The immune system, immunopathology. Infectious diseases

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Physiologic function

Protection + defence against external and/or internal noxae

- Defence against infection incl. toxic products
- Autotolerance against body-own antigenes
- Immunologic internal control (removal of old, defective, some mutated cells)

Failure possible due to inadequate immune function and/or too violent (event. evasive) noxae

Factors affecting immunity

Alteration of the immune system due to:

- Aging
- Sex and hormonal influences
- Malnutrition
- Toxins (environmental, chemicals, …)
- Trauma, burns, surgery
- Medication incl. immunosuppressive drugy, anaesthesia
- Concurrent diseases (diabetes mellitus, chronic renal failure, malignancy, HIV, …)
- Stress, sleep disturbance, psychological well-being, …

Exercise immunology

- Dose and type of exercise dependent effect on immunity
- Moderate exercise enhances immune functions, reduces stress
- Rise in number of blood phagocytes and their activity during the exercise and approx. 2-4 hours after it (if > 30 min), up to 24 hours after prolonged exercise
- Increased cytotoxicity of NK cells
- Increase in lymphocytes in blood
- Regular execise may protect against dangerous systemic low-grade inflammation (due to production of antiinflammatory cytokines)

Exercise immunology

- Intense and/or long-duration exercise → immune impairment, incl. suppression of lymphocytes, possible increased risk of infection
- Suppression of the NK cell activity, even several hours after the exercise (vigorous training – repeated decline – posible cumulative effect?)
- High intensity exercise (>80% of maximal oxygen consumption) → immune function suppression + tissue damage → acute-phase response with complement activation, release of cytokines
- Immune system recovery in 6-24 hours

Clinical implications

- Regular exercise in aging people may prolongate normal function of the immune system (lower decline, better immunologic balance, delay of age- and/or disease associated apoptosis (brain, heart)
- Lower inhibition of immune system after intense exercise in aged patients (x young) – such exercise possible

Clinical implications

- During mild viral/bacterial infection exercise in otherwise healty people possible, if symptoms located above the neck („neck check“) – sneezing, throatache, rhinitis – and are not worse after 10 minutes of moderate activity.
- If headache, head throbbing start after short term activity → stop and rest
- If systemic signs (fever, fatigue) or symptoms below the neck (cough, diarrhea, vomiting, muscle/joint ache → no exercise

Exercise during COVID-19

- Similar general rules:
  - symptoms above neck – exercise is OK, but possible reduction in intensity and/or lenght (a walk instead of a run), according to actual situation
  - symptoms below neck and/or systemic signs – exercise postponement
  - slow return to activity during the recovery (2-3 wks. of rest esp. after heart problems)
  - 150 minutes of exercise weekly in healthy people, if possible
- Pandemic rules according to the situation:
  - social distancing
  - cleaning of the equipment
  - outside activities, if possible

Immunity

Innate: not adaptive, non-specific

no immunologic memory (not stronger with more exposures)

Adaptive (specific):

- specific recognition and response to the particular antigen
- effective reaction to diverse pathogenes/antigenes
- memory – rapid response to subsequent exposure to the specific antigen
- activation of other defense mechanisms

Phases of immune response

- Recognition: receptors (innate non-specific, later adaptive specific) binding to the pathogene
- Amplification: start of reaction, production and/or release of humoral factors incl. cytokines (soluble mediators), activation and/or proliferation of immune cells
- Effector phase: removal of antigenes (phagocytosis, lysis, neutralization, …)
- Termination of the immune response (very important, if not complete – tissue damage and/or chronic inflammation possible)
- Memory – specialized long-living T- and B-lymphocytes

Non-specific defenses of innate immunity

- Mechanic barrier functions: skin + mucosa (epithelium, cilia in respiratory tract)
- Secretory factors: lysozyme in secretions (tears), acid pH in stomach, vagina, acid urine
- Microbiome colonisation: commensal microorganisms preventing overgrowth of pathogenes

Innate immunity

- **Cells:** neutrophils, macrophages (phagocytosis, killing of bacteria), eosinophils (antiparasitic, allergic response), basophils, natural killer cells, mast cells
- **Complement:** complex system of interacting plasma proteins, effector mechanism for specific immunity, or direct activation possible
- **Toll-like receptors** on macrophages, neutrophils, dendritic cells; if activated by binding of pathogenes, induce the secretion of pro-inflammatory cytokines

- **Rapid response -** early host response

Mechanisms of nonspecific immunity

- Fever

- Inflammation
- extravasation
- phagocytosis
- complement

- NK cells

- Interferons - against viral infection

Natural killer cells

- **NK cells:** subtype of large granular cytotoxic lymphocyte that constitute a major component of the innate immune system. NK cells able of direct killing of cells infected by viruses, intracellular pathogenes, play a major role in the anti-tumor immunity

Adaptive immunity

- Pre-activation necessary (days – weeks)
- Threat present for longer time at a higher level (activation threshold)
- Active immunity: natural contact with the antigen or artificial (vaccination) – usually permanent/long standing activity
- Passive immunity: natural transmisssion of antibodies (placenta, breast milk) or artificial (injection of preformed antibody/antitoxin) – temporary activity

Cell-mediated adaptive immunity

- Direct cellular reaction to antigenes
- Mediated by T-lymphocytes:
  - cytotoxic T-cells CD8+, direct killing
  - helper T-cells CD4+, cytokine production – activation of other immune mechanisms incl. innate immunity, inflammation
  - regulatory/suppressor T-cells – prevention of responses against self-antigenes and commensal microoganisms

Cytokines

- Mediators produced by many cells, incl. lymphocytes and macrophages
- Regulation of lymphocyte proliferation / maturation
- Attraction of immune cells into the focus of inflammation
- Activation of variable immune cells functions
- Stimulation of hemopoesis

Humoral immunity

- Mediated by antibodies (serum globulins), which are produced by plasma cells, i.e. differentiated B-lymphocytes
- Plasma cells mature when exposed to antigen
- Memory cells can react more quickly to later exposures to the same antigen

- Immunoglobulins directly attack antigenes, activate the complement system, stimulate some hypersensitive reactions

Antibody (immunoglobulin) isotypes

- IgG- most common in serum, secreted in secondary response
- IgM- secreted in primary response; also part of antigen receptor on B-cells
- IgA- most common in secretions – mucosal immunity
- IgE- immediate hypersensitivity (allergy)
- IgD- part of cell surface antigen receptor

Antigen-presenting cells

- Antigens are “processed” by antigen-presenting cells (in lymphatic and/or other tissues)
- macrophages
- dendritic cells
- B cells
- Major Histocompatibility Complex plays a critical role in antigen presentation

Major Histocompatibility Complex

- A highly variable genetic locus on chromosome 6, which codes for cell surface compatibility
- Also called HLA (Human Leukocyte Antigens)
- Membrane proteins presenting antigenes for recognition by T-cells, which subsequently produce cytokines for regulation of both cellular and humoral immunity.
- Recognition and tolerance of all self-cell, all un-recognized cells will NOT be tolerated
- Certain MHC subtypes (alleles) associated with increased incidence of some autoimmune diseases

Immunological tolerance

Immune system distinction between self and non-self

"Thymic education"

T cells that might react with self-antigen
are eliminated in the thymus
(clonal deletion; early mechanism)

Clonal anergy – possible autoreactive cells are formed but are not
activated against certain antigens
(later mechanism)

