PARA3002 TUTORIAL

Parasite Control

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PARASITE CONTROL

Three main strategies utilized:

- drugs
  (to cure/curb/prevent infection);
- vaccines
  (to protect against infection/disease);
- environmental management
  (to prevent transmission).

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Infectious diseases (n=240)

Acinetobacter
Actinomycosis
African trypanosomiasis
Acquired immunodeficiency syndrome
Amoebiasis
Anaplasmosis
Angiostrongyliasis
Anisakiasis
Anthrax
Arcanobacterium haemolyticum
Argentina haemorrhagic fever
Ascariasis
Aspergillosis
Astrovirus
Babesiosis
Bacillus cereus
Bacterial pneumonia
Bacterial vaginosis
Bacteroides
Balantidiasis
Bartonellosis
Baylisascaris
BK virus
Black piedra
Blastocystosis
Blastomycosis
Bolivian haemorrhagic fever
Botulism
Brazilian haemorrhagic fever
Brucellosis
Bubonic plague
Burkholderia
Buruli ulcer
Calicivirus (Norovirus, Sapovirus)
Campylobacteriosis
Candidiasis (moniliasis, thrush)
Capillariasis
Carrion's disease
Cat-scratch disease
Cellulitis
Chagas disease
Chancroid
Chickenpox
Chikungunya
Chlamydia
Chlamydophila pneumoniae
Cholera
Chromoblastomycosis
Clonorchiasis
Clostridium difficile colitis
Coccidioidomycosis
Colorado tick fever
Common cold (acute viral rhinopharyngitis, acute coryza)
Creutzfeldt-Jacob disease (CJD)
Crimean-Congo haemorrhagic fever
Cryptococcosis
Cryptosporidiosis
Cutaneous larval migrans
Cyclosporiasis
Cysticercosis
Cytomegalovirus
Dengue fever
Desmodesmus
Diantamoebiasis
Diphtheria
Diphyllobothriasis
Dracunculiasis
Ebola haemorrhagic fever
Echinococcosis
Ehrlichiosis
Enterobiasis
Enterococcus
Enterovirus
Epidemic typhus
Erythema infectiosum (fifth disease)
Exathem subitum (sixth disease)
Fasciolasis
Fasciolopsiasis
Fatal familial insomnia
Filariasis
Food poisoning (Cl. perfringens)
Free-living amoebae
Fusobacterium
Gas gangrene (Cl. myonecrosis)
Geotrichosis
Gerstmann-Straussler-Scheinker syndrome
Giardiasis
Glanders
Gnathostomiasis
Gonorrhoea
Granuloma inguinale (donovanosis)
Group A Streptococcus
Group B Streptococcus
Haemophilus influenzae
Hand, foot & mouth disease
Hantavirus pulmonary syndrome
Heartland virus disease
Helicobacter pylori
Haemolytic uremic syndrome
Haemorrhagic fever with renal syndrome
Hepatitis A
Hepatitis B
Hepatitis C
Hepatitis D
Hepatitis E
Herpes simplex
Histoplasmosis
Hookworm
Human bocavirus
Human ewingii ehrlichiosis
Human granulocytic anaplasmosis
Human metapneumovirus
Human monocytic ehrlichiosis
Human papillomavirus
Human parainfluenza virus
Hymenolepiasis
Epstein-Barr virus infectious mononucleosis
Influenza
Isosporiasis
Kawasaki disease
Keratitis
Kingella kingae
Kuru
Lassa fever
Legionellosis (Legionnaire's disease)
Legionellosis (Pontiac fever)
Leishmaniasis
Leprosy
Leptospirosis
Listeriosis
Lyme disease
Lymphatic filariasis
Lymphocytic choriomeningitis
Malaria
Marburg haemorrhagic fever
Measles
Middle-East respiratory syndrome
Melioidosis
Meningitis
Meningococcal disease
Metagonimiasis
Microsporidiosis
Molluscum contagiosum
Monkeypox
Mumps
Murine typhus (endemic)
Mycoplasma pneumonia
Mycetoma
Myiasis
Neonatal conjunctivitis
New -variant CJD
Nocardiosis
Onchocerciasis
Opisthorchiasis
Paracoccidioidomycosis
Paragonimiasis
Pasteurellosis
Pediculosis capitis
Pediculosis corporis
Pediculosis pubis
Pelvic inflammatory disease
Pertussis
Plague
Pneumococcus
Pneumocystis pneumonia
Pneumonia
Poliomyelitis
Prevotella
Primary amoebic meningoencephalitis
Progressive multifocal leukoencephalopathy
Psittacosis
Q fever
Rabies
Relapsing fever
Respiratory syncytial virus
Rhinosporidiosis
Rhinovirus
Rickettsia
Rickettsialpox
Rift valley fever
Rocky Mountain spotted fever
Rotavirus
Rubella
Salmonellosis
Severe acute respiratory syndrome
Scabies
Schistosomiasis
Sepsis
Shigellosis
Shingles
Smallpox
Sporotrichosis
Staphylococcal food poisoning
Staphylococcus
Strongyloidiasis
Subacute sclerosing panencephalitis
Syphilis
Taeniasis
Tetanus
Tinea barbae
Tinea capitis
Tinea corporis
Tinea cruris
Tinea manum
Tinea nigra
Tinea pedis
Tinea unguium
Tinea versicolor
Toxocariasis (ocular)
Toxocariasis (visceral)
Trachoma
Toxoplasmosis
Trichinosis
Trichomoniasis
Trichuriasis
Tuberculosis
Tularemia
Typhoid fever
Typhus fever
Ureaplasma urealyticum
Valley fever
Venezuelan equine encephalitis
Venezuelan haemorrhagic fever
Vibrio vulnificus
Vibrio parahaemolyticus
Viral encephalitis
Viral pneumonia
West Nile fever
White piedra
Yersinia pseudotuberculosis
Yersiniosis
Yellow fever
Zygomycosis

