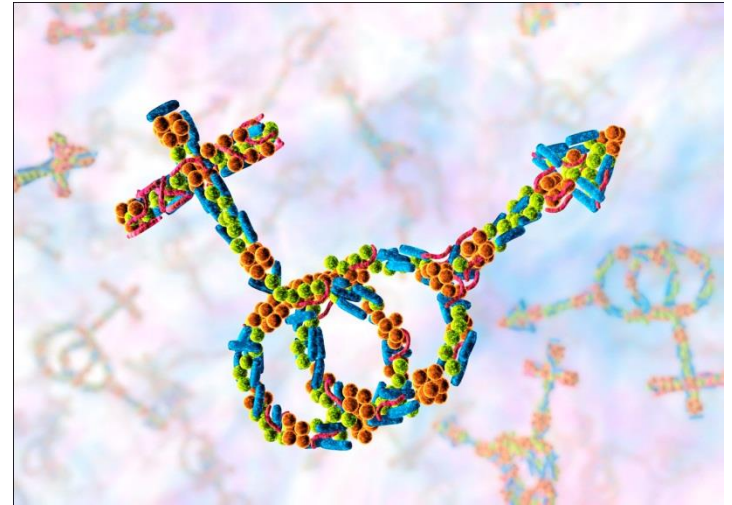
Water: *Vibrio cholerae*,
infective hepatitis virus
(*Hepatitis A and Hepatitis E*) may be found water.

Food: Contaminated food may
be source of infection.
Presence of pathogens in
food may be due to
external contamination,
(e.g. food poisoning by
Staphylococcus).



Methods of transmission of infection

- **Contact**
(sexual intercourse):
syphilis, gonorrhoea.
- **Inhalation:** influenza, tuberculosis, smallpox, measles, mumps, etc.



Methods of transmission of infection

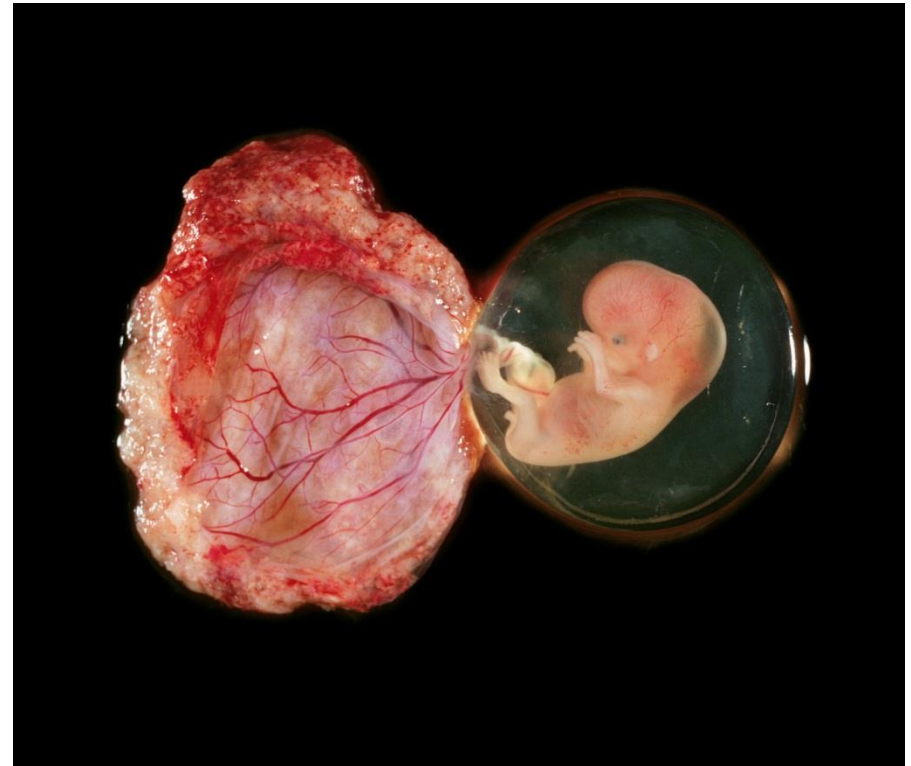
- **Ingestion:** cholera (water), food poisoning (food) and dysentery (hand borne).
- **Inoculation:** tetanus (infection), rabies (dog), arbovirus (insect) and serum hepatitis, i.e. hepatitis B (infection).



Human hand contaminated with colonies of bacteria (blue/pink patches)

Methods of transmission of infection

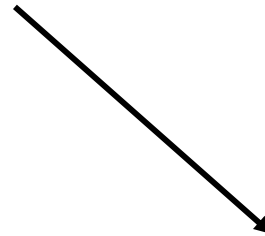
- ***Congenital:***
syphilis,
rubella,
toxoplasmosis,
cytomegaloviruses



Eight week old fetus attached to its placenta by the umbilical cord

Methods of transmission of infection

- ***Insects***: they act as mechanical vector (dysentery and typhoid by housefly) or biological vector (malaria) of infectious disease
- ***Iatrogenic and laboratory infections***: infection may be transmitted during procedures