Cancer immunology

Immune surveillance

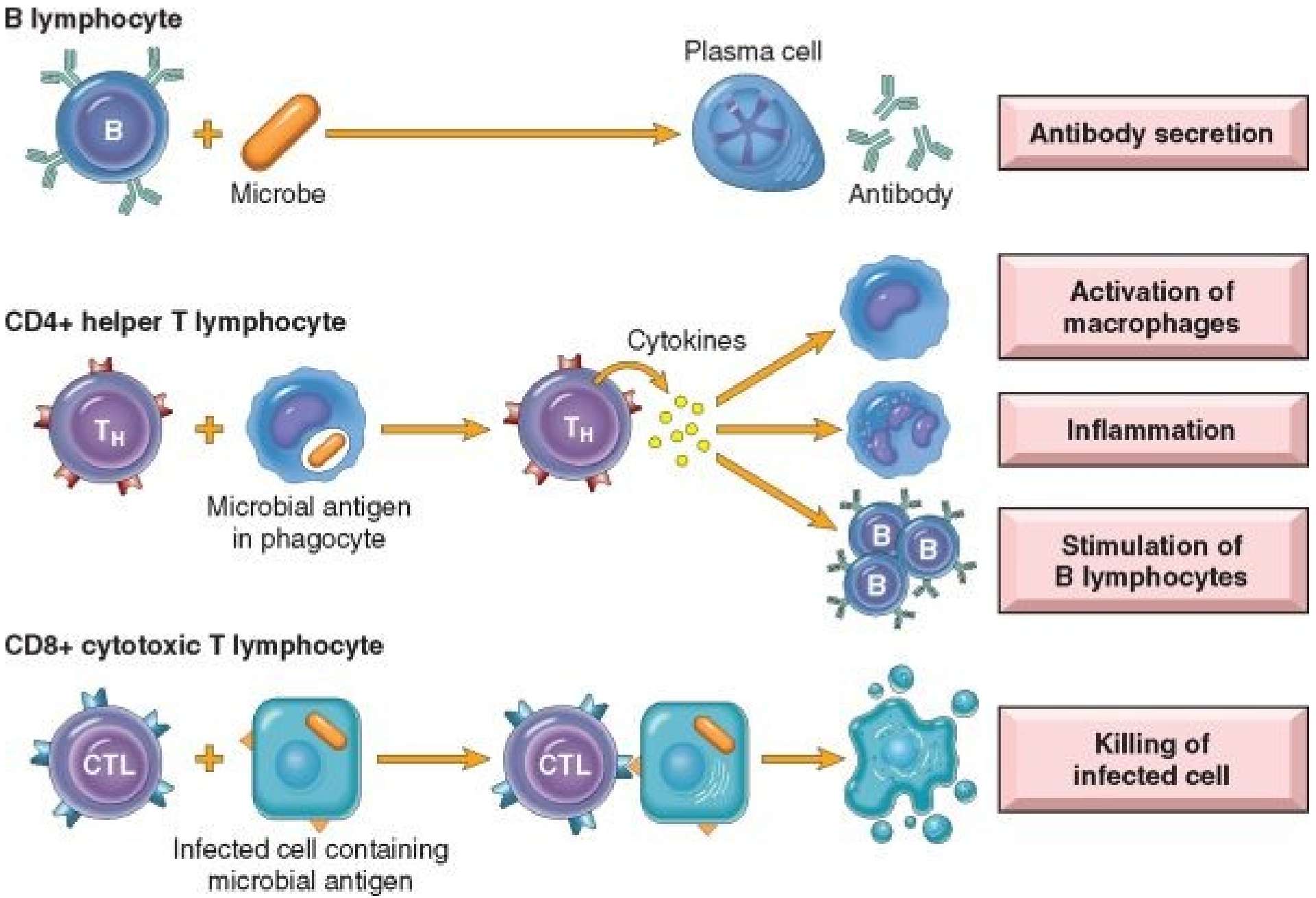
NK cells - early defense mechanism

MHC Class I activates these cells;

many tumor cells lack MHC Class I

Cytotoxic T cells - antigen specific

(both types of cells have similar killing mechanisms)



Robbins Pathologic Basis of Diseases

Disorders of the immune system

Exaggerated immune reaction

- Hypersensitivity reactions
- Autoimmune disorders

Transplantation immunology/immunopathology

Defective immune reaction

- Immunodeficiency (primary, secondary)

Hypersensitivity reactions

- sensitisation (previous exposition to an antigen) + repeated exposure → possible pathologic (excessive) response: hypersensitivity – imbalance between effector mechanisms of immune responses and control (+limiting) mechanisms
- antigens exogenous (chemicals, organic substances incl. microbes, …); endogenous (autoimmune diseases)
- association with inheritance of particular susceptibility genes (HLA, non-HLA)

Hypersensitivity

Classification according to the immunologic mechanism (→ mode of tissue injury and disease, manifestations) + time of response

Commonly multiple mechanisms in any one disease

- Antibody-mediated allergies are immediate and subacute hypersensitivities
- The most important cell-mediated allergic condition is delayed hypersensitivity

Hypersensitivity reactions contribute to:

Type I- rhinitis; asthma; hives; anaphylaxis

Type II- often directed against blood cells; various
types of hemolytic anemia
drug molecules can interact with blood cells
and form immunogenic structures

Type III- immune complex disease
usually complexes are cleared, but if not, are
deposited in tissue and cause inflammation

Type IV- contact dermatitis (basis for TB skin test)

Hypersensitivity reactions
Immediate (type I) hypersensitivity

- Rapid immunologic reaction occurring within minutes after the combination of an antigen with antibody bound to mast cells in individuals previously sensitized to the antigen („allergen“).
- Systemic disorder or local reaction.
- Anaphylaxis; allergies; bronchial asthma (atopic forms)
- Vascular dilatation, edema, smooth muscle contraction, mucus production, tissue injury, inflammation

Immediate (type I) hypersensitivity

Anaphylaxis: systemic reaction mostly after injection of an antigen into a sensitized individual. In minutes → shock (may be fatal).

- Causes: foreign proteins incl. vaccines, polysaccharides, drugs (penicillin), food (nuts, shellfish), insect toxins
- Starts with itching, hives, and skin erythema
- Contraction of bronchioles → respiratory distress. Laryngeal edema → hoarseness
- Vomiting, abdominal cramps, diarrhea
- Vascular shock, widespread edema

Immediate (type I) hypersensitivity

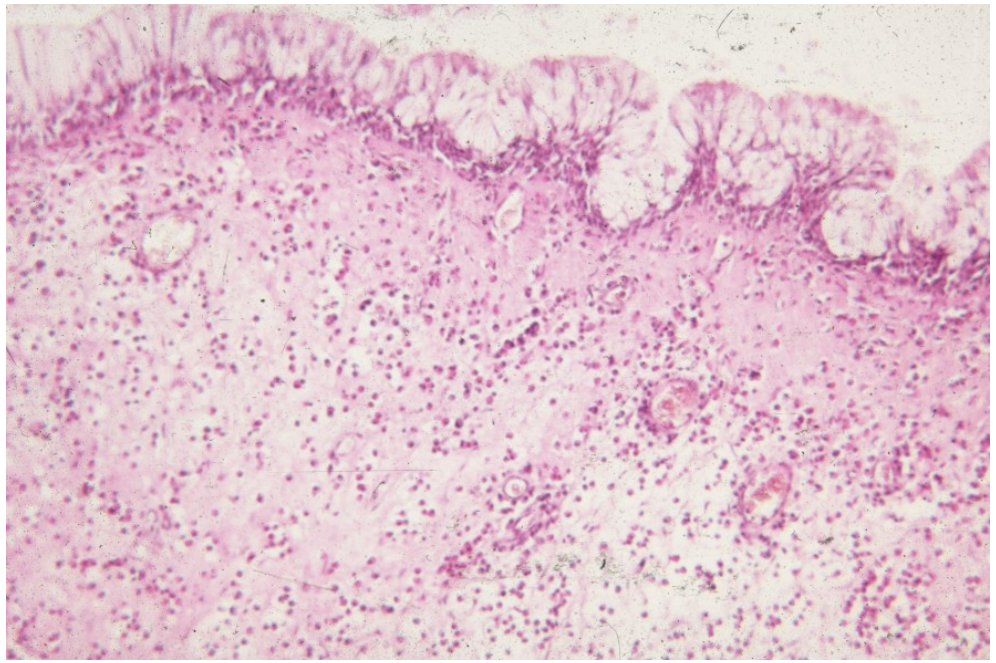
- Local reactions: diverse, according to the entry of the allergen. Localized cutaneous swellings (skin allergy, hives);

  nasal and conjunctival discharge (allergic rhinitis and conjunctivitis);

  hay fever; bronchial asthma;

  allergic gastroenteritis (food allergy).

Allergic rhinitis



Atopy

- **Genetically determined susceptibility to immediate hypersensitivity reactions.**
- **Atopy:** predisposition to develop localized immediate hypersensitivity reactions to a variety of inhaled and ingested allergens.
- ↑ serum IgE levels,
- Positive family history of allergy in 50% of atopic individuals.
- Atopic eczema, allergic rhinitis, asthma (+ secondary hyper-responsiveness of bronchial mucosa to non-specific irritants, e.g. cold, tobacco smoke,… Secondary neural triggering.)

Antibody-mediated (type II) hypersensitivity

- Onset usually slow (1–3 hours) after antigen exposure
- Production of IgG, IgM → bind to antigen on target cell or tissue → phagocytosis or lysis of target cell, recruitment of leukocytes
- Inflammation; in some diseases functional problems without cell or tissue injury (type V hypersensitivity – thyroid hyperfunction - Graves‘ disease)
- Malaise, weakness, rash, hoarsness, abdominal cramps, diarrhea, hypotension

Immune complex–mediated (type III) hypersensitivity

Antigens widely distributed through the body or blood.

