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PATHOGENICITY AND VIRULENCE

The 7th lecture for 2nd-year students
March 23, 2015

Resistance of biofilm towards toxic substances – revision

MICROBES IN THE BIOFILM FORM ARE ALWAYS MORE RESISTANT THAN IN THE PLANKTONIC FORM

- Higher resistance applies also to disinfectants and antibiotics
- Differences in sensitivity sometimes amount up to 3 orders
- General mechanism of the higher resistance is not known
- In each microbe-antimicrobial combination the mechanism can be different

Possible causes of higher resistance of biofilm – revision

1. More difficult penetration of toxic matter through the biofilm
2. Character of environment in the biofilm is altered
3. Also the microbial population in the biofilm is altered

Biofilm and disease 1 – revision

Biofilm takes part in the pathogenesis of

1. chronic infections in general
2. infections of implanted devices

- the progress of these infections is slow
- they are without distinctive symptoms
- acute exacerbations occur occasionally
- the effect of antibiotic therapy is transitory only
- after stopping antibiotics infections recur (even if bacteria grown from them appear sensitive *in vitro*)

Biofilm and disease 2 – revision

Chronic infections of natural bodily surfaces

dental caries (oral streptococci, mainly *Streptococcus mutans*)

periodontitis (Gram-negative oral anaerobes)

otitis media (*Haemophilus influenzae*)

osteomyelitis (*Staphylococcus aureus*)

cholecystitis and cholangoitis (enterobacteria)

prostatitis (*Escherichia coli*)

subacute bacterial endocarditis (oral streptococci)

pneumonia in cystic fibrosis (*Pseudomonas aeruginosa*)

Biofilm and disease 3 – revision

Chronic infections of artificial surfaces

central venous catheters (coagul. neg. staphylococci, candidae)

prosthetic heart valves (*Staph. aureus*, *Staph. epidermidis*)

joint prostheses (*Staphylococcus aureus*, *Staph. epidermidis*)

surgical sutures (*Staphylococcus aureus*, *Staph. epidermidis*)

vascular grafts (Gram-positive cocci)

endotracheal tubes (various bacteria and yeasts)

intrauterine contraceptive devices (*Actinomyces israelii*)

urinary catheters (*E. coli* or others, mainly Gram-negative rods)

contact lenses (*Pseudomonas aeruginosa*, Gram-positive cocci)

Pathogenicity

Pathogenicity = ability of a microbe to be harmful to health and to cause disease

Infectiousness = ability to cause infection

Infection – broader term than disease

In the disease the symptoms of disease are present (the infection is manifest)

But the infection may proceed without symptoms (inapparent infection)

Apart from infections microbes can cause food poisoning, as well

Ecological remark

Ecology = science on mutual relations among organisms and relations between organisms and their environment

Symbiosis = close association of two different organisms

Three forms of symbiosis:

Mutualism – both partners benefit from the association and are unable to survive without it

Commensalism – the association is beneficial for one partner and indifferent to the other

Parasitism – the association benefits one partner and harms the other (the host)

→ consequence = pathogenicity

Infection

The definition of infection is not easy

- **Infection** = situation when the etiological agent of infection invades an organism and multiplies in it; or it settles on bodily surfaces and acts adversely there

- **Colonization** = settlement of bodily surface by a nonpathogenic microbe (or by a pathogen that does not cause pathological symptoms there)

History of infectious diseases – I

Leviticus (3rd book of Moses) – ban of pork

Quarantine (= 40 days) – plague

Fracastoro (1485-1553): „De contagione“

1676 van Leeuwehoek – observed bacteria

1838 Schönlein – mould in hair during favus

1850 Davaine – bacteria in sheep with anthrax

1857 Pasteur – microbes → spoil wine and beer

1865 Villemin – microscopically: bacteria in TBC

1869 Pasteur – parasites in silkworm

1876 Lister – antisepsis

1876 Robert Koch and Louis Pasteur – anthrax

History of infectious diseases – II

Physiological thesis of Hippocrates:

The disease (incl. the infectious one) = consequence of certain inadequacy of organism

Microbial antithesis of Pasteur and Koch:

The cause of the infectious disease is a microbe

Ecological synthesis:

= synthesis of physiological thesis and microbial antithesis – for the occurence of the infectious disease 1. the microbe, 2. the host and 3. their environment are responsible