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Diseases for which drugs are available (n=160)

67%

means 33% are untreatable

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Diseases with drug-resistance problems (n=55)

34%

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Infectious diseases (n=240)

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Vaccination-preventable diseases (n=24)

Haemophilus influenzae
Meningococcal disease
Mumps
Hepatitis A
Hepatitis B
Hepatitis D
Tetanus
Diphtheria
Ebola haemorrhagic fever
Human papillomavirus
Pertussis
Pneumococcus
Influenza
Poliomyelitis
Tuberculosis
Typhoid fever
Rabies
Viral encephalitis
Chickenpox
Measles
Rotavirus
Rubella
Yellow fever
Cholera

10%

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The great debate

Chemotherapy versus Vaccination

Which is best?

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DRUGS

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DRUG USE

Huge range of chemicals used for parasite:

chemotherapy (curative)
- **static drugs (arrest development, reversible)**
- **cidial drugs (irreversible damage - lethal)**

chemoprophylaxis (preventive)
- **stop infection**
- **limit infection**

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Parasite targets

Huge diversity of parasites in terms of:
- **organismal biodiversity (multiple phyla)**
- **developmental cycles (eggs/larvae/adults)**
- **food requirements (energy sources)**
- **metabolic pathways (aerobic/anaerobic)**
- **types of hosts (vertebrate/invertebrate)**
- **location within host (tissue/organ specificity)**

All present challenges to chemical treatment

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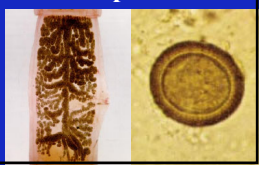
PARASITE METABOLISM

Parasites may utilize/usurp host metabolism
They exhibit many specialized adaptations
- **absence of circulatory system in helminths**
- **absence of digestive tract in cestodes**
- **absence of mitochondria in some protozoa**
- **alternation of metabolism between parasitic and free-living stages**
- **metabolic diapause**



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Pharmaceuticals

Pharmacodynamics - action of drug on body
Pharmacokinetics - action of body on drug

Action based on selective toxicity (parasite first)

Contra-indicated use - side-effects
- synergism/antagonism
With-holding period - 100-1000x ADI
(acceptable daily intake)
Maximum residue limits

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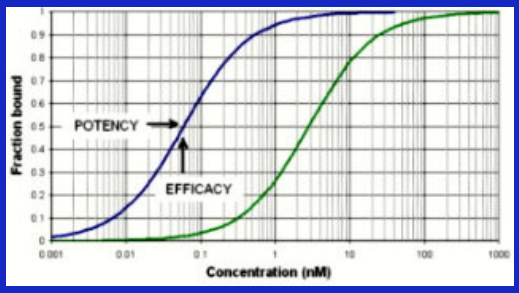
Pharmacodynamics (PD)