Formation of insoluble antigen-antibody complexes.

- Deposition of antigen-antibody complexes (vessel wall)→ complement activation → recruitment of leukocytes → release of enzymes and other toxic molecules
- Inflammation, necrotizing vasculitis (necrosis of the vessel wall)
- Headache, chest pain, nausea, hematuria

Immune complex–mediated (type III) hypersensitivity

- Systemic lupus erythematosus nuclear antigens; nephritis, skin lesions, arthritis, others
- Poststreptococcal glomerulonephritis streptococcal cell wall antigen(s); may be “planted” in glomerular basement membrane; nephritis

T cell–mediated (type IV) hypersensitivity

- Contact dermatitis; multiple sclerosis; type I diabetes; rheumatoid arthritis; inflammatory bowel disease (i.e. Crohn disease); tuberculosis
- Perivascular cellular infiltrates; edema; granuloma formation; cell destruction
- Fever, arthralgia, enlarged lymph nodes, hives (urticaria)

T cell–mediated (type IV) hypersensitivity

- Rheumatoid arthritis: unknown antigen in joint synovium; role of antibodies? Chronic arthritis with inflammation, destruction of articular cartilage and bone
- Crohn disease: unknown antigen; role for commensal bacteria; chronic intestinal inflammation, obstruction, risk of fistulae, peritonitis

T cell–mediated (type IV) hypersensitivity

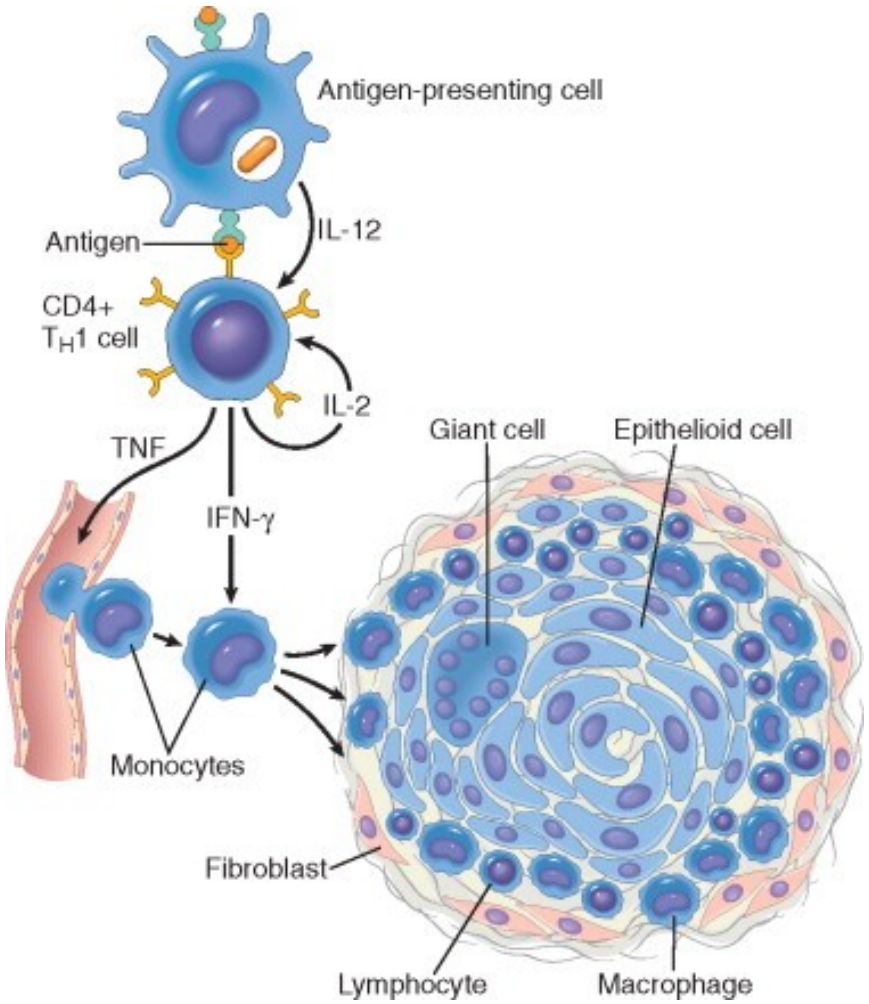
- Peripheral neuropathy; Guillain-Barré syndrome?: protein antigens of peripheral nerve myelin; neuritis, paralysis
- Contact sensitivity (dermatitis): various environmental antigens (e.g., poison ivy); skin inflammation with blisters – vesicular dermatitis

Clinical implications

- Anaphylaxis or other type I hypersesitivity: emergency, immediate action necessary
- Type IV reactions: possible in response to lotions, gels, etc. – observation of skin reaction
- In people with known hypersensitivity – skin test
- Latex sensitivity/allergy in a therapist possible

Granulomatous inflammation

- Persistent or nondegradable antigens, (tubercle bacilli)
- Infiltrate dominated by macrophages in 2-3 weeks.
- Activated macrophages transform into epithelium-like cells epithelioid cells.
- Granuloma: microscopic aggregation of epithelioid cells usually surrounded by a layer of lymphocytes.
- Granulomatous inflammation typically associated with strong T-cell activation with cytokine production



from Robbin's Pathologic Basis of Disease

AUTOIMMUNITY

- Ability of immune system to differentiate between self and non-self antigens
- Immune system response against self antigens

Autoimmune diseases

- *Autoimmunity arises from a combination of the inheritance of susceptibility genes, which may contribute to the breakdown of self-tolerance, and environmental triggers, such as infections and tissue damage, which promote the activation of self-reactive lymphocytes.*

- Autoantibodies (AA) in clinically normal people.
- Physiologic AA in removal of breakdown products after tissue damage (antigen-antibody complex removed by macrophages)
- Imbalance between control mechanisms (normally preventing pathologic self-reactivity) and pathways leading to the generation and activation of pathogenic effector lymphocytes.

Autoimmune diseases

- Pathologic autoimmunity: presence of immune reaction specific for self-antigen
- + primary pathogenic, not secondary to tissue damage
- + absence of other cause
- Commonly uncertain „pure“ autoimmunity – term immune-mediated inflammatory diseases

Factors influencing autoimmune disease

Internal triggering factors

- genotype / HLA
- cytokines
- apoptosis genes
- primary immunodeficiency
- hormones

External triggering factors

- infections
- UV
- drugs
- chemicals (including food)
- stress

Autoimmune diseases

- *Most autoimmune diseases are complex multigenic disorders*
- Many autoimmune diseases associated with infections, clinical flare-ups often preceded by infectious prodromes
- Disease occurrence in clusters, discordance in identical twins
- Many infectious diseases similar to autoimmune disease in pathology (Lyme disease)

Autoimmune diseases

Changes in self-antigens, that make them look like non-self to the immune system, due to:

Viral or bacterial infection

Irradiation

Medication

Smoking

Hormones

- Females are much more likely to develop autoimmune illness
- Rise in hormones associated with pregnancy may even cause abortion of the fetus

Drugs and foods

- **gluten – celiac disease**
- saturated fats – diferent AI diseases (oxygen radicals)
- **D- penicilamine, hydralazine, oral contraceptives, isoniaside** induction of autoantibodies
- silicone´s polymers (sclerodermia, systemic lupus, rheumatoid arthritis)

Autoimmune diseases

- Different autoimmune diseases show substantial clinical, pathologic, and serologic overlaps.
- Precise phenotypic classification often problematic.