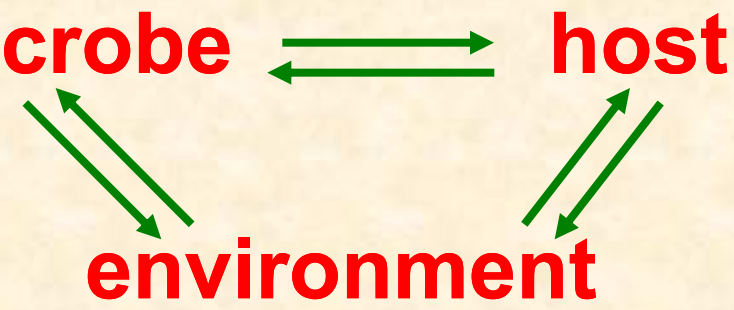
Koch´s postulates

A particular microbe is the etiological agent, if

1. it is present in every case of the disease and its localization in the body corresponds to the damages observed;
2. it is isolated from the host and kept in pure culture for several generations;
3. by means of the microbe grown in this way it is possible to imitate the disease in another host;
4. it is again isolated from the experimentally infected host.

Relationship between the microbe and the host

The relationship is dynamic and influenced by the environment:



Illness is not a rule – peaceful coexistence is usually better for the parasite

In spite of that the host tries to get rid of the parasite – to destroy, remove or at least to localize it

Pathogenicity

Pathogenicity = the ability to cause a disease

It depends on both microbial and host species

Particular microbial species is pathogenic for a specific host species only, for another species it may be non-pathogenic

This host species is susceptible to the relevant microbial species, to a different microbial species it can be resistant

Primary and opportune pathogens

Primary (obligate) pathogens → cause disease even in otherwise healthy individuals = chiefly agents of classical infections (diphtheria, typhoid fever, plague, gonorrhea, tetanus, influenza, morbilli etc.)

Opportunistic (facultative) pathogens → cause disease under certain conditions or at a certain disposition only = usually members of normal flora

- when they reach another site in the body
- or when the immunity of the individual is lowered

Natural and experimental pathogenicity – examples

Microbes naturally pathogenic for man & animals:

***Staph. aureus, Francisella tularensis, Clostridium botulinum,* rabies v., tick-borne encephalitis v.**

Microbes pathogenic for animals experimentally:

***Bacillus anthracis, Streptococcus pneumoniae, Clostridium tetani* – mouse**

***Mycobact. tuberculosis,* rickettsiae – guinea pig**

***Treponema pallidum,* herpes simplex v. – rabbit**

Microbes pathogenic for man only:

Neisseria gonorrhoeae, Haemophilus ducreyi

Microbes non-pathogenic for man:

Majority of soil and water microorganisms

Opportunistic pathogens – I

Typical opportunistic pathogen:

Escherichia coli

A part of normal colonic flora (but <1 % only)

Outside the large intestine = pathogen

- **cystitis, pyelonephritis, urosepsis**
- **cholecystitis, peritonitis**
- **wound infections**

At lowered immunity (newborns):

- **meningitis**
- **diarrhea (EPEC – serotypes O55, O111)**

Opportunistic pathogens – II

Another opportunistic pathogen:

Staphylococcus epidermidis

Part of normal skin and mucosal flora

Outside the skin and mucosae = pathogen

- **wound infections (also surgical: sternum, eye)**
- **cystitis**

At lowered immunity:

- **above all blood stream infections in individuals with i.v. catheters, infections of implants and other devices**
- **sepsis in newborns and neutropenic individuals**

Virulence

Virulence = degree (measure) of pathogenicity

Virulence = property of certain strain of the microbe
– a pathogenic species can incorporate highly virulent strains as well as almost avirulent ones

Indicator of strain virulence: ability to kill

LD_{50} = 50% lethal dose (the amount of microbe that is able to kill exactly ½ of experimental animals)