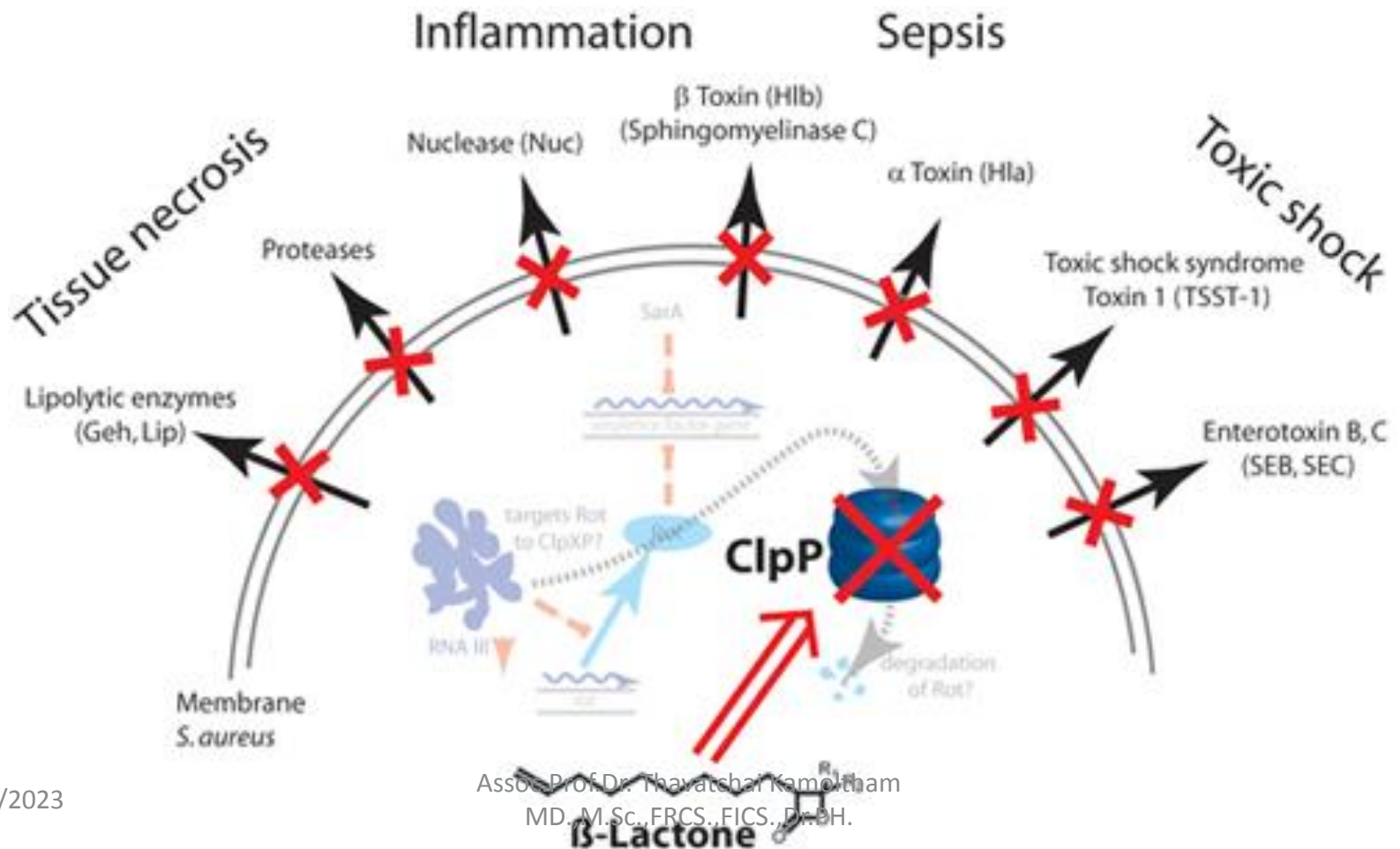


Characters of pathogens

- Bacteria should be able **to enter** the body.
- Organism should be able **to multiply** in the tissue.
- They should be able **to damage** the tissue.
- They must be capable **to resist** the host defense.

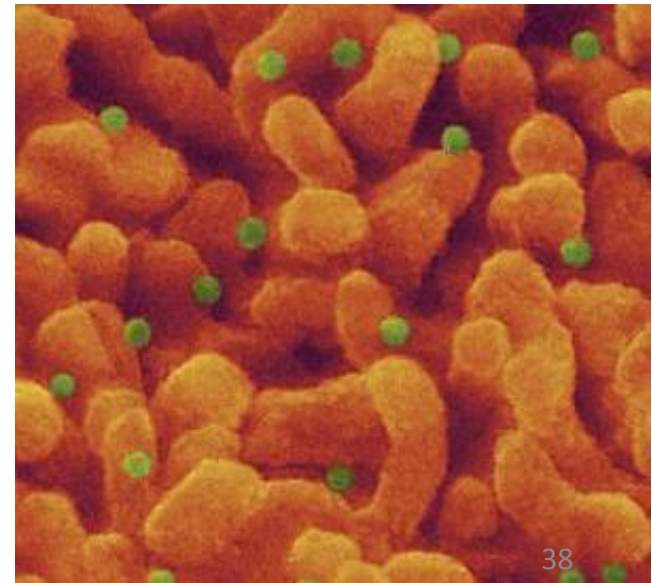
Pathogenecity is referred to the ability of microbial species to produce disease.

Virulence is referred to the ability of microbial strains to produce disease.

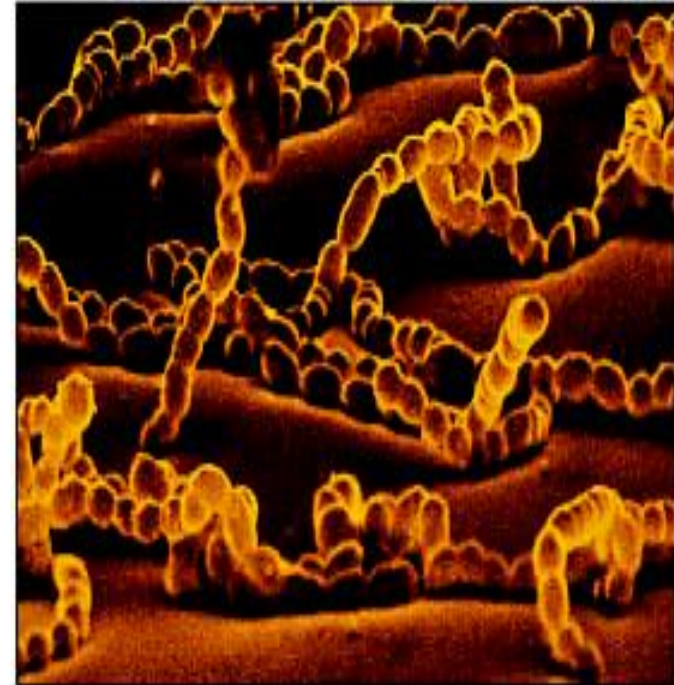
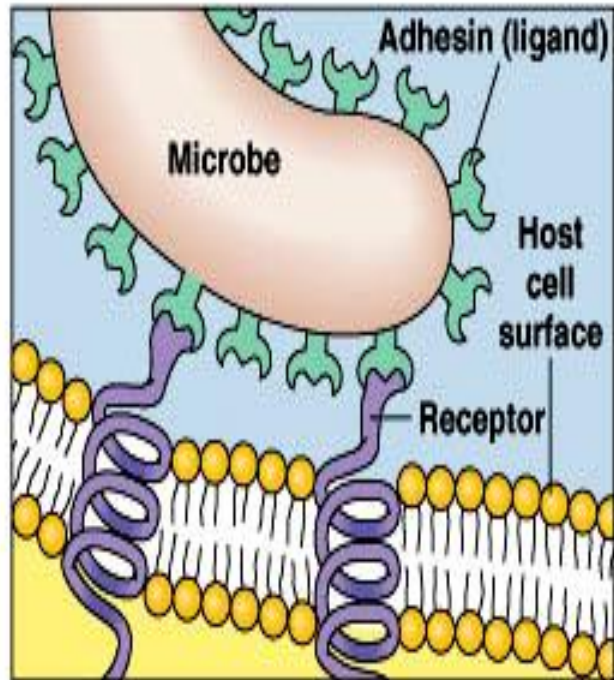


Factors of Virulence

- **Adhesion:** The initial event in the pathogenesis of many infections is the **attachment of the bacteria to body surfaces**. This attachment is specific reaction between surface receptors and adhesive structures on the surface of bacteria (adhesins).



Adherence of bacteria



(a) Surface molecules on a pathogen, called adhesins or ligands, bind specifically to complementary surface receptors on cells of certain host tissues.