DOSE – RESPONSE CURVE



stimulants, depressants, toxins, substitutes

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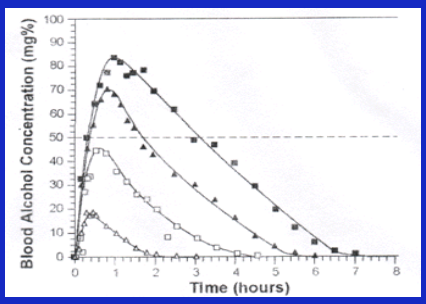
Pharmacokinetics (PK)

CONCENTRATION-TIME CURVE



ADME (Absorption, Distribution, Metabolism, Excretion)

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Products

Names - one international non-proprietary name
- regional nonproprietary names (country)
- several proprietary names (brands)

Oral - tablets, pills, capsules, bolus
liquids, emulsions

Parenteral - ampoules, vials, implants
(s.c., i.m., i.v., i.p., i.t.)

Topical - liniments, lotions, ointments, dips, shampoos, washes, pour-ons, spot-ons, collars, creams, sprays, powders, aerosols

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Targets for antibiotics

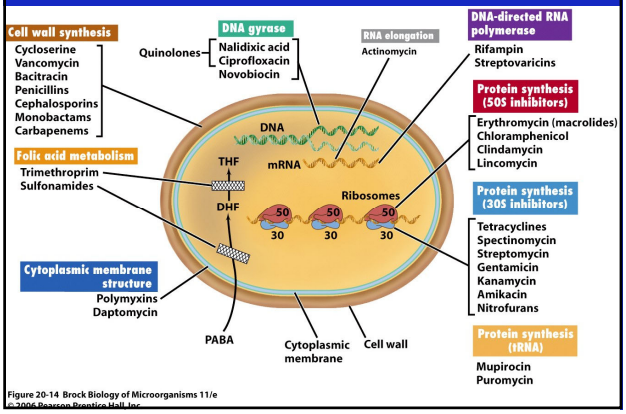

Figure 20-14 Brock Biology of Microorganisms 11/e
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CHEMOTHERAPY

Anti-parasitic drugs exhibit selective activity on:

- DNA synthesis (alkylation, purine, cofactor)
- protein synthesis (inhibition, translation)
- energy metabolism (electron transport, reduction)
- neurotransmission (blockers, inhibition)
- membrane function (vacuoles, permeability)
- microtubule function (paralysis)
- hem(oglobin) interaction (disruption)

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Drug Resistance

Parasites subject to sub-lethal drug concentrations
- wrong dose (poor weight estimation)
- interrupted time course (poor compliance)
- antagonistic drug interactions

Selective pressure for survival advantage
- phenome-genome (mutation, lateral gene transfer)
- inheritance (resistant progeny)

Mechanisms of resistance
- alter target (lower affinity)
- alter uptake (decrease influx, increase efflux)
- inactivate drug (enzymatic modification)

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VACCINES

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How do hosts survive it all?

- Become resistant or tolerant
  (survival of fittest - Red Queen hypothesis)
- Ameliorate disease
  (minimize acute-chronic damage)
- Develop protective immunity
  (memory, premunition)

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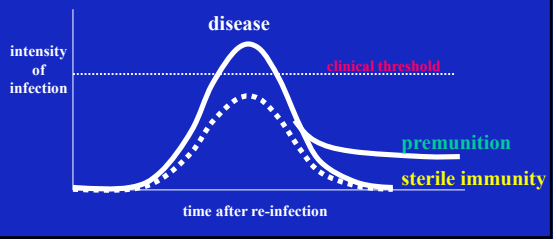
Three types of immunity

Previous exposure confers:
- clinical immunity (disease prevented)
- sterile immunity (parasites eradicated)
- concomitant immunity (some parasites persist)



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Immunity to Parasites

PROTOZOA	HELMINTHS
• acute disease	• chronic disease
• parasite multiplication	• no multiplication
• intracellular location	• extracellular location
• cell-mediated immunity	• humoral immunity
• cytotoxic T cells	• Ab opsonization
• helper T cells (Th1/Th2)	• then mϕ, NK, eo
• strong protection	• weak protection

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THREE LINES OF DEFENSE

first line BARRIER	second line INNATE	third line ADAPTIVE (ACQUIRED)
external coverings & secretions	phagocytes & inflammation	cell-mediated & humoral responses
nonspecific	nonspecific	specific

