

# BIOL215: MICROBIOLOGY FOR HEALTHCARE PROFESSIONALS

## Lecture notes for Exam 4

DR. PRYOR

### ANTIVIRAL DRUGS

#### 1. NUCLEOSIDE ANALOGS

- mimic **nucleosides** (“building blocks”) of DNA and RNA  
A T G C U
- block viral DNA or RNA from being **transcribed** or **translated**

##### Ex. Azidothymidine (AZT) “Retrovir”

- mimics T (thymidine)...a thymidine analog
- used to treat HIV

##### Ex. Acyclovir “Zovirax”

- mimics G (guanosine)...a guanosine analog
- used to treat **herpetic** diseases, such as HSV-1 and HSV-2

##### Ex. Valacyclovir “Valtrex”

- mimics G (guanosine)...a guanosine analog
- used to treat **herpetic** diseases, such as HSV-1 and HSV-2
- a **prodrug** = converted in the body into acyclovir

##### Ex. Ribavirin “Copegus”

- mimics G (guanosine)...a guanosine analog
- used to treat viral hepatitis

#### 2. COMPETITIVE ENZYME INHIBITORS

- bind to the active sites of enzymes that are needed for viral replication

##### Ex. Oseltamivir “Tamiflu”

- blocks **neuraminidase**
- virions cannot escape host cell
- used to treat influenza

##### Ex. NNRTIs (Non-Nucleoside Reverse Transcriptase Inhibitors)

- “non-nukes”
- blocks **reverse transcriptase**
- reverse transcriptase enzyme is needed for RNA viruses
- **reverse transcription** converts RNA into DNA, which is then used by the host cell

- ex. Efavirenz “Sustiva”
- used to treat HIV

### 3. INTERFERONS

- proteins secreted by virus-infected host cells
- interfere with viral replication

**Ex. Pegylated interferon  $\alpha$ -2a “Pegasys”**

- used to treat viral hepatitis
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### VIRAL VACCINES

- prevent viral diseases
- “immunizations”
- train the host’s immune system to attack viruses
- they do not cause the viral disease

#### 1. Live, attenuated vaccines

- intact virions that have been weakened
- some patients will have some symptoms and signs of the disease, but mild
- most effective, longest-lasting type of vaccine

#### 2. Inactivated “killed” vaccines

- intact virions that have been destroyed
- patients will NOT have some symptoms and signs of the disease
- less effective, shorter-lasting type of vaccine

#### 3. Subunit vaccines

- virus parts
  - patients will NOT have some symptoms and signs of the disease
  - less effective, shorter-lasting type of vaccine
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## ONCOVIRUSES

- cancer-causing viruses

Ex. **HPV** – can cause cervical, anal, vaginal and vulvar, and penile cancers

Ex. **EBV (HSV-4)** – can cause lymphomas (cancers that attack the immune system)

Ex. **HSV-8** – a herpes virus

– can cause Kaposi's sarcoma: lesions on skin and internal organs

– common in AIDS patients

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## EUKARYOTE INFECTIONS AND DISEASES

**Eukaryotes** - can be unicellular or multicellular

- have nucleus and organelles

- highly variable

- include **fungi** (already discussed), **protists**, and **helminths**

### PROTISTS:

#### • Malaria

- caused by protist *Plasmodium* spp.

- transmitted by *Anopheles* sp. Mosquitoes

- over 200,000,000 new cases per year! (mostly in the tropics)

- infect red blood cells

- anemia (destruction of RBCs)

- jaundice (liver failure)

- renal failure (kidneys)

- brain damage

Malaria **prophylaxis** (prevention with drugs) includes:

- **chloroquine** ("Aralen") –but many strains of *Plasmodium* resistant to this drug

- **mefloquine** ("Lariam") – but there are psychiatric side-effects

Malaria **diagnosis** includes:

- blood smear (not 100% accurate)

- travel history

- immunological tests (ex. "test strips" similar to pregnancy test)

Malaria and **sickle cell anemia (SCA)**:

- people with SCA are resistant to malaria
- most common in Africans and African-Americans
- there is a gene for SCA

<b>Genotype</b>	<b>Phenotype</b>	<b>Malaria Resistance</b>
<b>Homozygous dominant</b> (no SCA gene)	No SCA	None
<b>Heterozygous dominant</b> (one SCA gene)	<b>Carrier</b> but no SCA	High (heterozygous advantage)
<b>Homozygous recessive</b> (two SCA genes)	SCA	High (but die from SCA)

### • Toxoplasmosis

- caused by protist *Toxoplasma gondii*
- transmitted by housecat feces or undercooked wild game
- 60,000,000 people in USA infected
  
- symptoms and signs usually mild
- can cause neurological problems in fetus of pregnant women
- can also affect AIDS patients severely
- linked to OCD and schizophrenia?
  