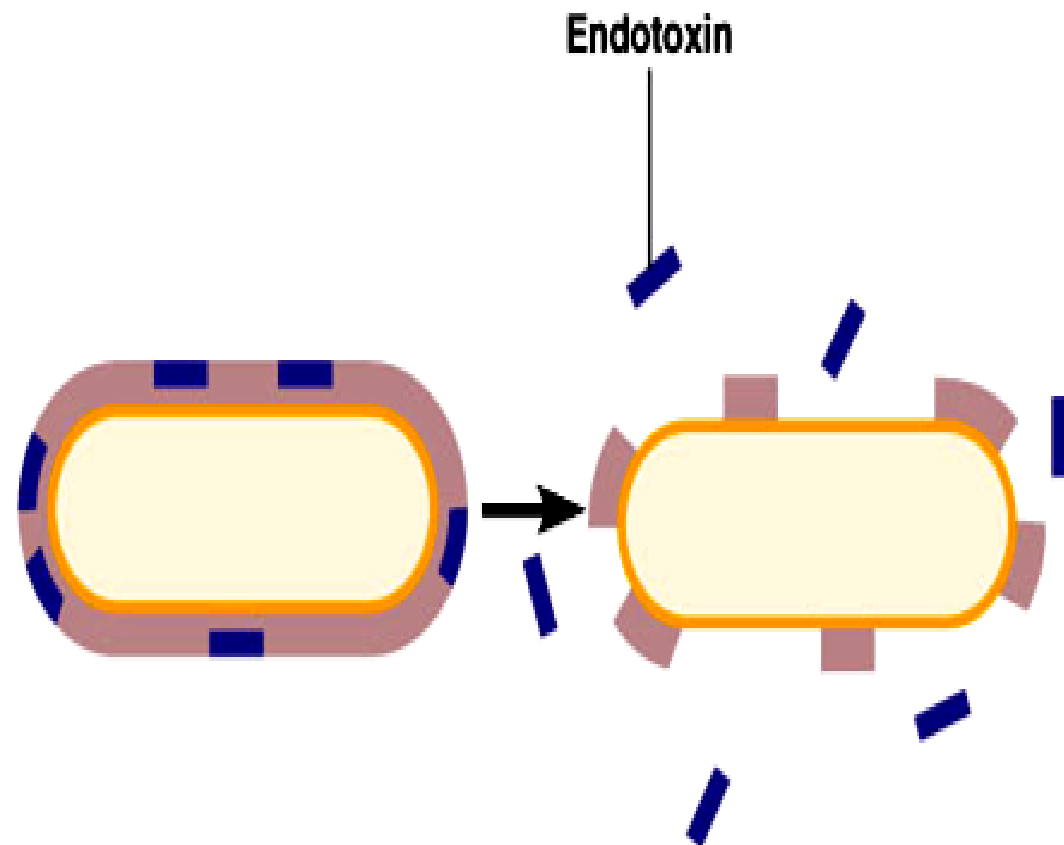
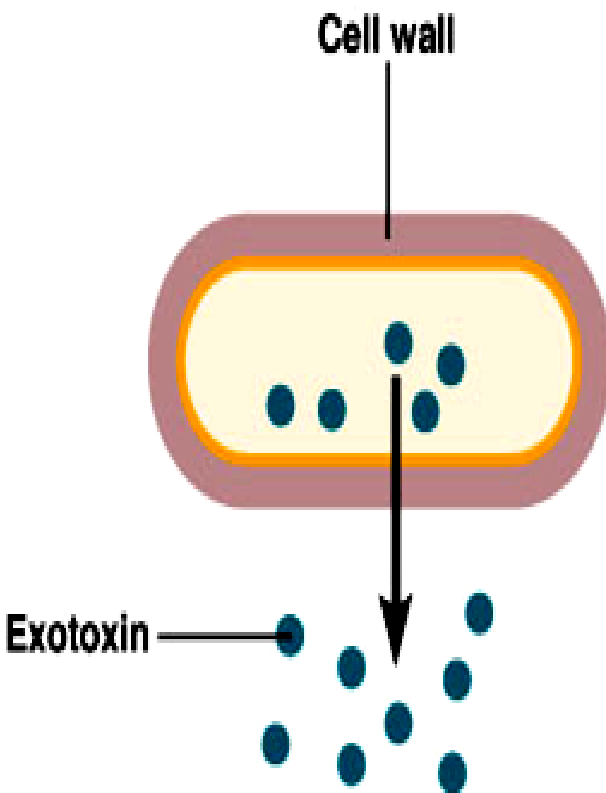
2/23/2023

(b) *E. coli* bacteria (green) on human bladder cells.

(c) Bacteria adhering to human skin.

Factors of Virulence

- ***Invasiveness*** is the ability of organism to **spread in a host tissue** after establishing infection.
 - Less invasive organisms cause ***localized*** lesion.
 - Highly invasive organisms cause ***generalized*** infection (septicemia).
- ***Toxigenicity***. Bacteria produce two types of toxins – ***exotoxins*** & ***endotoxins***



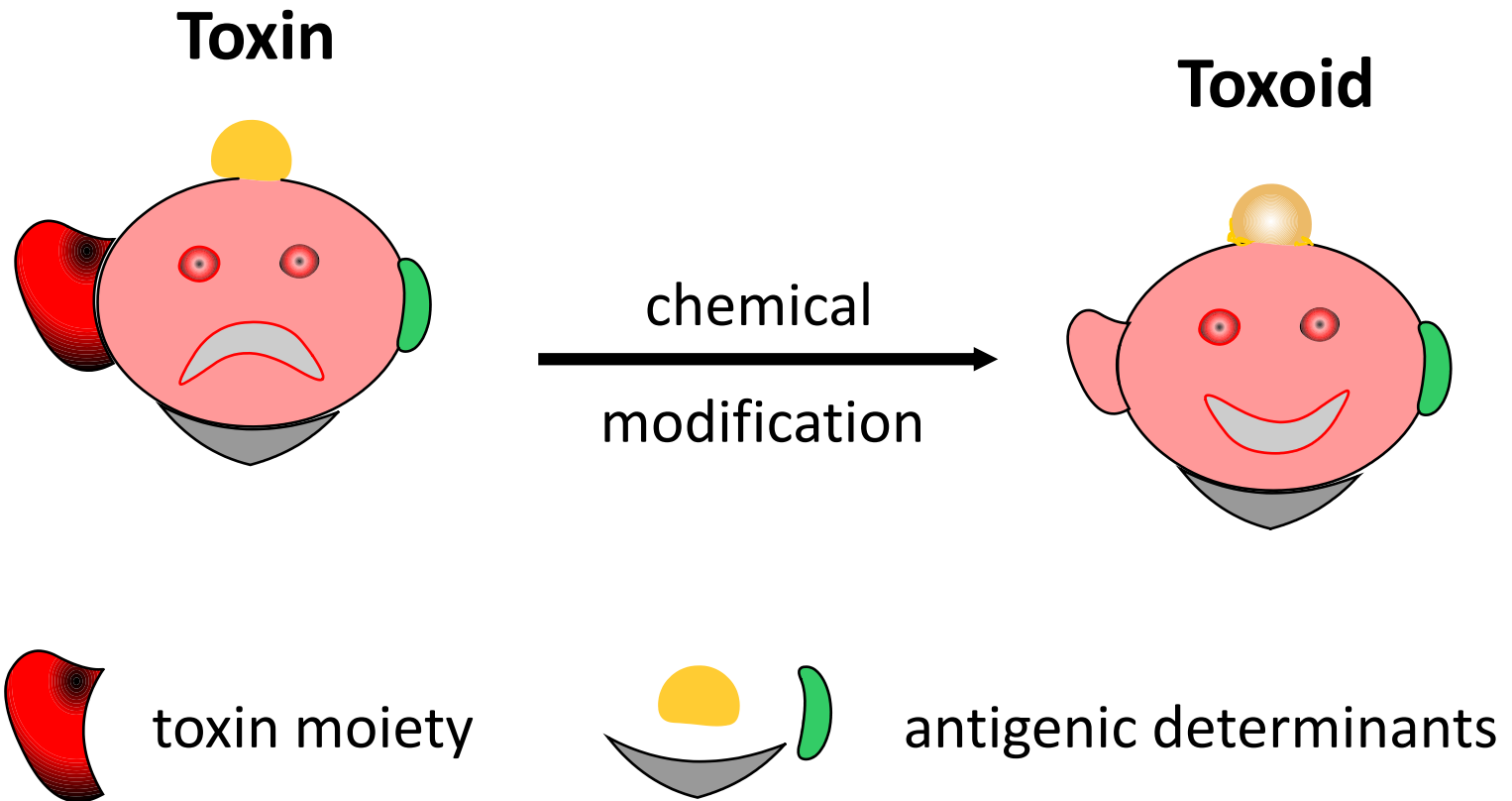
(a) Exotoxins are produced inside mostly gram-positive bacteria as part of their growth and metabolism. They are then secreted or released following lysis into the surrounding medium.