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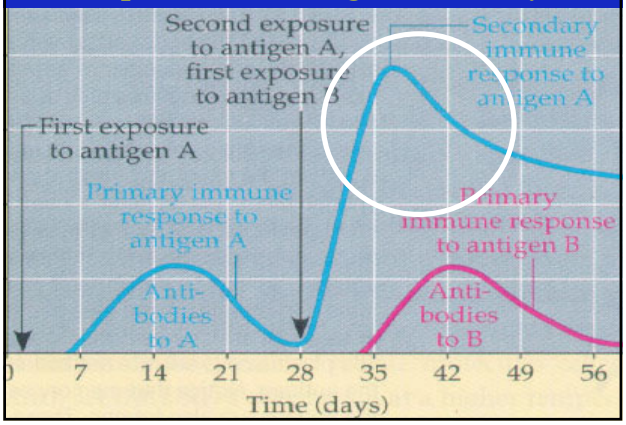
Exploit immunological memory



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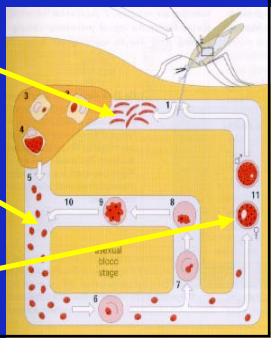
Vaccination rationale

Three vaccination strategies

- anti-infection (prevent establishment)
- anti-disease (prevent symptoms)
- anti-transmission (prevent dissemination)



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Vaccination

Vaccine type:

- live attenuated organisms
- killed organisms
- subcellular vaccines

Problems:

- reversion
- allergy
- contamination

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Vaccine production

Direct from parasites (poor quantity, good quality)

- culture parasites
- harvest antigens
- purify immunogens

Via molecular biology (good quantity, poor quality)

- recombinant vaccines
- DNA vaccines

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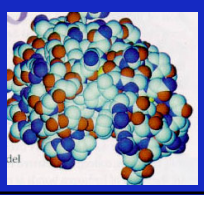
Targets

Elements considered as candidate vaccines

- internal proteins
- cytoskeletal proteins
- parasite enzymes
- molecules similar to host proteins



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Vaccine optimization

Small antigens cleared rapidly from host
Need to prolong exposure to achieve response

- use carrier molecules
- use adjuvants
- use delivery systems
- use slow release depots

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The great debate

Chemotherapy	Vaccination
• broad spectrum (targets whole groups)	• narrow activity (species specific)
• short-acting	• long-lasting
• re-infection possible	• re-infection prevented
• drug resistance	• reversion of virulence
• drug residues	• hypersensitivity
• environmental toxins	• contamination

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ENVIRONMENTAL MANAGEMENT

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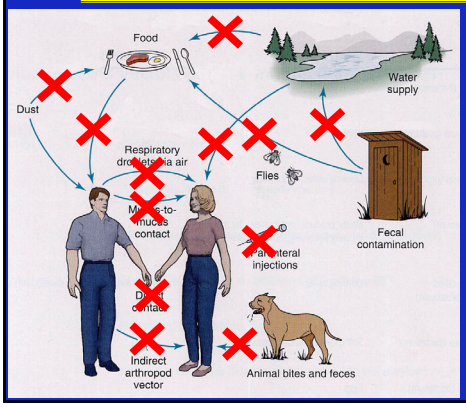
Biological interventions (break cycle)



Sources
- people
- animals

Routes
- faecal-oral
- respiratory
- vector-borne
- contact

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Biological interventions

Target:
- hygiene
- sanitation
- vectors
- reservoir hosts
- environments
- behaviours

It is all about education!

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Strategies

Change:
- Physical conditions
  - Sanitation, water treatment, sewage treatment, food hygiene…
- Biological entities
  - Vector control, animal reservoirs, breeding sites…
- Sociological behaviour
  - Hygiene, healthcare, nutrition, housing, agricultural practices…

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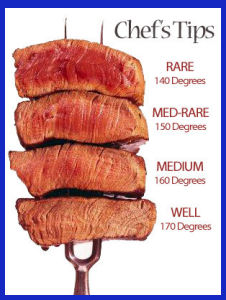
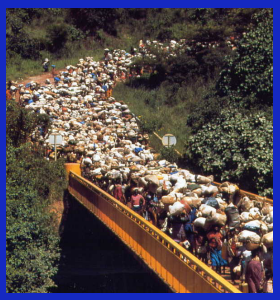
Greatest Challenge

How to change human behaviour?





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