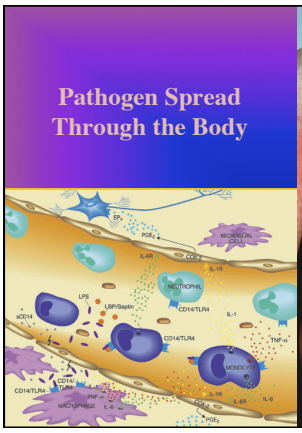
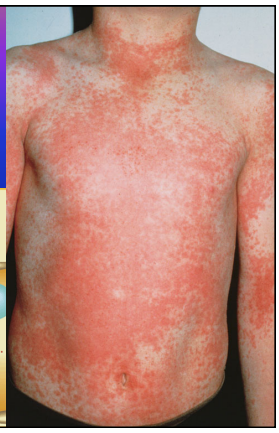
Pathogen Spread Through the Body





Summary

- **Successful Pathogens:**
  1. **Enter the body via skin defect, through respiratory, digestive, or urogenital systems, or through the conjunctiva.**
  2. **Adhere to and colonize/enter specific cells in body. Inflammation may be initiated.**
  3. **May penetrate through an epithelial cell layer. Have invasins. Initiate local inflammatory response.**
  4. **Evade phagocytic cells and chemical components of inflammation.**
- **Next Step: Spread through the body (if causing systemic infection) and evasion of immune responses.**

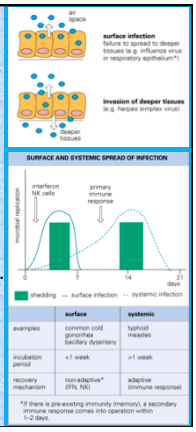
Localized versus Systemic Infections (Fig 15.1&15.2)

- **Why do some organisms leave the surface of the body or from a localized infection to spread through the body?**
- **Can depend on characteristics of pathogen.**
- **Localized Infections:**

1. **Some organisms don't spread systemically because deeper environments not suitable for reproduction. Example: Rhinovirus (colds).**
2. **Some organisms enter and exit using the same surface. No opportunity for deeper penetration. Example: Influenza virus.**
3. **No need to enter deeper tissues. Can undergo complete "cycle" and leave body before specific defenses mounted. No advantage to causing a systemic infection.**

- **Systemic Infections:**

1. **Environment not ideal at point of entrance. Spread systemically to maximize growth potential.**
2. **Principle target not at entry site. Spread systemically to reach target.**
3. **Many pathogens: reason for systemic spread not known.**



Rates of Replication and Systemic Spread (Table 15.1)

- Rate of pathogen replication affects systemic spread.
- The slower an organisms doubling time, the more likely it causes systemic infection.
  - Slow replication: longer time required for specific defenses to develop. More opportunity for organism to spread.
- Doubling times *in vitro* vs. *in vivo* can be significantly different.
  - *In vitro*: conditions set for optimal growth, no body defenses to combat.
  - *In vivo*: nutrients or environment not optimal and innate/adaptive defenses slow rate of reproduction.

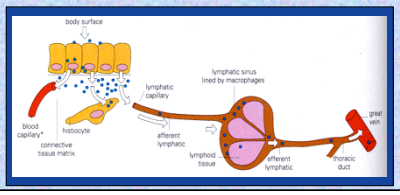
REPLICATION RATES OF MICROORGANISMS

microorganism	situation	mean doubling time
most viruses	in cell*	< 1 h
many bacteria, e.g. *Escherichia coli, staphylococci*	in vitro	20–30 min
Salmonella typhimurium	in vitro in vivo	30 min 5–12 h
Mycobacterium tuberculosis	in vitro in vivo	24 h many days
Mycobacterium leprae†	in vivo	2 weeks
Treponema pallidum†	in vivo	30 h
Plasmodium falciparum	in vitro/in vivo (erythrocyte or hepatic cell)	8 h

*but some viruses show greatly delayed replication or delayed spread from cell to cell
†cannot be cultivated in vitro

Spread Through the Body (Fig 15.6)

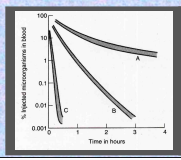
- After entry and multiplication in local cells or tissues, pathogen usually transported to regional lymphatic tissue or lymph nodes.
  - Immune response begins in lymph nodes.
  - Some pathogens target lymphatic tissue (slows immune responses).
- Becomes race between pathogen reproduction rates and how effectively lymph node filters out organism (resident phagocytes).
- Factors affecting pathogen removal:
  - Rate of lymph flow: high rate of flow (acute or severe inflammation) favors pathogen.
  - Pathogen load: high numbers favors pathogen passage through lymph node.
- If pathogen wins, organisms enter blood stream and spread systemically.



Survival of Pathogens in Blood Stream

- Survival of pathogens in blood stream depends on:

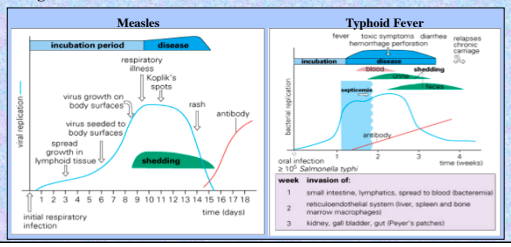
1. Species of pathogen.
2. Immune status of host.
3. Whether organisms remain in plasma or circulate on/inside cellular component of blood.
   - If free in plasma: must withstand chemical (complement, antibodies) and cellular (phagocytes) components of blood.
   - On/within blood cells, pathogen more protected.
4. Point where organisms enter blood.
   - Organisms entering pulmonary circulation have greater chance of spreading than organisms entering through digestive tract.
     - Blood from lungs returns immediately to heart, then distributed throughout body.
     - Blood from digestive system passes through liver. Many pathogens removed by Kupffer cells (resident macrophage).