(b) Endotoxins are part of the outer portion of the cell wall (lipid A; see Figure 4.12c) of gram-negative bacteria. They are liberated when the bacteria die and the cell wall breaks apart.

Factors of Virulence - Exotoxins

- **Heat labile protein**.
- Diffuse readily into the surrounding medium.
- **Highly potent**, e.g. 3 kg botulinum can kill all the inhabitants of world.
- They are generally formed by Gr+ bacteria and also by Gr- organisms like **Shigella, V.cholerae, E.coli**.
- Exotoxin is specifically **neutralized antitoxin**.
- Can be separated from culture by filtration.
- Action is **enzymatic** and it has **specific** tissue affinity.
- **Specific pharmacological effects** for each exotoxin.
- Cannot cause pyrexia in a host.
- Can be **toxoided**.

Modification of Toxin to Toxoid



Factors of Virulence - Endotoxins

- **Endotoxin** (lipid a portion of lipopolysaccharide) has biological activities causing *fever, muscle proteolysis, uncontrolled intravascular coagulation and shock.*
- These may be mediated by production from mononuclear cells of IL-1, probably IL-6.

Characters of Endotoxins

- Proteins polysaccharide lipid complex **heat stable.**
- Forms part of cell wall (don't diffuse into the medium).
- Obtained only by cell lysis.
- They have no enzymatic action.
- Effect is non-specific action.
- No specific tissue affinity.
- Active only in large doses 5 to 25 mg.
- Weakly antigenic.
- Neutralization by antibody ineffective.
- Cannot be toxoided.
- Produce in Gram negative bacteria.

Factors of Virulence

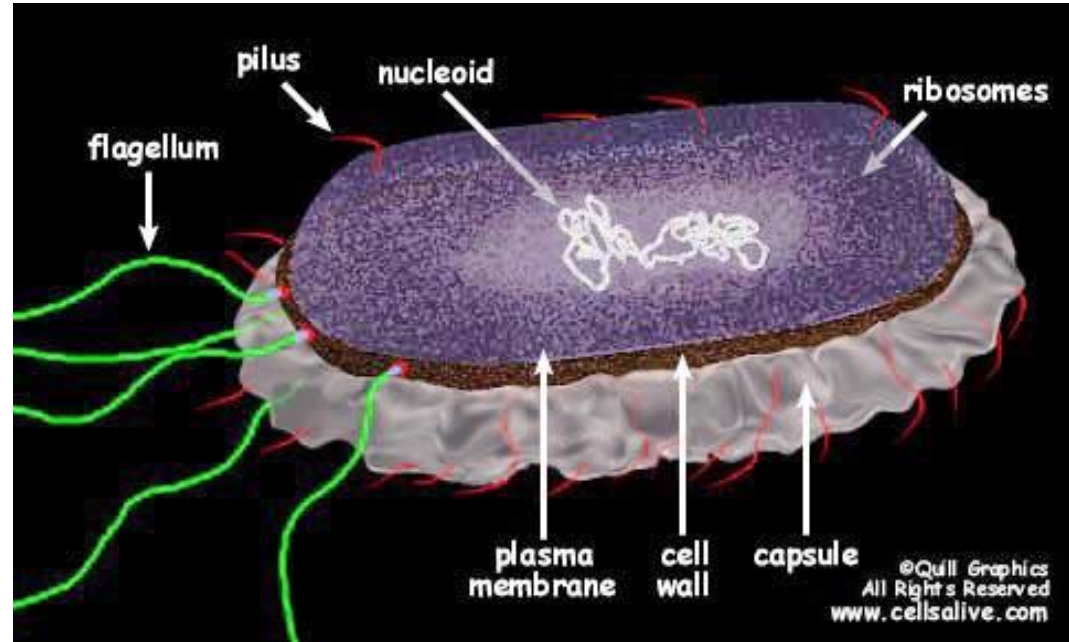
- *Communicability* is the ability of parasite to spread from one host to another. It determines the survival and distribution of organism in a community.
- *Coagulase* (S.aureus) which prevents phagocytosis by forming fibrin barrier around bacteria.
- *Fibrinolysin* promotes the spread of infection by breaking down the fibrin barrier in tissues.

Factors of Virulence

- *Hyaluronidase* split hyaluronic acid (component of connective tissue).
- *Leucocidins* damage polymorphonuclear leucocytes.
- *Ig A1 proteases*: split IgA and inactivates its antibody activity.
- *Hemolysin* is produced by some organisms capable of destroying erythrocytes.

Factors of Virulence. Bacterial appendages

Capsulated bacteria like **Pneumococcus**, **K.pneumoniae** and **H.influenzae** stand phagocytosis



Surface antigen, e.g. Vi-antigen of *S. typhi* and K- antigen of *E.coli* resisted phagocytosis and lytic activity of complement.