Autoimmune diseases

- **DISEASES MEDIATED BY ANTIBODIES AND IMMUNE COMPLEXES**

Organ-specific autoimmune diseases

Autoimmune hemolytic anemia
Autoimmune thrombocytopenia
Myasthenia gravis (muscle weakness)
Graves disease (thyroid hyperfunction)

Systemic autoimmune diseases

Systemic lupus erythematosus (SLE)

Diseases caused by autoimmunity or by reactions to microbial antigens

Polyarteritis nodosa (vessel wall inflammation + necrosis)

Autoimmune diseases

DISEASES MEDIATED BY T-CELLS

Organ-specific autoimmune diseases

Type 1 diabetes mellitus
Multiple sclerosis (brain)

Systemic autoimmune diseases (+ possible role of antibodies)

Rheumatoid arthritis (mainly joints, soft tissues inflammation)
Systemic sclerosis (mainly soft tissues inflammation)
Sjogren syndrome (chronic inflammation of salivary, lacrimal glands)

Diseases caused by autoimmunity or by reactions to microbial antigens

Inflammatory bowel disease (Crohn disease, ulcerative colitis)
Inflammatory myopathies (muscles)

Incidence of autoimmune diseases

- Rheumatoid arthritis 1-3%
- Sjögren´s sy 1/20 000
- Vasculitis 1/100 000

- <u>Prevalence of autoimmune diseases</u>

5-7% of population

Diagnosis

clinical picture

laboratory

autoantibodies

autoreactive lymphocytes

autoantigens

related genes

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

- Chronic systemic autoimmune disease
- Cause unknown
- Affects almost any organ(s)
- Characterized by chronic inflammation

SLE

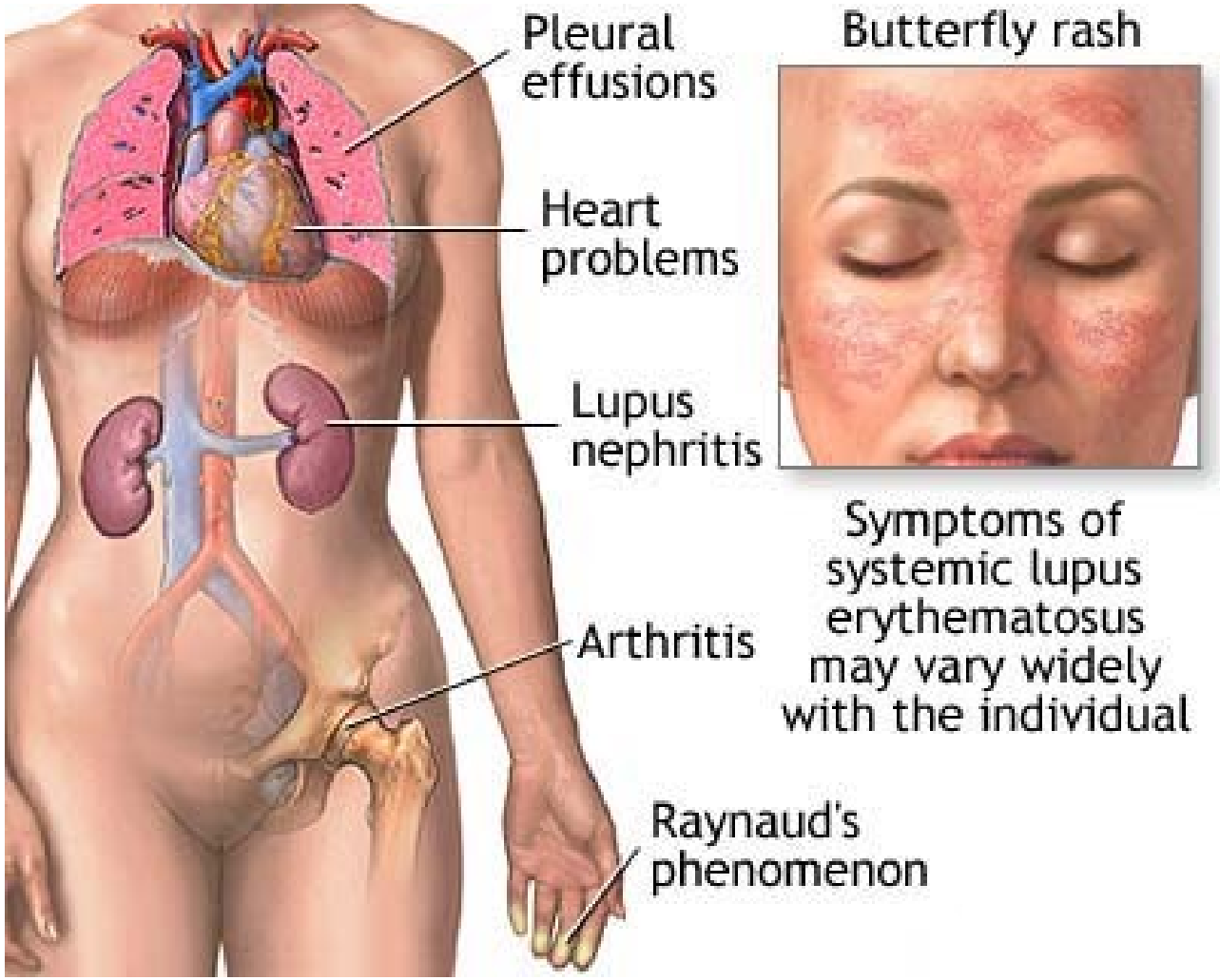
- The course of the disease is variable and unpredictable.
- Rare acute cases result in death within weeks to months.
- Appropriate therapy: flare-ups and remissions, years or even decades.
- *The most common causes of death are renal failure and intercurrent infections*.

SLE – typical case

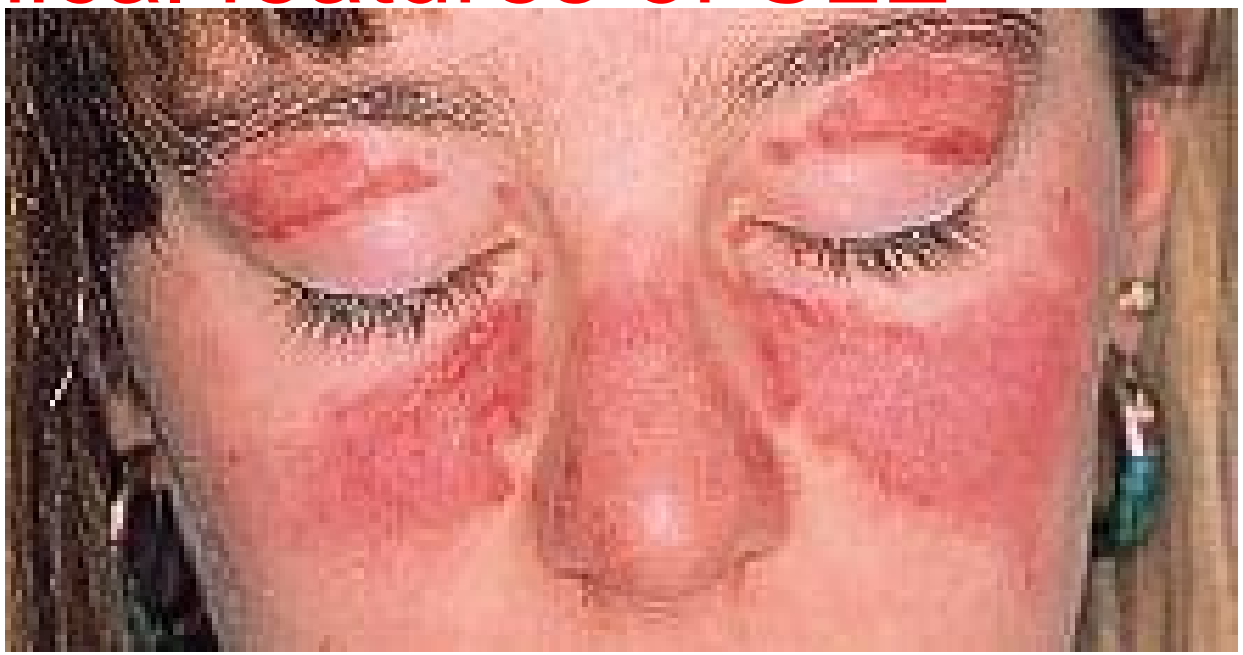
young woman with some of the following features:

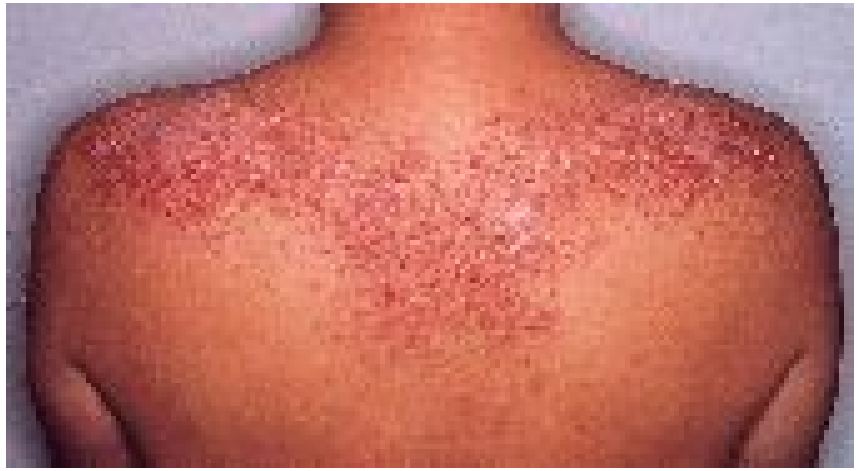
- a butterfly rash over the face,
- fever,
- pain but no deformity in one or more peripheral joints (feet, ankles, knees, hips, fingers, wrists, elbows, shoulders),
- pleuritic chest pain
- photosensitivity