		Leucocyte associated			
	Free in plasma	Mononuclear cells	Polymorphs	Erythrocyte associated	Platelet associated
Viruses	Poliovirus Yellow fever Hepatitis B	Measles Epstein–Barr virus Herpes simplex Cytomegalovirus HIV		Colorado tick fever virus Human parvovirus B19[b]	Murine leukaemia virus LCM virus (see Glossary)
Rickettsiae Bacteria	All types Pneumococci *Leptospira* *B. anthracis* *Borrelia recurrentis*	*Mycobacterium leprae* *Listeria* *Brucella*	Pyogenic bacteria	*Bartonella bacilliformis*	
Protozoa	Trypanosomes	*Leishmania* *Toxoplasma gondii*		Malaria *Babesia*	

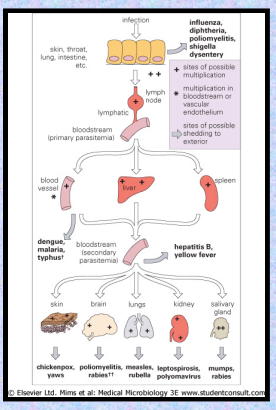
Systemic Infections Evolve by "Stepwise" Growth of Pathogens in the Body (Fig 15.4&15.5)

- In systemic infections, pathogens frequently don't go immediately to their final destination(s).
- As spread occurs, different sites are infected and growth occurs before pathogen spread to tissue where signs and symptoms occur.
- This is incubation and/or prodromal stage of infection. Disease frequently contagious.



Localization Within the Body (Fig 15.3)

- The mechanism used by pathogens to target specific organs from the circulation is poorly understood. Theories:
  1. Adhesins/receptors on pathogens target particular types of endothelial cells.
     - Not proven.
  2. Pathogens randomly adhere to all endothelial cells but only multiply/ cause disease in certain organs.
     - Not convincingly demonstrated.
  3. Local inflammation targets pathogens to specific organs due to slow blood flow and sticky endothelium.
     - What initiates the inflammation?



Organism Spread via the Blood (Table 15.2)

- Though targeting mechanisms are not understood, many organisms spread via the blood stream and invade specific organs.

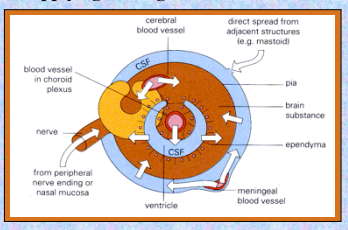
CIRCULATING MICROBES THAT INVADE ORGANS VIA SMALL BLOOD VESSELS

microbe	disease	principal organs invaded*
viruses		
hepatitis B	hepatitis B	liver
rubella	congenital rubella	placenta (fetus)
varicella-zoster virus	chickenpox	skin, respiratory tract
polio	poliomyelitis	brain, spinal cord
mumps	mumps	parotid, mammary glands
bacteria		
Rickettsia rickettsi	Rocky Mountain spotted fever	skin
Treponema pallidum	secondary syphilis	skin, mucosae
Neisseria meningitidis	meningitis	meninges
protozoa		
Trypanosoma cruzi	Chagas' disease	heart, skeletal muscle
Plasmodium spp.	malaria	liver
helminths		
Schistosoma spp. (larvae)	schistosomiasis	veins of bladder, bowel
Ascaris lumbricoides (larvae)	ascariasis	lung
Ancylostoma duodenale (larvae)	hookworm	lung

*in liver, sinusoids; elsewhere, capillaries, venules

Spread Through the Nervous System (Fig 15.7)

- Some virus move systemically utilizing nerve fibers (either within nerve cells or support cells for nerves). This mechanism of spread is protected from both inflammatory and immune surveillance. Few pathogens can utilize this route.
- Most pathogens of nervous system enter from blood stream using vessels supplying meninges or brain.



Alternate Mechanisms of Spread

- Organisms may spread by penetrating internal cavities of the body.

1. Cerebrospinal fluid (CSF) is located between nervous tissue (brain and spinal cord) and surrounding meninges. Organisms that penetrate this space are protected from host defense systems (blood-brain barrier).
2. The pleural cavity surrounds the lungs (between lung tissue, diaphragm, and ribs). The cavity is lined by a pleural membrane rich in phagocytic cells. Inside the cavity is pleural fluid that facilitates respiration by preventing tissue adherence. If pathogens reach this space, they spread in the fluid and may penetrate the pericardium (membrane and fluid-filled space surrounding the heart).
3. The peritoneal cavity is the space where the digestive system and abdominal organs are separated from the abdominal wall by a membrane system called the peritoneum. The peritoneum is rich in phagocytic cells. Organisms entering the peritoneal cavity can spread throughout the abdomen invading almost any abdominal organ and cause peritonitis.