Infecting dose

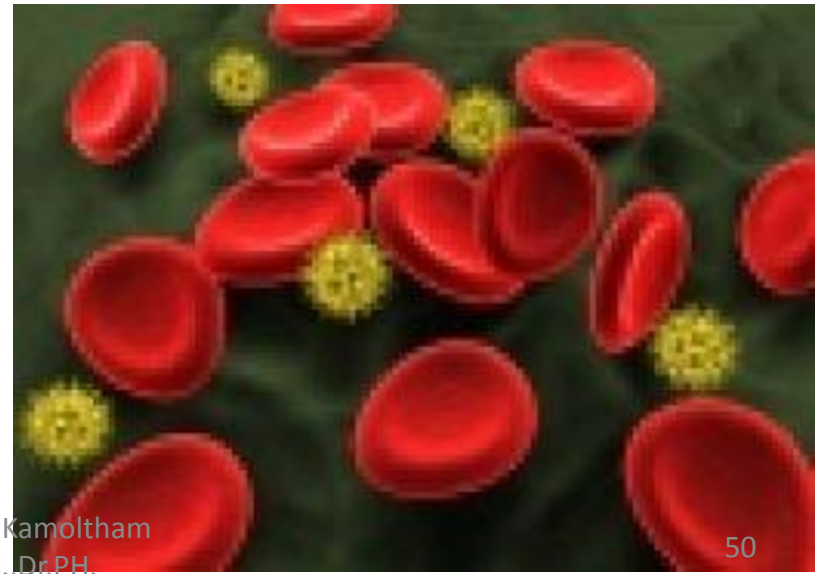
- The *minimum infection dose* (MID) or *minimum lethal dose* (MLD) is the minimum number of organism required to produce clinical evidence of infection or death of susceptible animal.

- *Route of infection*

- *Vibrio cholerae* is effective orally. No effect when it is introduced subcutaneously.
- *Streptococci* can initiate infection whatever be the mode of entry.

Types of infectious diseases

- Infectious diseases may be
- **localized** or **generalized**
- **superficial** or **deep-seated**.
- Circulation of bacteria in the blood is known as **bacteremia** (viruses – **virusemia**).



Types of infectious diseases

- ***Septicemia*** *ภาวะโลหิตเป็นพิษ* is the condition where bacteria circulate and multiply in the blood, form toxic products and cause swinging type of fever.
- ***Pyemia*** is a condition where pyogenic bacteria produce septicemia with multiple abscesses in the internal organs such as the spleen, liver and kidney.

Types of infectious diseases

Depending on the spread of infectious disease in the community they may be classified into different types.

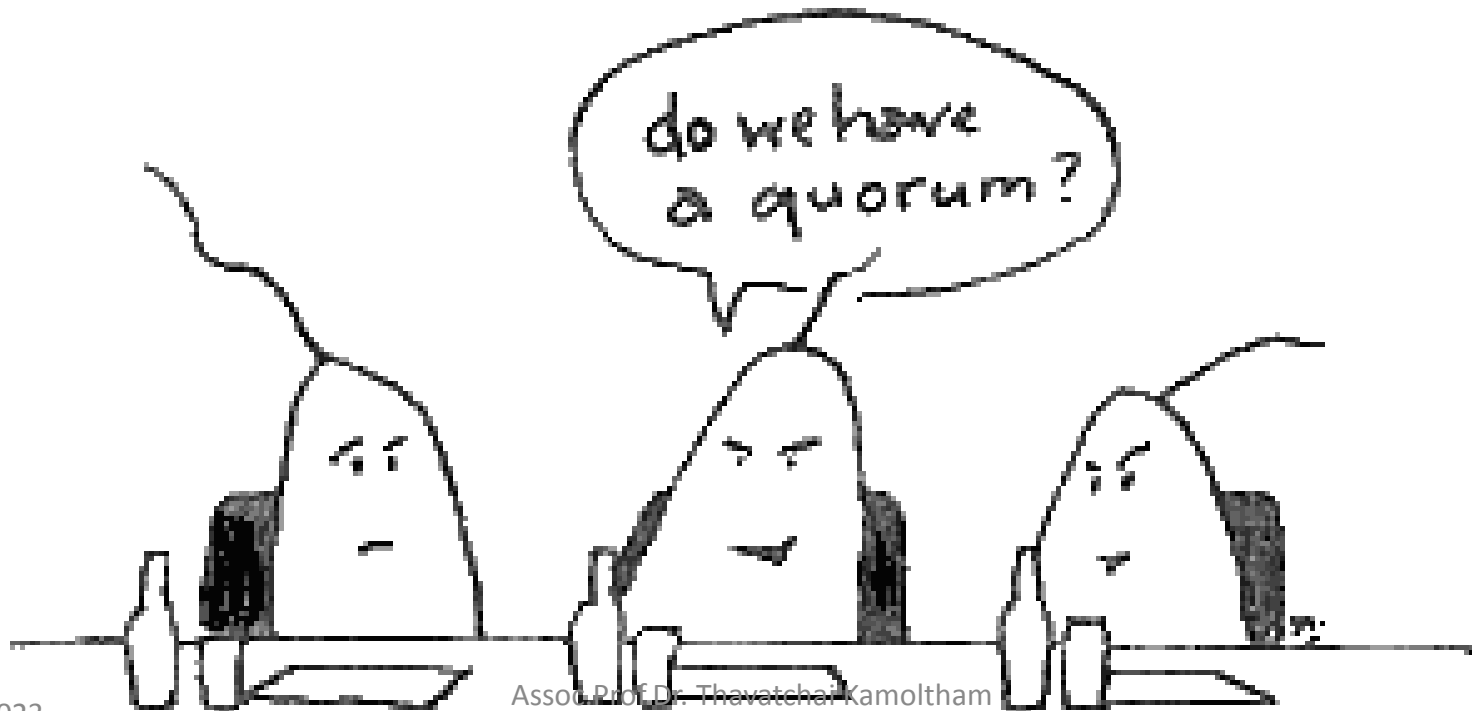
- **Endemic** โรคประจำถิ่น diseases are ones that are constantly present in a particular area. Typhoid fever is endemic in most parts of India. An **epidemic** disease is one that spreads rapidly, involving many persons in an area at the same time. **Influenza causes** annual winter epidemics in the cold countries.
- **Epidemics** โรคระบาด vary in the rapidity of spread. Waterborne disease such as **cholera and hepatitis** may cause explosive outbreaks, while disease, which spreads by person-to-person contact evolve more slowly.
- **Pandemic** การระบาดใหญ่ is an epidemic that spreads through many areas of the world involving very large numbers of persons within a short period (**Influenza, cholera, plaque**).