SLE


Pleural effusions
Heart problems
Lupus nephritis
Arthritis
Raynaud's phenomenon
Butterfly rash
Symptoms of systemic lupus erythematosus may vary widely with the individual

Clinical features of SLE





Special implications of SLE

- Physical and occupational therapy important part of treatment
- Individual plan, according to the phase (acute flare with mostly rest, gradual start of activities with energy conservation – fatigue common)
- Exercise to increase muscle strenght, prevent osteoporosis x avoid increased stress of inflamed joints
- Limit exposure to direct sunlight
- Immunosuppression due to therapy → risk of infection

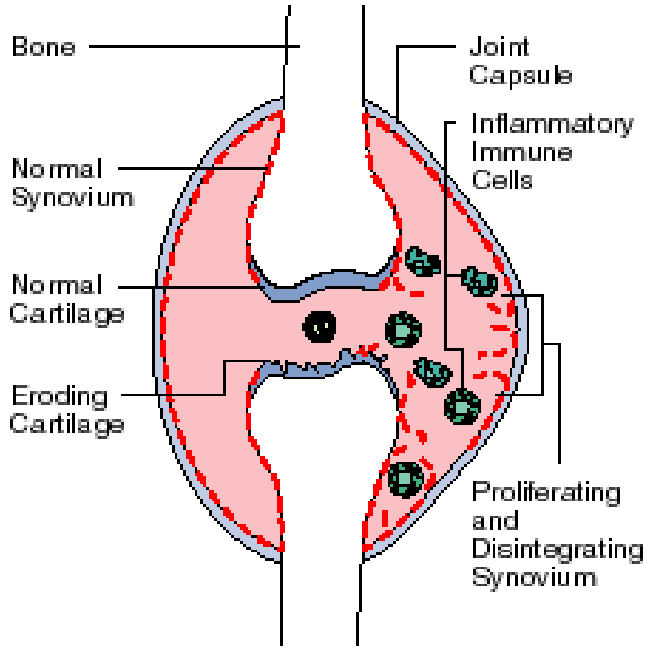
Rheumatoid arthritis

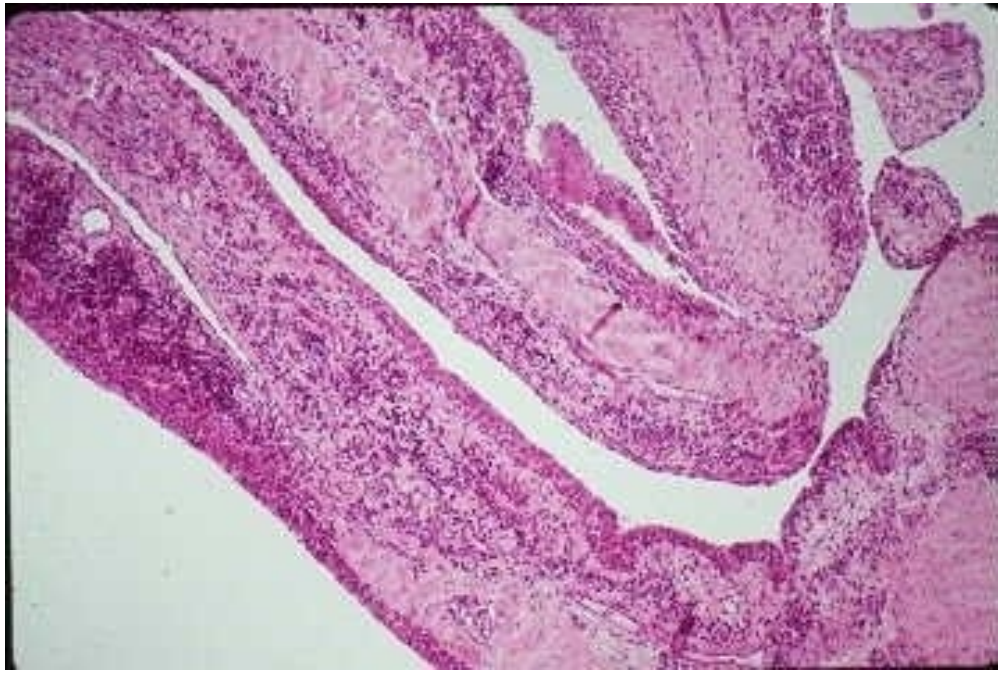
- Systemic autoimmune disease (joints, skin, blood vessels, heart, lungs, muscles, nerves)
- Genetic factors
- Etiology unknown, combination of gen. predisposition, environment (trigger), autoimmunity
- Rheumatoid factor (RF) in 80%
- Start commonly between ages 25-50 years
- Women 3:1 men
- Prolonged morning joint stiffness (≥ 1 hour)

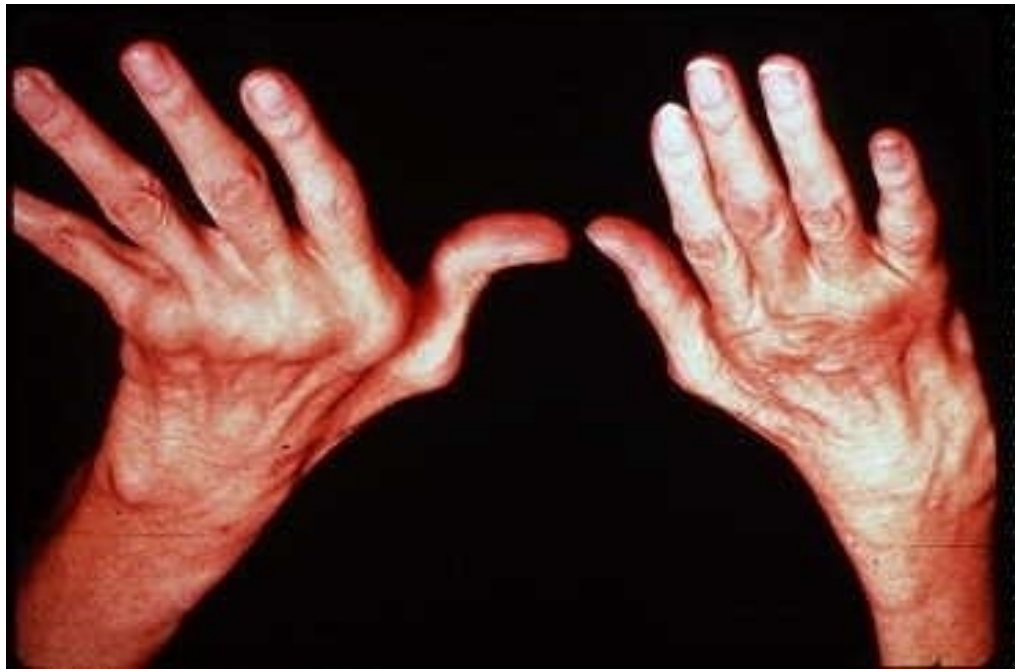
Rheumatoid arthritis

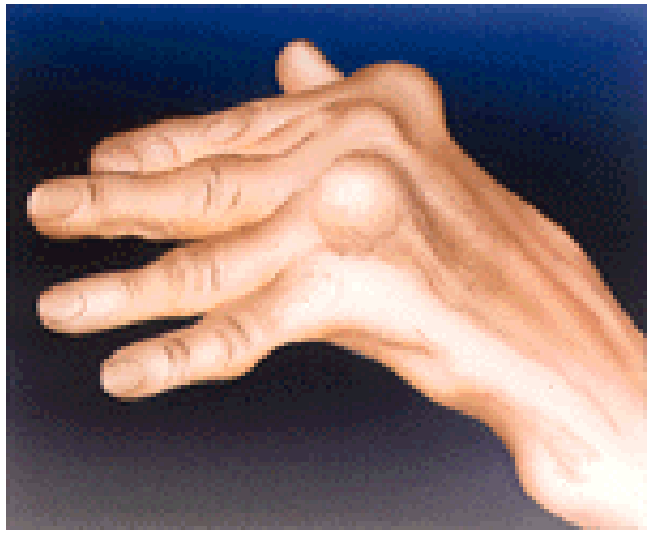
- Chronic nonpurulent proliferative inflammation of synovial joints, symmetrical
- Proliferation of synovial lining cells, oedema, fibrin deposition → pannus (synovial cells + granulation tissue + inflammatory cells) →
- Erosion of articular cartilage and adjacent bone (osteoclasts) →
- Fibrous ankylosis → bony ankylosis

Variable course, usual start in hands or other small joints.
Arthritis + morning stiffness
Worsening limitation of motion
Rheumatoid nodules in organs or tissues – skin, lungs (!x ca), myocardium,…
Systemic signs (fatigue, malaise, weight loss, fever, …)









Special implications

- Part of diagnostic staff (localisation, type and duration of joint pain)
- Signs of possible progression (increased intensity of pain, more joints affected)
- True arthritis – pain during active + passive motion x tendinitis – more in active motion
- Patient education (type of exercise)
- Functional status and rehabilitation

Systemic sclerosis

- Chronic inflammation with progressive interstitial and perivascular fibrosis in the skin, subcutaneous tissue, muscles and multiple organs
- gastrointestinal tract, kidneys, heart, muscles, and lungs (interstitial fibrosis) frequently involved
- death from renal failure, cardiac failure, pulmonary insufficiency, or intestinal malabsorption
- *limited scleroderma*, in which the skin involvement is often confined to fingers, forearms, and face.

