Introduction to Infectious Diseases notes

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Introduction to infectious diseases

- The body is a great environment for bacteria and viruses to proliferate. Bacteria need water, warmth, and nutrients to live "alone" and thrive. Higher-order organisms function much the same. Viruses are parasitic by nature; they need another organism to replicate their DNA. Most pathogens are bacteria or viruses.

- Asia, Nov. 2002, pneumonia - infection of the lungs, outbreak in Guangdong province. Lungs have a large surface area (~tennis court).

SARS: severe acute respiratory syndrome, new infection (February - March 2003), rapid and "contactless" contagion.


Koch's postulates: you have to be able to identify the virus in every case of the disease.

Culture bacteria (infected) autonomously, infect other organisms, culture the ensuing infected bodies independently from civet cats and raccoon dogs, reservoirs of SARS-associated virus, on sale?

Viruses can mutate: RNA viruses have no checkpoint for validity of replication.

- Many specific treatments have been developed for identified infectious diseases (syndromes clear with correct system recognition). Epidemiology: history of the disease, track communicable diseases, maps of endemic diseases.

The body has built inflammatory responses, immune responses, to fight infectious diseases. They also can be dangerous to human health, innate and adaptive immunity against invincible.
Human tuberculosis and malaria

- Key initial process of human infectious diseases:
  - invasive live microbes
  - production of transmissible progeny
  e.g. avian influenza virus; size or number of mutations of progeny matter

- Malaria mostly in tropical areas

  Some historical elements:
  - 2400 BC in a Chinese medical document (before any)
  - 6th century BC in India (etiology)
  - Hypothesis: swampland areas & mosquitoes
  - 1860s and next: Pasteur, Koch (tried to attenuate)

  Transmission of a vector, or etiological agent, not disease!

  - 1880: Laveran within red blood cells
  - 1897: Ross observed sporozoites in blood-feeding mosquitoes
  - 1898: Grassi: Anopheles mosquitoes only

  Eradication of A. mosquito habitats and niches does not always eradicate disease

- Malaria is a parasite that lives in two hosts: blood-feeding A. mosquitoes and humans

  - High morbidity and mortality
  - Mono prophylactic treatment ⇒ resistance

- Malaria describes intra-erythrocytic asexual development of Plasmodium in human red blood cells (h RBC)

  - Parasite delivered through dermis, then vascular bed, in hepatocytes (25 in liver)
  - Without any symptoms, then 1st-second-long invasion of RBC, deploy quickly
  - Escape and re-invasion (symptoms from anemia, inflammation)

  - Plasmodium falciparum in human hosts: ring form, trophozoite and schizont stages

  - Systemic inflammatory process → fever

  - Severe malaria: cerebral m., severe anemia, acute respiratory distress
  - or massive febrile episodes (93 out 100 cases in sub-Saharan African children)

  - Accumulation of platelets in brain microvessels (⇒ hemorrhage)
  - RBCs adhere (via "knobs") to endothelial cells (Grau & Sheffield 2005)

  - In a pro-inflammatory manner (cytokine & chemokine cascade)
during intra-erythrocite development, plasma membrane asymmetry disrupted
flip-flop enzymes dysfunctional.

Tuberculosis: pulmonary disease
historical notes: Koch (1885 - 1890) cultured microorganisms in agar for colonies
lung parenchyma disrupted by bacteria
symptoms & signs: cough, spuim, haemoptysis, weight loss, fever, malaise

Mycobacterium tuberculosis inhaled by 100 individuals
progress to cavitory TB only in 5 to 10 cases (phagocytosis)
extracellular progeny AND intracellular quiescent bacteria

balancing protective immunity (IFNγ, NO, TNFα, IL12, IL23)
and immunopathology

The inflammatory cascade: shock and multi-organ failure
Geert Schmid-Schönbein

- the inflammatory process plays out in the microcirculation: 10^11 capillaries
  in muscle, networks* fed by a range of arterioles (arcade) (vs. 10^4 veins)
in human lung, tree-like structure of blood vessels
* terminal arterioles → capillaries → collecting venules
very low Reynolds’ numbers Re (honey-like, not water-like)

the network of lymphatic vessels surrounds the arterioles

- pressure-flow relationship
  in skeletal muscle microcirculation

many diseases have cell activation & inflammation as hallmarks:
cardiovascular disease, stroke, diabetes, hypertension, myocardial ischemia, cancer, ...
physiological shock and multi-organ failure

cascade: cell response = ion exchange, pseudopods from actin polymerization,
degranulation, inflammatory mediators, endothelial permeability
upregulation of membrane adhesion molecules
cascade (c'd): tissue degradation, neutrophil entrapment in microvessels, transmigration, platelet attachment, aggregation, thrombosis, red cell aggregation, protease release, oxygen free radical formation, apoptosis, organ dysfunction.

- initial repair: down-regulation of anti-inflammatory genes, up-regulation of pro-inflammatory genes (cytokines...), monocyte & T-lymphocyte infiltration.

- repair: release of growth factors, growth of connective tissue, revascularization, "resolution of inflammation." sometimes, no healing, no resolution of the inflammation; why?

(pictures of actin depolymerization, pore formation, neutrophil infiltration, apoptosis)
(pictures of the attachment of platelets and white blood cells to post-capillary venules)

-scapillaries venule WBC adheres to the endothelium only if RBC push them against walls, infiltration later, once adhesion has occurred.

-central mechanisms for cardiovascular cell activation:
- inflammatory mediators (1), depletion of anti-i. mediators, fluid shifts, transients of gas pressure or temperature, juxtacrine activation, bio-implant interfaces.

(1) bacterial sources, endotoxins, oxidized products, LTB₄, PAF
(2) NO for instance

in shock (1) are "leukotaxin peptide", "chaptotic factor...": plasma - transported what organ shows neutrophil activation? pancreas! (insulin + digestion) actually, inflammatory mediator produced if pancreatic enzyme leipzig prevent or another digestive protease (2)

intestinal mucosa normally protects you from inflammatory mediators = digestive enzymes, both the liquid and the proteinated fractions can kill you -> several fragments act (800 - 1500 Da)
Routes of exposure: injection, ingestion, inhalation, mucous membranes
Attire: closed shoes, long pants, goggles, coats, gloves
\*100 in case of emergencies
Wash well if exposed to hazardous materials, MIT medical
Evacuate if asked to
Have a safe experience!