Stages of infectious disease

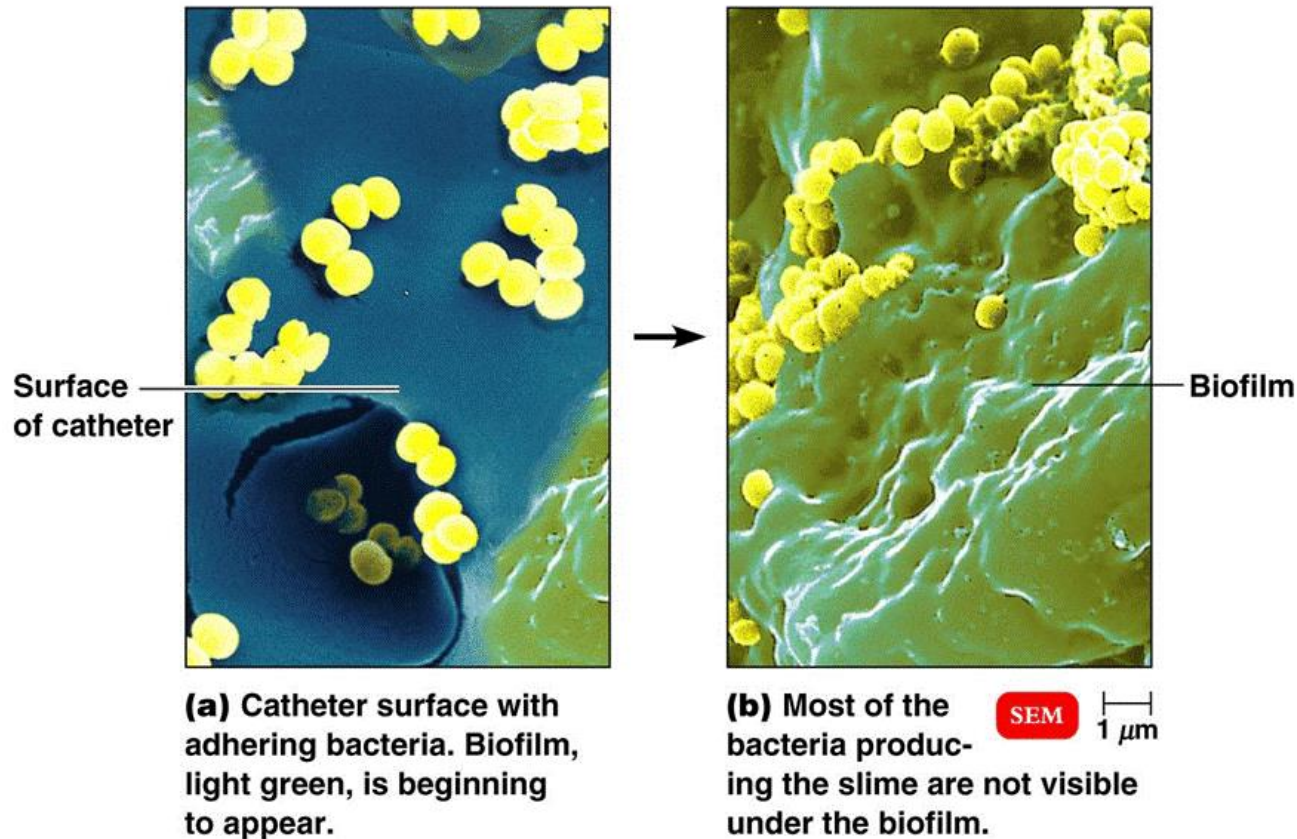
- ***Incubation period*** – no symptoms.
- ***Prodromal period*** – mild and generalized symptoms (fever, weakness, headache).
- ***Invasive stage*** – symptoms specific to the disease.
- ***Decline stage*** – symptoms subside.
- ***Convalescence*** – no symptoms, health returns to normal.

Quorum Sensing

Many groups of bacteria can communicate - by releasing and detecting chemical **pheromones** to gauge their population density - the molecular structure of a key protein in this interbacterial communication has been solved.



Quorum sensing provides an explanation for why some disease-causing virulence factors are not expressed during the early stages of encounter with the human host



Copyright © 2007 Pearson Education, Inc., publishing as Benjamin Cummings.

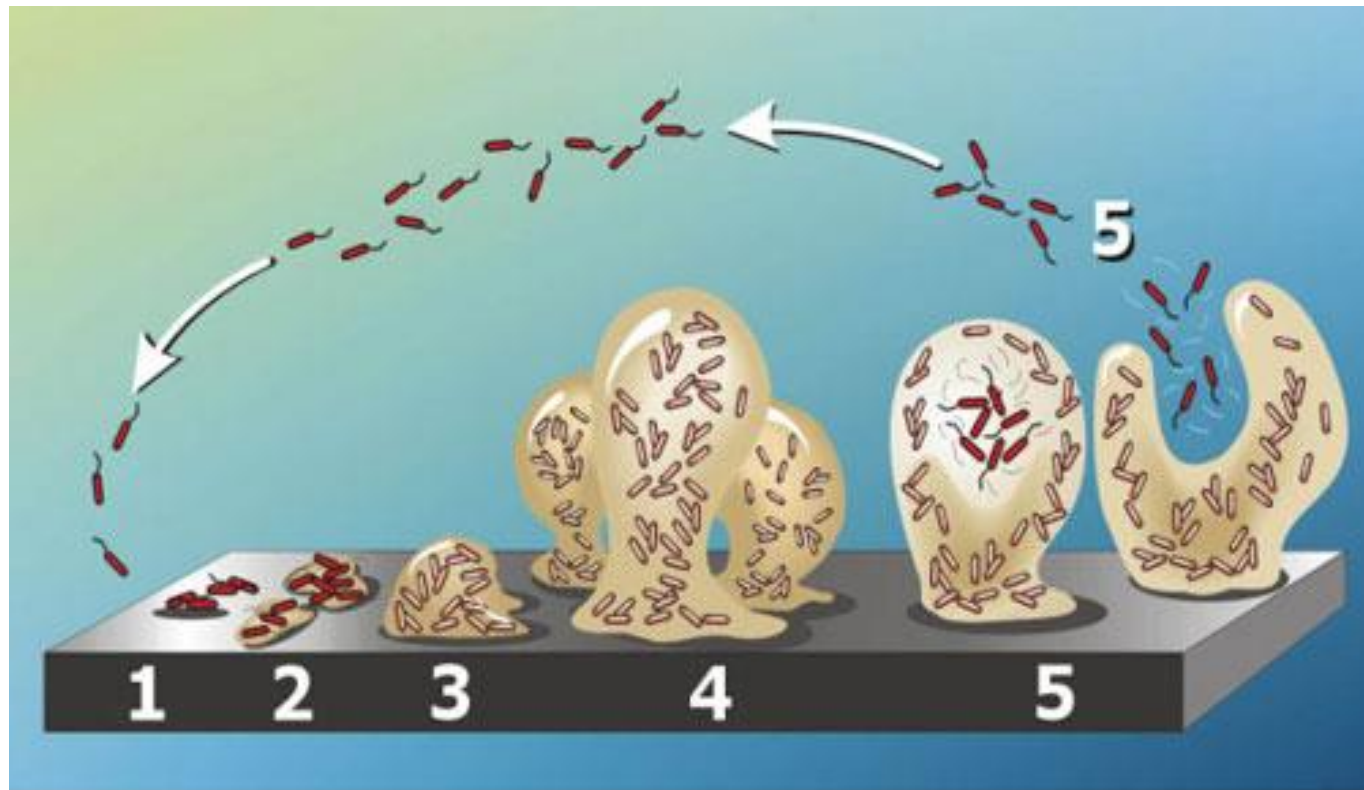
Biofilm Bacteria

- Biofilm bacteria can be up to **1000 times more resistant** to antimicrobial stress (e.g. antibiotics and disinfectants) than free-swimming bacteria of the same species.
- **Plaque** is a biofilm on the surfaces of the teeth which secretes acids that destroy teeth and gums