- tx: **pyrimethamine** (“Daraprim”)
- Martin **Shkreli** raised price 5000% (from \$13 per pill to \$833 per pill)
- in 2018, he was sentenced to prison and \$7.4 million in fines

### • Trichomoniasis

- caused by protist *Trichomonas vaginalis*
- vaginal infection
- 3 million infected in USA
- vaginal and abdominal pain
- discharge from urethra and vagina
- **dysuria** (painful urination)
- trt: **metronidazole** (“Flagyl”)

### • Trypanosomiasis

- caused by protist *Trypanosoma* sp.
- blood infection, transmitted by insect bit
- 300,000 infected in USA
  
- fever, headache
- brain infection
- sleepiness, coma, death
  
- in Americas, called **Chagas** disease
- spread by **kissing bug**
- characterized by **Romañas eyes** (swollen eyelid from bug feces)
  
- in Africa, called **sleeping sickness**
- spread by **tsetse fly**
- characterized by **Winterbottom’s sign** swollen lymph node, neck
  
- trt: **arsenic** compounds

### ● Amoebiasis

- caused by protist *Entamoeba histolytica*
- GI infection
- **fecal-oral** route of transmission (dormant cyst ingested)
- diarrhea and **dysentery** (bloody diarrhea)
- ORT: **Oral Rehydration Therapy** (lots of fluids, with electrolytes – sugar, salts)
- antidiarrheal drugs (ex. **Loperamide** “Imodium AD”) NOT recommended
- can lead to severe, life-threatening dehydration:
  - headache, dizziness, weakness
  - dry mucous membranes
  - dark urine, low urine output
  - sunken eyes (sunken **fontanelles** in infants)
  - poor skin **turgor** (pinched skin slow to spring back)
  - slow **capillary refill** (pressed nails, gums slow to return to pink)
  - **tachycardia** (fast heart rate)
  - **tachypnea** (fast breathing)
  - **hypotension** (low BP)

\* many other protists can also cause GI infection (*Balantidium*, *Cryptosporidium*, *Giardia*...)

### HELMINTHS:

#### ● Pinworm

- *Enterobius vermicularis*
- most common helminth infection in USA (up to 50% of children)
- fecal-oral transmission of eggs
- eggs hatch in intestines, males and females mate
- female lays sticky eggs around anus
- extremely itchy anal region
- sticky tape test (Scotch tape on anus, on slide and look under microscope)
- trt: **pyrantel** (“Pin-X”)

#### ● Tapeworm

- *Taenia* sp.
- fecal-oral transmission of eggs
- eggs hatch in intestines
- worm expels egg-filled body segments via feces
- worms absorb nutrients from digested food
- trt: **praziquantel** (“Biltricide”)

## SEXUALLY-TRANSMITTED DISEASES (STDs) or SEXUALLY TRANSMITTED INFECTIONS (STIs)

### 1. Chlamydia

- caused by *Chlamydia trachomatis* bacteria
- intracellular bacteria (live inside host cells)
- in men: mild or no symptoms
  - pus discharge (**purulent** discharge)
  - painful urination (**dysuria**)
- in women: more severe infection
  - purulent discharge
  - dysuria
  - **cervicitis** (infection of cervix)
  - **urethritis** (infection of urethra)
  - **salpingitis** (infection of fallopian tubes)
  - infertility
  - **PID** (pelvic inflammatory disease)
  - **ectopic** pregnancy (outside of uterus)