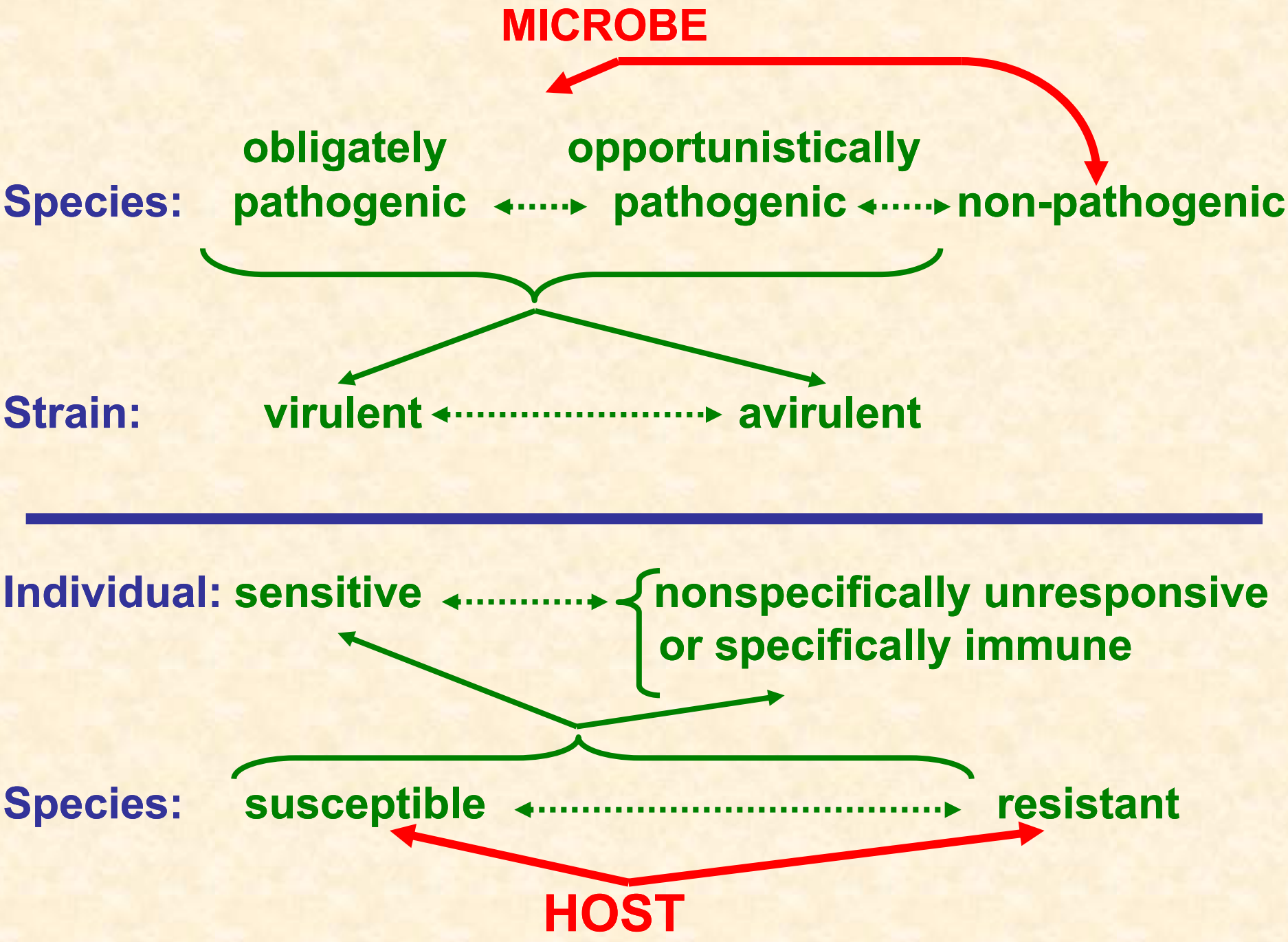
Increasing virulence: repeated passages of the strain (be cautious with the strains from dissection material)

Attenuation = artificial weakening of virulence (attenuated strains serve for the preparation of vaccines)

Attenuation – an example

BCG-vaccine against TBC (bacille Calmette-Guérin)

- Original strain – *Mycobacterium bovis* – is less pathogenic for man than *Mycob. tuberculosis*
- The selected strain was „tormented“ 12 years on potato with bile until it lost most of its virulence (it is almost avirulent)
- In a normal newborn BCG causes only a local process in the site of injection or in a regional lymph node
- Very rarely in an immunodeficient newborn it can cause the generalized infection


MICROBE
obligately pathogenic
opportunistically pathogenic
non-pathogenic
Species:
Strain:
virulent
avirulent
Individual:
sensitive
nonspecifically unresponsive
or specifically immune
Species:
susceptible
resistant
HOST

Recommended reading material

Paul de Kruif: Microbe Hunters

Paul de Kruif: Men against Death

Axel Munthe: The Story of San Michele

Sinclair Lewis: Arrowsmith

André Maurois: La vie de Sir Alexander Fleming

Hans Zinsser: Rats, Lice, and History

Michael Crichton: Andromeda Strain

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Thank you for your attention