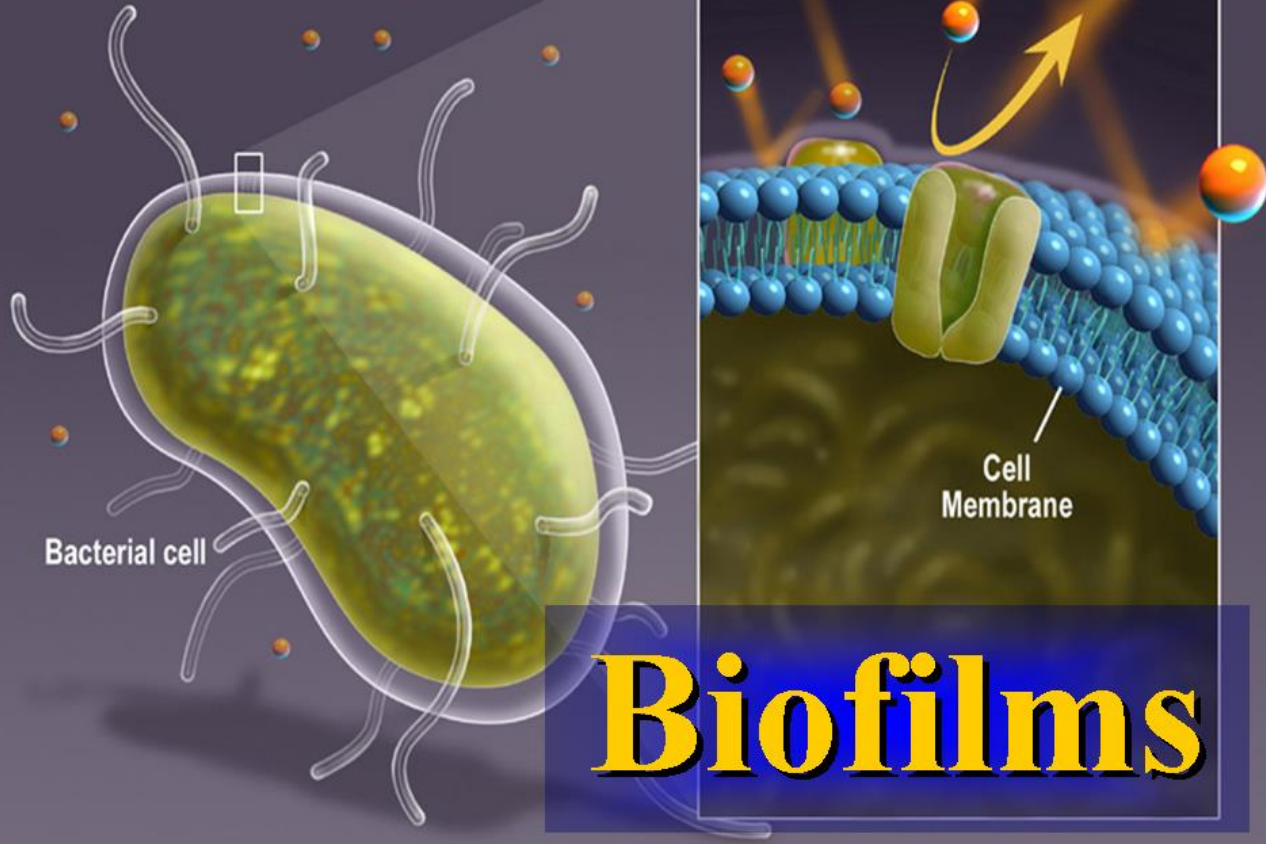


Dental plaque as seen under a scanning electron microscope

5 stages of *P.aeruginosa* biofilm development
1, initial attachment; 2, irreversible attachment;
3, 4 - maturation ; 5, dispersion.



Cellular Resistance



These communities represent a higher order of structure and function than is found when bacteria are grown in broth culture

Biofilm communities are responsible for much of the biological activity attributed to bacteria in the wide range of habitats occupied by these biochemically complex microorganisms

Uncovering the Hidden Antibiotic Potential of Cannabis

Maya A. Farha, Omar M. El-Halfawy, Robert T. Gale, Craig R. MacNair

, Lindsey A. Carfrae, Xiong Zhang, Nicholas G. Jentsch,

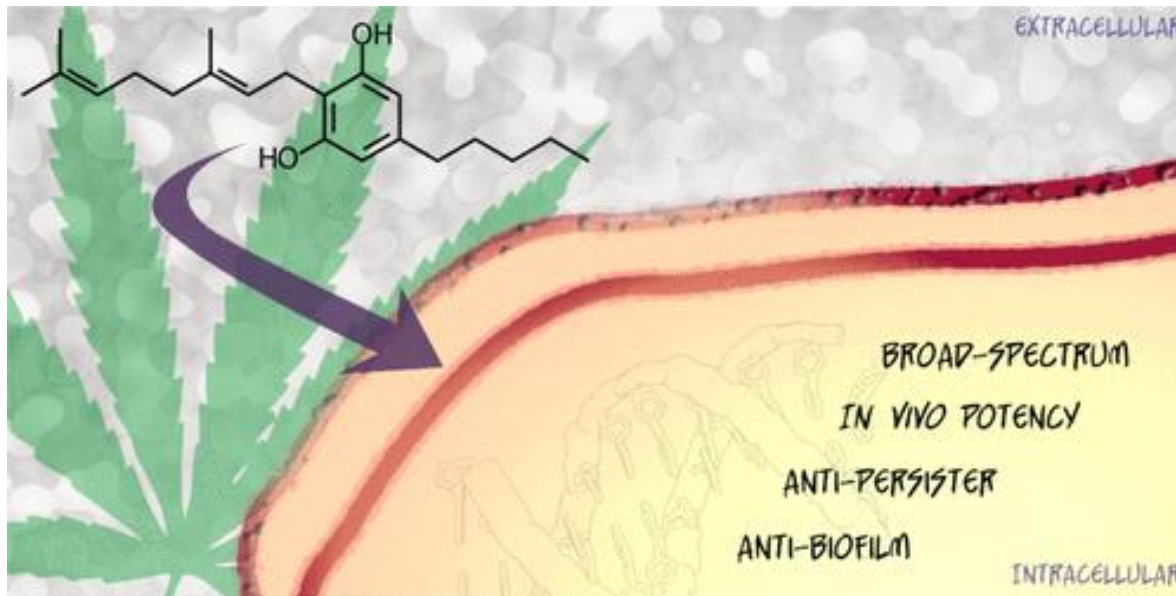
Jakob Magolan

Department of Biochemistry and Biomedical Sciences, McMaster University, Hamilton, Ontario L8N 3Z5, Canada