### 2. Syphilis

- caused by *Treponema pallidum* bacteria
- primary stage: - lesions on genitals called **chancres**
- secondary stage: - **rash** anywhere on body
- tertiary stage: - masses on skin, organs, bones called **gummas**
  - **neurosyphilis** (dementia, seizures, psychosis)
  - **Argyll-Robertson pupil** (prostitute's eye) – pupil response lost

### 3. Gonorrhoea

- caused by *Neisseria gonorrhoeae* bacteria
- in men: mild or no symptoms (similar to chlamydia)
- in women: more severe infection (similar to chlamydia)
- also can lead to infection of:
  - heart (endocarditis)
  - eyes (ophthalmia)
  - throat (pharyngitis)
  - anus (proctitis)
  - brain (encephalitis, meningitis)
  - joints (arthritis)

#### 4. Genital Herpes

- caused by **HSV-2** virus
- latent phase and lytic cycle phase
- lesions on or around genitals (can also be oral)

#### 5. Genital warts (papillomas)

- caused by **HPV** virus
- can be treated with:
  - cryosurgery (freeze with liquid N)
  - excision (cut off)
  - electrocautery (burn off with electricity)
  - laser treatment (burn off with laser light)
- strains HPV 6 and 11 linked to **genital warts**
- strains HPV 16, 18, 31, and 45 linked to **cervical cancer**
- HPV viruses can be “cleared” from the body naturally over time, in some cases

#### 6. Viral hepatitis

- caused by **HAV, HBC, HCV** virus
- liver damage

#### 7. Vaginitis (vaginosis)

- caused by either:
  - ***Candida albicans*** (fungi – “yeast infection”)
  - ***Gardnerella vaginalis*** (bacterial vaginitis – “BV”)
  - ***Trichomonas vaginalis*** (protist)

#### 8. AIDS

- caused by **HIV** virus
  - transmitted by:
    - blood
    - semen
    - vaginal secretions
    - anal/rectal mucus
    - breast milk
  - HIV kills immune system cells called “**T cells**”
  - clinical definition of AIDS is when the CD4 T cell count is less than 200 cells/ $\mu$ L blood
  - this will be explained next (immune system)
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## THE IMMUNE SYSTEM

Two basic aspects:

**Nonspecific** (innate) immunity

**Specific** (adaptive) immunity

### **Nonspecific (Innate) Immunity:**

- born with it
- responds to all microbes

#### **1. Skin**

- dry
- outer skin cells are sloughed, along with attached microbes
- acidic secretions inhibit microbes
- antimicrobial compounds kill or inhibit microbes
- salty (inhibits microbes)

#### **2. Mucous membranes**

- mucus is sticky (traps microbes)
- mucus contains antimicrobial compounds

#### **3. Lacrimal glands**

- tears are antimicrobial and wash away microbes

#### **4. Fever**

#### **5. Inflammation**

- redness (called **rubor**)
- warmth (called **calor**)
- swelling (called **tumor**)
- pain (called **dolor**)

#### **6. White blood cells (leukocytes)**

- include phagocytic cells that ingest microbes and microbe-infected cells

### **Specific (Adaptive) Immunity:**

- develops with exposure to microbes
- responds to specific microbes

#### **1. T Cells**

- mature in thymus
- move around the body
- lymphocytes that circulate through the lymphatic system and circulatory system

#### **3 types of T cells:**

##### **Helper T cells (TH)**

- have **CD4** receptors
- assist other T cells
- stimulate B cells
- most important cells in specific immunity

##### **Cytotoxic T cells (TC)**

- have **CD8** receptors
- destroy infected cells, cancerous cells, etc.
- release perforin, which lyses infected host cells

##### **Regulatory T cells (TREG)**

- have **CD4** receptors
- control T cell response
- prevent overreaction and underreaction

#### **2. B cells**

- mature in bone marrow
- move around in the body
- lymphocytes that circulate through the circulatory system

#### **3. Plasma cells**

- B cells stimulated by TH cells change into plasma cells
- plasma cells produce and release antibodies

#### **4. Antibodies**

- also called immunoglobulins (Ig)
- Y-shaped proteins produced by plasma cells
- bind to antigens (very specific)
- antigens include parts of microbes and "allergens" such as pollen, peanuts, etc.