Systemic sclerosis

- female-to-male ratio of 3 : 1, with a peak incidence in the 50- to 60-year age group
- Raynaud's phenomenon*:* episodic vasoconstriction of the arteries and arterioles of the extremities, in virtually all patients and precedes other symptoms in 70% of cases.
- Dysphagia attributable to esophageal fibrosis and its resultant hypomotility in more than 50% of patients

Organ-specific autoimmune diseases

Endocrine system

- Autoimmune (Hashimoto's) thyroiditis - hypofunction
- Hyperthyroidism (Graves' disease; thyrotoxicosis)
- Type I diabetes mellitus (insulin-dependent or juvenile diabetes)
- Insulin-resistant diabetes
- Autoimmune adrenal insufficiency (Addison's disease)

Organ-specific autoimmune diseases

Neuromuscular system

- Myasthenia gravis
- Autoimmune polyneuritis
- Multiple sclerosis

Organ-specific autoimmune diseases

GIT

- Chronic ulcerative colitis
- Malignant pernicious anaemia with chronic atrophic gastritis
- Autoimmune hepatitis, AI pancreatitis
- Primary biliary cirrhosis
- Chronic sclerosing cholangitis

Diabetes

Hyperglycaemia

Different mechanisms cause different forms

Genetic and environmental component to all forms

Diabetes gives rise to complications;

microvascular- nephropathy, neuropathy, retinopathy

macrovascular - cardiovascular disease

Two major forms of diabetes:

Type 1 diabetes (autoimmune)

Type 2 diabetes (metabolic)

Multiple sclerosis

- autoimmune brain disorder, genetic + environmental factors (infection as trigger), T lymphocytes reaction against myelin + macrophagic activation by cytokines – demyelinisation
- Brain white matter plaque (active, inactive), gliosis – sclerosis
- muscular weakness, paraesthesia, sensoric dysfunction (ocular), etc.

Myasthenia gravis

Disease marked by progressive weakness and loss of muscle control

Classified as a B cell disease

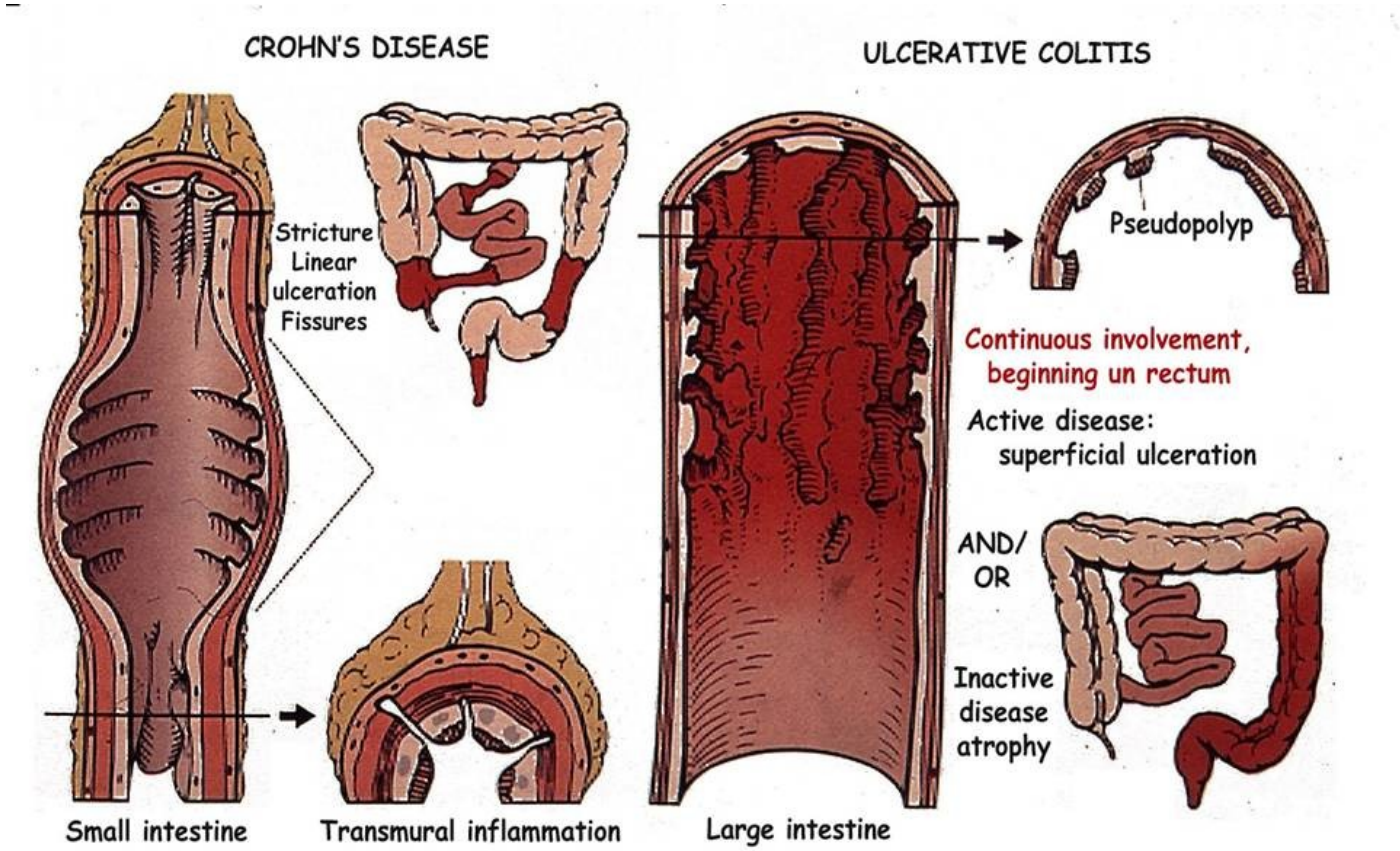
Autoantibodies against nicotinic acetylcholine muscle receptors

Celiac disease

- Sensitivity to gluten
- recurring abdominal bloating and pain
- chronic diarrhea/constipation
- failure to thrive in infants/loss of weight
- fatigue
- unexplained anemia
- dermatitis herpetiformis Duhring

- Autoantibodies

IBD – inflammatory bowel diseases



IMMUNODEFICIENCIES

- Primary – genetic, uncommon
- Secondary – acquired, very common

Primary immunodeficiencies

- Depends on the stage of immune development that is affected

- The earlier the defect, the more severe the effect

- SCID (severe combined immunodeficiency syndrome)
  essentially no protection against infection
  difficult treatment (bone marrow transplants, etc.)