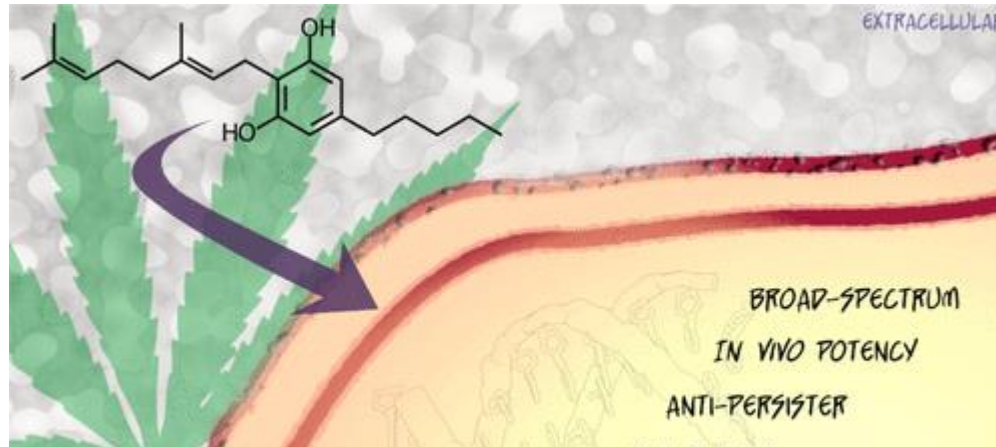
Michael G. De Groote Institute of Infectious Disease Research, McMaster University, 1200 Main Street West, Hamilton, Ontario L8N 3Z5,

Canada <http://orcid.org/0000-0002-2947-8580>

and **Eric D. Brown*** [Cite this:](#) *ACS Infect. Dis.* 2020, 6, 3, 338–346



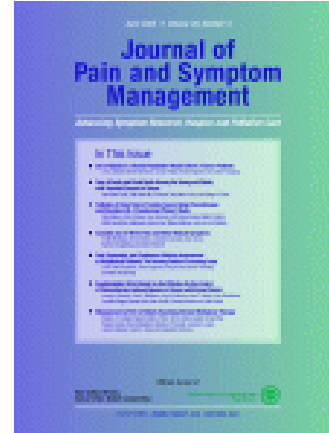
Uncovering the Hidden Antibiotic Potential of Cannabis



- *Cannabis sativa* has long been known to contain antibacterial cannabinoids, but their potential to address antibiotic resistance has only been superficially investigated.
- Cannabinoids exhibit antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA), inhibit its ability to form biofilms, and eradicate preformed biofilms and stationary phase cells persistent to antibiotics.
- Demonstrate *in vivo* efficacy of **cannabigerol CBG** in a murine systemic infection model caused by MRSA.
- Cannabinoids work in combination with polymyxin B against multidrug resistant Gram-negative pathogens, revealing the broad-spectrum therapeutic potential for cannabinoids.



ScienceDirect



Journal of Pain and Symptom Management

Volume 29, Issue 4, April 2005, Pages 358-367

Cannabis Use in HIV for Pain and Other Medical Symptoms

Emily Woolridge MB BS, BSc. Cite <https://doi.org/10.1016/j.jpainsymman.2004.07.011> Get rights and content

- the major benefits of **antiretroviral therapy** on survival during HIV infection,
- an increasing need to manage symptoms and side effects during long-term drug therapy.
- Up to one-third HIV patients (27%, 143/523) reported using cannabis for treating symptoms.
- **Patients reported improved appetite (97%), muscle pain (94%), nausea (93%), anxiety (93%), nerve pain (90%), depression (86%), and paresthesia (85%).**
- Many cannabis users (47%) reported associated memory deterioration.

Cannabis and Infection

[The antimicrobial effect behind *Cannabis sativa*](#)

[L Schofs, MD Sparo... - ... Research & Perspectives, 2021 - Wiley Online Library](#)

... **Cannabis** sativa preparations have a long history of medical applications, including the treatment of **infectious diseases**. This review collects the information about the activity of *C. sativa* ...

บันทึก อ้างอิง อ้างโดย [17](#) บทความที่เกี่ยวข้อง ทั้งหมด [9](#) ฉบับ

[\[PDF\] letfreedomgrow.com](#)

[History of **cannabis** and its preparations in saga, science, and sobriquet](#)

[EB Russo - Chemistry & biodiversity, 2007 - Wiley Online Library](#)

... **infectious disease** that remain challenges for 21st century medicine. Information gleaned from the history of **cannabis** ... techniques and standardization of **cannabis**-based medicines that ...

บันทึก อ้างอิง อ้างโดย [622](#) บทความที่เกี่ยวข้อง ทั้งหมด [14](#) ฉบับ

[\[HTML\] **Cannabis** use and fungal **infections** in a commercially insured population, United States, 2016](#)

[K Benedict, GR Thompson III... - ... **infectious diseases**, 2020 - ncbi.nlm.nih.gov](#)

... , and fungal contamination of **cannabis** has been described. In a ... **cannabis** were 3.5 (95% CI 2.6–4.8) times more likely than persons who did not use **cannabis** to have a fungal **infection** ...

บันทึก อ้างอิง อ้างโดย [18](#) บทความที่เกี่ยวข้อง ทั้งหมด [14](#) ฉบับ

Cannabis and Infection

[Cannabis and its secondary metabolites: their use as therapeutic drugs, toxicological aspects, and analytical determination](#)

J Gonçalves, T Rosado, S Soares, AY Simão... - Medicines, 2019 - mdpi.com

... , production, use and sale of **cannabis**, and has led inclusively ... allowed a better understanding of **cannabis** derivatives as ... therapy, neurodegenerative **diseases**, and **infectious diseases**. ...

[Heavy cannabis use associated with reduction in activated and inflammatory immune cell frequencies in antiretroviral therapy–treated human immunodeficiency virus ...](#)

JA Manuzak, TM Gott, [JS Kirkwood](#)... - ... **Infectious Diseases**, 2018 - academic.oup.com

... suggest that **cannabis** use is associated with a potentially beneficial reduction in systemic inflammation and immune activation in the context of antiretroviral-treated HIV **infection**. ...

[Beneficial effects of cannabis on blood–brain barrier function in human immunodeficiency virus](#)

[RJ Ellis](#), [S Peterson](#), [M Cherner](#)... - ... **Infectious Diseases**, 2021 - academic.oup.com

... As depicted schematically in Figure 1, we hypothesized that an interaction between HIV serostatus and **cannabis** use such as that in PWH with a leaky BBB, **cannabis** would improve ...

Cannabis and Infection

Modulation of the immune system in **cannabis** users

R Pacifici, P Zuccaro, S Pichini, PN Roset, S Poudevida... - Jama, 2003 -
jamanetwork.com

... , as the log-transformed number of **cannabis** "joints") and the ... **Cannabis** use was associated with a decrease in levels of IL-... promote the progression of **infectious diseases** and tumors, ...

Effect of **cannabis** use on human immunodeficiency virus DNA during suppressive antiretroviral therapy

A Chaillon, M Nakazawa, C Anderson... - ... **Infectious Diseases**, 2020 -
academic.oup.com

... effect of **cannabis** on HIV DNA was not evident when **cannabis** was used in combination with any other drugs, highlighting the complex interplay between drug use and viral **infections**. ...

Antioxidant activity and evidence for synergism of **Cannabis** sativa (L.) essential oil with antimicrobial standards

A Nafis, A Kasrati, CA Jamali, N Mezrioui... - Industrial Crops and ..., 2019 - Elsevier

... for the first time the antimicrobial potential of Moroccan **Cannabis** sativa essential oil (EO) singly or ... strategy to overcome the intense use of antibiotics against some **infectious diseases**.