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扶住 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) spontaneously infect other organisms culture the ensuing infected bodies independently from civet cats and raccoon dogs, reservoirs of SARS - associated virus, can take? viruses can mutate: RNA viruses have no checkpoint for validity of replication.

- Many specific treatments have been developed for identified infectious diseases (syndrome clear syndromic recognition is key epidemiology: history of the disease, track communicable diseases, maps of endemic d.

- The body has built inflammatory responses to fight infectious diseases. They also can be dangerous to human health: inhale and adaptive immunity against inviculum.
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:
    - 2700 BC in a Chinese medical document
    - 6th century BC in India
  - Hypothesis...
    - swampy areas & mosquitoes
  - 1860s and next: Pasteur, Koch (tried to attenuate)
  - 1880: Laveran within red blood cells
  - 1897: Ross observed sporozoites in blood-feeding mosquitoes
  - 1898: Grassi: Anopheles mosquitoes only

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

- 1910: Ross observed sporozoites in blood-feeding mosquitoes
- 1898: Grassi: Anopheles mosquitoes only

- Evacuation 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 intraerythrocytic 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 reinvasion (symptoms from anemia, inflammation)
- Plasmodium falciparum in human hosts: ring form, trophozoite and schizont stages
- Systemic inflammatory process → fever
  - seen in vitro, not in RBC!

- Severe malaria: cerebral m., severe anemia, acute respiratory distress
  - or more debile episodes (93 out 100 cases in sub-Saharan African children)
  - Accumulation of platelets in brain microvessels (⇒ hemorrhage)
  - RBCs adhere (via "knobs") to endothelial cells (Lyman & Sheffield 2005)
  - in a pro-inflammatory manner (cytokine & chemokine case
during intra-erythrocitic development, plasma membrane asymmetry disrupted, flip-flop enzymes dysfunctional.

Tuberculosis: pulmonary disease.
Historical notes: Koch (1885-1890) cultivated microorganisms in agar for colonies in lung parenchyma disrupted by bacteria. Symptoms & signs: cough, spitum, 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 number 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 blood aggregation, protease release, oxygen free radical formation, apoptosis, organ dysfunction

- initial repair: downregulation of anti-inflammatory genes, upregulation 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)

- trigger mechanisms for cardiovascular cell activation:
  - inflammatory mediators (1), depletion of anti-X mediators, fluid shear, transients of gas pressure or temperature, juxtaglomerular activation, bio-implant interfaces.
    - (1) bacterial sources, endotoxins, oxidized products, LT-B4, PAF
    - (2) NO for instance

in shock (1) are "leukotaxin peptide," "chagogen factor,"...: plasma -> transported to what organ shows neutrophil activation? pancreas! (insulin + digestion)

actually, inflammatory mediator produced if pancreatic enzyme bypass prevent or another digestive protease

intestinal mucus normally protects you from inflammatory mediators = digestive enzymes

both the liquid and the proteinated fractions can kill you -> several fragments act (800 - 1500 Da)
Biosecurity and laboratory preparedness

- routes of exposure: injection, ingestion, inhalation, mucous membranes
- attire: closed shoes, long pants, goggles, coats, gloves
- x 100, in case of emergencies
- wash well if exposed to hazardous materials, MIT medical
- evacuate if asked to
- have a safe experience!