BioMedical Parasitology

Chemotherapy versus vaccination

Prof Peter O'Donoghue

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Control of parasitic disease

Three main strategies: **How?**

- **Drugs** (cure/curb/prevent infection)
- **Vaccines** (protect against infection/disease)
- **Environmental management** (prevent transmission)

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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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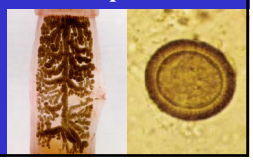
PARASITE METABOLISM

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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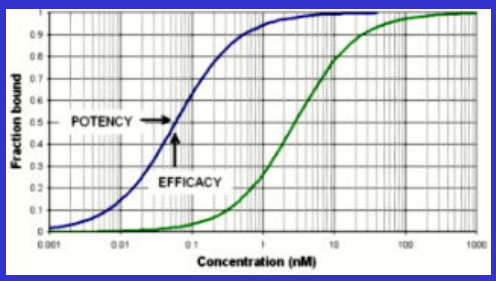
Pharmacodynamics (PD)

DOSE – RESPONSE CURVE



stimulants, depressants, toxins, substitutes

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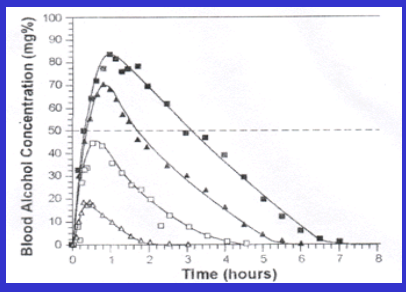
Pharmacokinetics (PK)

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

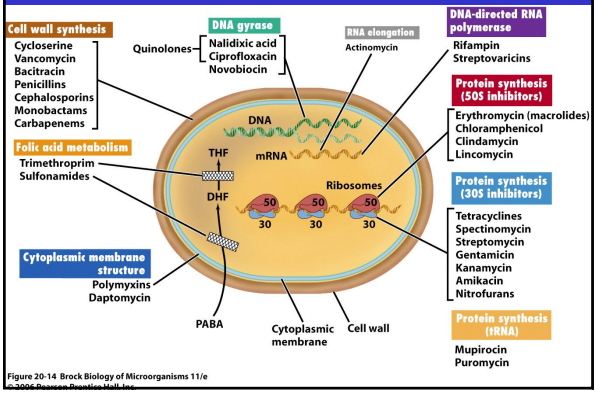

Figure 20-14 Brock Biology of Microorganisms 11/e

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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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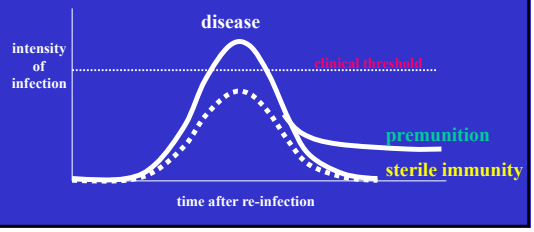
Three types of immunity

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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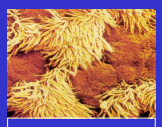
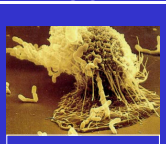
THREE LINES OF DEFENSE



first line
BARRIER

external coverings & secretions

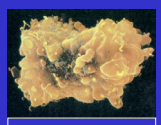
nonspecific



second line
INNATE

phagocytes & inflammation

nonspecific



third line
ADAPTIVE
(ACQUIRED)

cell-mediated & humoral responses

specific

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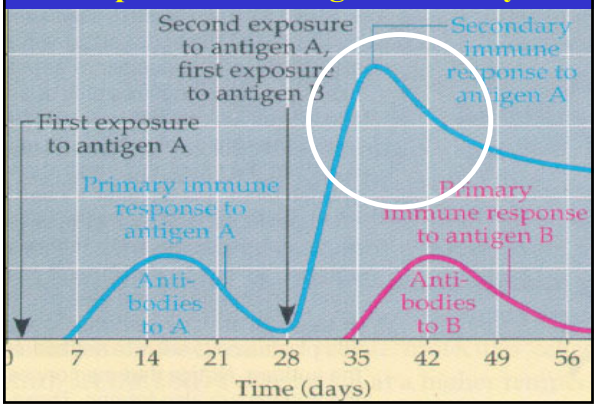
Exploit immunological memory



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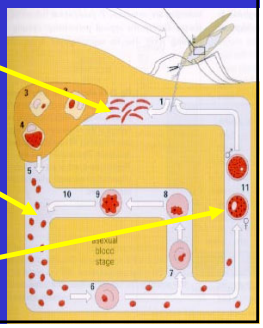
Vaccination rationale

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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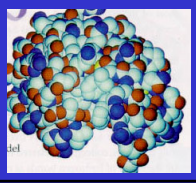
Targets

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 versus Vaccination

Which is best?

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The great debate

Chemotherapy versus 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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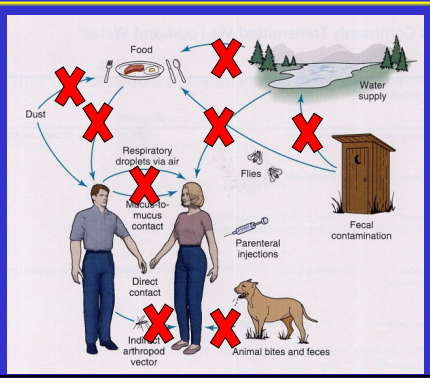
Break transmission cycle

Stop infections from happening in the first place



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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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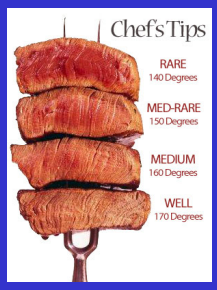
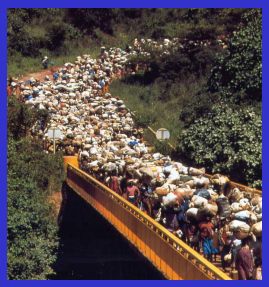
Greatest Challenge

How to change human behaviour?





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Greatest Challenge

How to change human behaviour?

Your turn!

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