PRIMARY IMMUNODEFICIENCY

- genetically determined
- humoral and/or cellular arms of adaptive immunity (mediated by B and T lymphocytes, respectively)
- defense mechanisms of innate immunity (NK cells, phagocytes, or complement)
- manifestation mostly in infancy, (6-24 months)
- susceptibility to recurrent infections by opportunistic pathogenes, or systemic i. by microorg. normally superficial, or unusually extensive i. by common path.
- autoimmune diseases

T-cell defect

- Bacterial sepsis
- Cytomegalovirus, Epstein-Barr virus, severe varicella, chronic infections with respiratory and intestinal viruses
- Fungal infections (*Candida, Pneumocystis jirovecii)*
- Aggressive disease with opportunistic pathogens, failure to clear infections

B-cell defect

- Streptococci, staphylococci, *Haemophilus*
- Enteroviral encephalitis
- Severe intestinal giardiasis
- Recurrent sinopulmonary infections, sepsis, chronic meningitis

Granulocyte defect

- Staphylococci, *Pseudomonas*
- *Candida, Nocardia, Aspergillus*

Complement defect

- Neisserial infections, other pyogenic infections

Common variable immunodeficiency CVID

- relatively common, heterogeneous group of disorders (dg. by exclusion), both sexes, children - adolescents
- hypogammaglobulinemia
- sporadic and inherited forms
- B cells in normal numbers, not able to differentiate into plasma cells
- abnormalities in T helper cell–mediated activation of B cells
- hyperplastic B-cell zones in lymphoid tissue

SECONDARY IMMUNODEFICIENCY

Due to impaired synthesis and function:

- protein, vitamin and energy deficiency in malnutrition, cachexia in disseminated cancer, anorexia, alcoholism
- prevalent monoclonal Ig in some lymphoproliferative diseases
- bone marrow infiltration or fibrosis (leukemia, myelofibrosis)
- suppression of cell mediated immunity due to acute viral infection (CMV, EBV, measles, etc.), bacterial and protozoal infection – macrophagic dysfunction (leprosy, leishmaniasis)

SECONDARY IMMUNODEFICIENCY

- iatrogenic (immunosuppressive and cytostatic drugs, radiotherapy, splenectomy – pneumococcus sepsis)
- diabetes mellitus and other metabolic diseases
- chronic stress
- sarcoidosis (↓ T-cell function)
- certain age groups (old, newborn, immature infants)

Increased catabolism or loss: nephrotic syndrome and renal failure, inflammatory intestinal diseases (IBD, lymphangiectasia)

SECONDARY IMMUNODEFICIENCY

Humoral immunodeficiency

- intestinal lymphangiectasia, IBD → ↓ all Ig classes, commonly + lymphopenia
- nephrotic sy, chronic diarrhea → ↓ IgG
- iatrogenic immunosuppression/cytostatic therapy
- B-cell malignancies
- Splenectomy – spleen B-cell – Ab x polysaccharide antigens – encapsulated microorganisms (pneumococci)

SECONDARY IMMUNODEFICIENCY

Cellular immunodeficiency

- temporal after acute viral infection (CMV, EBV, measles, etc.)
- AIDS

SECONDARY IMMUNODEFICIENCY

Combined immunodeficiency

- Severe general metabolic problems (DM, renal insufficiency), malnutrition, anorexia, chronic alcoholics – inadequate hormones, glucose, vitamins level

SECONDARY IMMUNODEFICIENCY

Defect of phagocytosis

- neutropenia in bone marrow insufficiency (irradiation, immunosuppressant/cytostatic th., some chemicals)
- autoantibodies
- ↑ loss in hypersplenism
- metabolic diaseases
- myeloid leukemia

SECONDARY IMMUNODEFICIENCY

Complement defficiency

- immunocomplex diseases
- sepsis
- severe liver disease

Clinical implications

- Increased risk of infections + commonly poor physiologic and psychologic health status + comorbidities + invasive procedures
- Infection control strategy necessary, esp. during the pandemics
- Minimize infection reservoirs (you, the client, reusable equipment, invasive devices)
- Stop the transmission (hand washing, clean/sterile techniques and equipment, face mask, maintain skin integrity)

HIV / AIDS

- Pandemic infection, affecting cells of the immune system → possible problems in any organ system
- Infection by opportunistic microorganisms → inflammation, tumors
- Direct influence of HIV on nervous systém
- Common co-infection with other infection (hepatitis C, hepatitis B, tuberculosis), esp. in high-risk behaviour

AIDS epidemics

- AIDS related illnesses still the leading cause of death among women of reproductive age
(15–49 years) globally
- 120 000 children dying of AIDS related illnesses (50% decline in 6 years)
- Increases in AIDS-related mortality over the past decade in the Middle East and North Africa (48%↑) and eastern Europe and central Asia (38%↑).

AIDS epidemics

- HIV infection in Europe: National epidemics concentrated among key populations at higher risk (men who have sex with men – MSM, injecting drug users; prisoners, sex workers, sexual partners of key population).

AIDS epidemics

- Europe, Australia and Canada: mortality rates

  among people living with HIV in the first five years after infection now ~ in the HIV-uninfected population
- Mortality among HIV-infected people increases with the duration of infection
- Increasing complications of chronic HAART – highly active antiretroviral therapy

HIV ISSUES

- Blood safety
- HIV treatment: antiretroviral therapy
- Prevention of mother-to-child transmission
- Co-management of tuberculosis and
  HIV treatment
- HIV testing in the general and most-at-risk population

HIV / AIDS - transmission

- Exchange of body fluids (blood, semen) – high-risk behaviour
- High-risk unprotected sex (vaginal, oral, anal), MSM
- Females: 2x↑risk (HIV viral load in semen important), sexually transmitted diseases (STD) further ↑ the risk (defect in mucosa)
- Children - during pregnancy, labor, breastfeeding
- Infected equipments (needle – intravenous drug use; 0,3% after needlestick injury in heathcare workers; tattoo, …)
- NOT transmitted: casual social or household contact, cups, drinking fountains, unbroken skin contact, sweat, tears, nonbloody saliva, urine, faeces…
- Postexposure prophylaxis possible

Phases of HIV infection

- Acute retroviral syndrome (3-6 wks after infection, in 40-90%, self-limited in 2-4 wks)
- Chronic phase (clinical latency, persistent generalized lymphadenopathy – PGL)
- Progression to AIDS (AIDS-related complex – ARC, AIDS indicator conditions: constitutional, neurologic, opportunistic infection, neoplasm

Acute HIV infection

- **Suspect:** Signs or symptoms of acute HIV infection with recent (within 2–6 weeks) high risk of exposure
- **Possible signs**: fever, lymphadenopathy, skin rash, myalgia/arthralgia, headache, diarrhea, oral ulcers, leucopenia, thrombocytopenia, transaminase elevation.

Acute HIV infection

- **High-risk exposures** include sexual contact with a person infected with HIV or at risk of HIV, sharing of injection drug use paraphernalia, or contact of potentially infectious blood with mucous membranes or breaks in skin.
- **Differential diagnosis:** Epstein-Barr virus (EBV)- and non-EBV (e.g., cytomegalovirus [CMV])-related infectious mononucleosis syndromes, influenza, viral hepatitis, streptococcal infection, syphilis

HIV neurologic disease

- Acute aseptic meningitis
- subacute and chronic: HIV-associated neurocognitive disorders (behavioral, cognitive, motor)
- HIV meningoencephalitis – AIDS-dementia complex, vacuolar myelopathy, myopathy and peripheral neuropathy
- before HAART, clinical signs of neurologic lesion in 40-60% of patients (HIV, opportunistic infection, tumor)
- now ↓– chronic encephalitis – microglial nodules + multinucleated giant cell, microfoci of necrosis

Opportunistic infections and neoplasms

- Protozoal and helmintic cryptosporidiosis, toxoplasmosis, giardiosis, etc.)
- Fungal (Pneumocystis, candidiasis, cryptococcosis, coccidiomycosis, histoplasmosis)
- Bacterial (mycobacteriosis – atypical, TB; salmonellosis, nocardiosis)
- Viral (CMV, Herpes simpex, Varicella-zoster, progressive multifocal leukoencephalopathy – JC polyoma virus)
- Neoplasms (Kaposi sarcoma – HHV 8, B-cell non-Hodgkin lymphomas, primary brain lymphomas – EBV, aggressive cervical and anal carcinomas – HPV)

LUNG INFECTIONS

- Pneumocystis
- Candidiasis, histoplasmosis, coccidiomycosis
- CMV (+ in combination)
- TBC
- Toxoplasmosis
- Nocardiosis

TBC

- early in the course of HIV infection
- reactivation/reinfection
- pulmonary and/or disseminated
- multiple and/or highly resistant mycobacteria common – new types of drugs necessary
- problems in combination therapy (HIV + TBC)

GIT INFECTIONS

Very common, persistent diarrhea

- Cryptosporidiosis, isosporidiosis (protozoa; watery diarrhea, major fluid loss; dg.- oocysts in the stool)
- Atypical mycobacteriosis (M. avium-intracellulare complex)
- Salmonella, Shigella
- CMV