**What do antibodies do?**

- bind to antigens (on microbes), thus immobilizing them = **neutralization**
  - marks the microbe for ingestion by phagocytic white blood cells = **opsonization**
  - stimulate **complement activation** = proteins in the blood that work together to destroy the microbe
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## Miscellaneous Infectious Diseases

(infectious disease = caused by microbes; “contagious”)

### Cardiovascular system:

- normally should be no microbes in bloodstream
- bacteria in blood = **bacteremia**
- viruses in blood = **viremia**
- fungi in blood = **fungemia**
  
- **sepsis (septicemia)** = bacterial toxins in blood
- can quickly lead to **septic shock** = dangerous decrease in blood pressure

Ex. **endocarditis** = infection and inflammation of heart lining or valves

- commonly caused by *Staphylococcus* and *Streptococcus*, and other bacteria; also viruses, fungi
- bacteria can enter bloodstream from dental procedures, heart valve transplant, tonsillectomy, other surgeries

Ex. **hemorrhagic fever** = internal bleeding

- can be caused by **Ebola** virus
- currently restricted to parts of Africa, but spreading
- **airborne** transmission (droplets, aerosol) from person-to-person
- high mortality rate (fatal)
- experimental treatment called “**Zmapp**” – antibodies that attack the virus are given to patient
- successfully cured American doctor who contracted it in Africa (Dr. Kent Bradley)

### Lymphatic system:

Ex. **plague** (bubonic plague = lymph nodes)

- caused by bacteria *Yersinia pestis*, spread by fleas
- killed 1/3 to ½ population of Europe in 14<sup>th</sup> Century
- still exists in some countries today

Ex. **tularemia**

- caused by bacteria *Francisella tularensis*
- from rabbits, and other mammals and insect bites
- increasing in USA

### Cutaneous (skin):

#### Ex. **impetigo**

- caused by bacteria *Staphylococcus aureus*
- all staph infections may be antibiotic-resistant (MRSA, etc.)
- flaking or peeling skin, scabs, often on face

#### Ex. **cellulitis**

- caused by bacteria *Staphylococcus aureus*
- inflammation in deep skin layers
- pain, swelling, warmth, redness
- can lead to sepsis

#### Ex. **staphylococcal scalded skin syndrome (SSSS)**

- caused by bacteria *Staphylococcus aureus*
- burned skin appearance
- **desquamation** = sloughed skin layers
- most common in newborns

### Ophthalmic (eyes):

#### Ex. **conjunctivitis**

- “pink eye”
- caused by wide variety of bacteria, viruses
- also causes **photophobia** = sensitivity to light

#### Ex. **keratitis**

- caused by protist *Acanthamoeba* sp., also HSV-1 and HSV-2
- infection of cornea and deep eye tissues
- increasing in USA, esp. from contact lens use

### Nervous system:

- normally should be no microbes in nervous system
- **Central nervous system** (brain, spinal cord, spinal fluid) – can test with **lumbar puncture** “spinal tap” between L3/L4 vertebrae, collect fluid, and examine microscopically or culture the sample
- **Peripheral nervous system** (nerves)

#### Ex. **meningitis**

- infection of **meninges** = membrane covering of brain
- caused by bacteria (such as ***Neisseria meningitidis*** – “meningococcus”), viruses, fungi
- headache, pain/stiff neck, fever, vomiting, unconsciousness

#### Ex. **encephalitis**

- infection of brain
- caused by arboviruses (viruses spread by insect bites)
- **ZIKA** virus = spread by mosquito bites, causes **microcephaly** (small brain) in babies of women infected during pregnancy

#### Ex. **meningoencephalitis**

- infection of meninges and brain
- caused by protist ***Naegleria fowleri*** (protist) --- brain-eating amoeba, contaminated water enters sinuses (via the nose)
- and caused by other microbes

### Respiratory system:

#### Ex. **pertussis** (whooping cough)

- caused by bacteria ***Bordetella pertussis***
- uncontrolled coughing, inflammation of airways and pharynx
- **DTaP vaccine** immunizes against pertussis

**Gastrointestinal system:**

Ex. salmonellosis/typhoid fever

- caused by bacteria *Salmonella enterica*
- spread by fecal-contaminated food or water
- rash, abdominal pain, fever
- “**Typhoid Mary**” – most famous carrier of typhoid (Mary Mallon), spread it to others on purpose