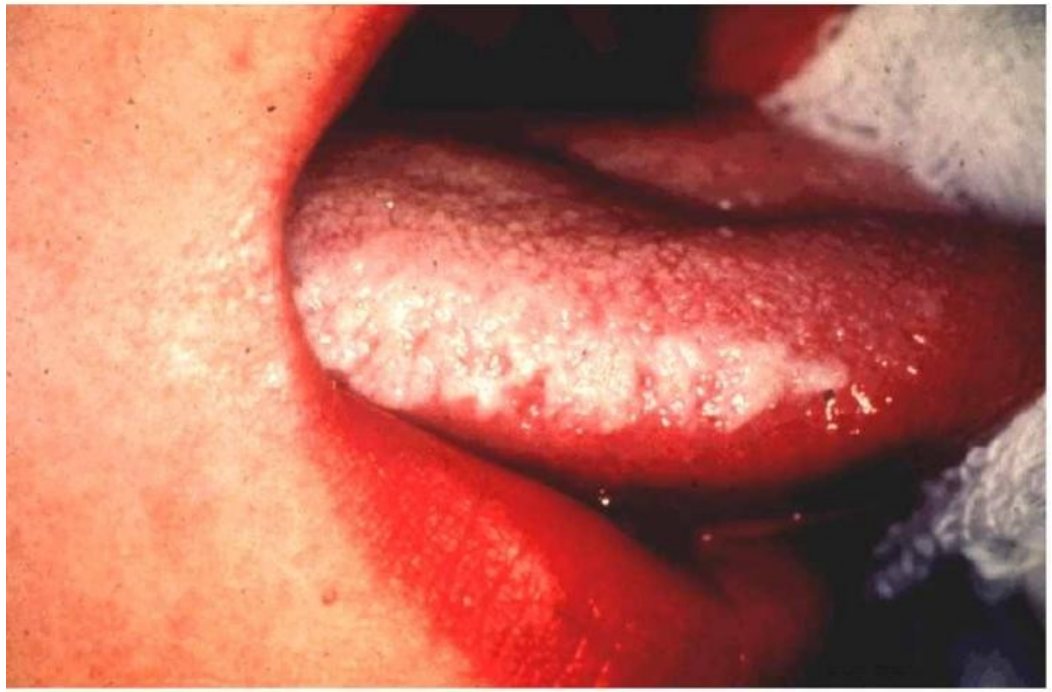
HIV + hepatitis co-infection

- Common coinfection of HIV + HBV and/or HCV
- ↑ acute HCV in HIV infected
- accelerated progression of chronic hepatitis to cirrhosis + liver failure
- problems in HAART / HCV drug interaction and toxicity
- value of the transplantation?

SKIN + ORAL INFECTIONS

- Chronic, relapsing, non-healing
- Commonly ulcers
- EBV + HIV – oral hairy leukoplakia
- Candida
- HSV, VZV

Oral hairy leukoplakia



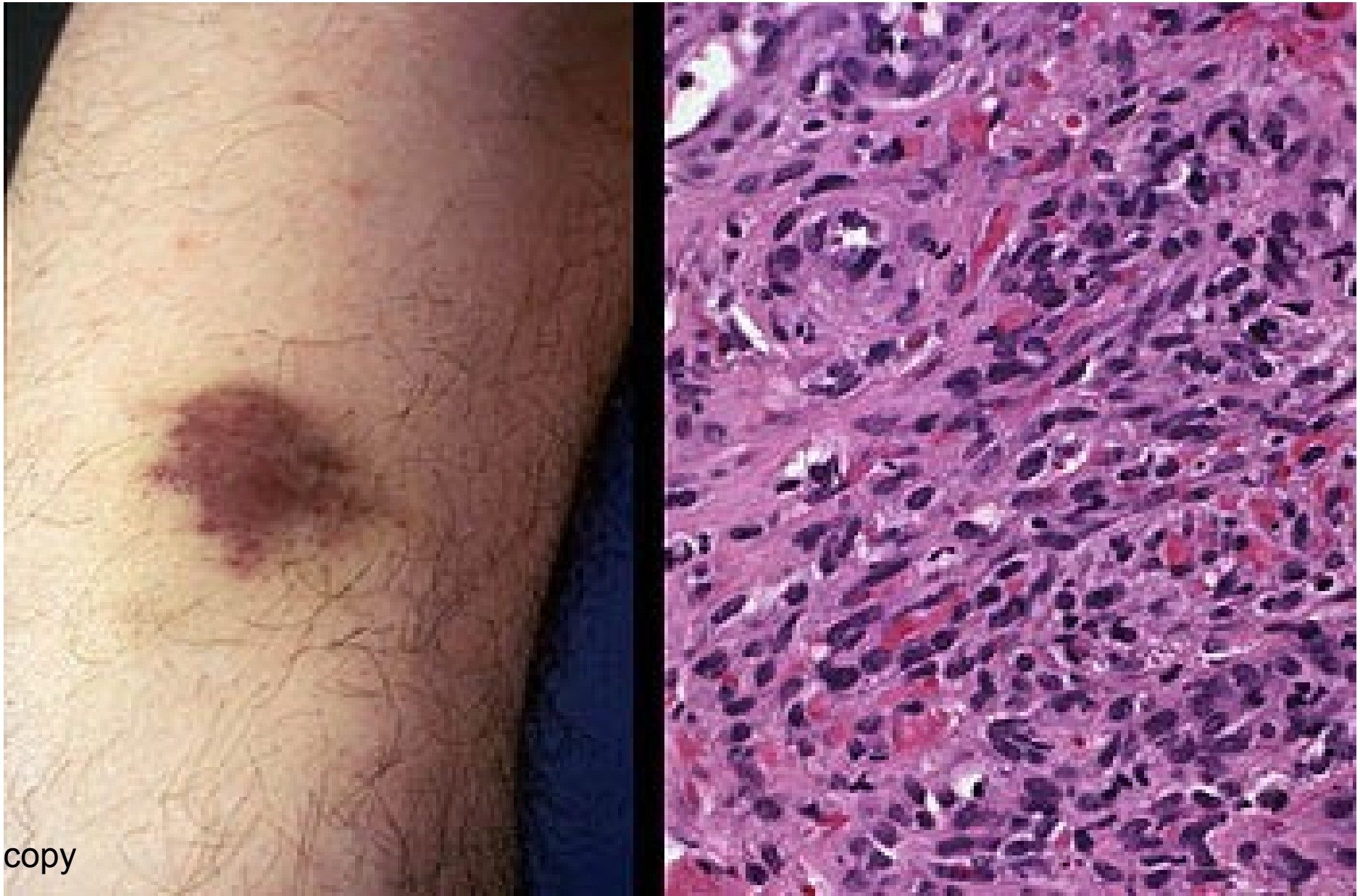
Musculoskeletal manifestations

- Myalgia/arthralgia
- Rheumatologic manifestations incl. joint inflammation
- Musculoskeletal pain syndrome / HIV wasting syndrome
- Delayed healing

HIV-associated neoplasia

- HHV-8: Kaposi‘s sarcoma
- EBV: non-Hodgkin‘s malignant lymphoma, primary brain ML
- HPV: agressive anal, cervical squamous cell carcinoma
- general increased risk of malignancy

Kaposi sarcoma



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HIV lymphoma

- Solitary lump or nodule, swelling, nonhealing ulcer
- The swelling may be ulcerated or may be covered with intact, normal-appearing mucosa.
- Usually painful, rapid growth.
- Common association with EBV
- Several histopathologic types, atypical localization

Human papilloma viruses

- Human papilloma virus lesions appear most commonly in immunocompromised individuals.
- Diagnosis based on history, clinical appearance, and biopsy.
- Common in early HIV infection.
- Spiky warts, raised, cauliflower-like appearance.

Noninfectious HIV-related comorbidities:

- The premature aging process in HIV-infected people
- 2x ↑ risk of myocardial infarction
- ↑ risk of osteoporosis incl. fractures (even in adolescents!)
- ↑ risk of chronic renal failure
- Non-AIDS tumors

HAART complications

- **Diarrhea, nausea , and vomiting.**
- **Lipodystrophy: fat in adipous tissue redistributed to other regions, i.e.face and limbs → thin, breasts, stomach and/or neck enlarge.**
- **Glucose intolerance, diabetes. Lactic acidosis.**
- **Liver toxicity – acute hepatitis incl. liver failure. Pancreatitis.**
- **Nephrotoxicity**
- **Neuropathy**
- **Osteonecrosis, osteoporosis, osteopenia**

Special implications

- Protect yourself (client unaware of HIV+, untrue report of HIV status)
- Help the diagnosis (encourage HIV test in unclear clinical signs)
- Special support according to the problems (wasting, osteoporosis, …)

Pathology of Infectious Diseases

Categories

Saprophytes: nonpathogenic; in dead organic matter

Parasites: living in or on an host on his the expense

– **Commensals:** normal inhabitants of skin and mucosa;

– **Pathogenic microorganisms:** Classic disease-causing pathogens

– **Opportunists or facultatively pathogenic** microorganisms:

in immunocompromised individuals in an “opportune” situation; frequently from the normal flora, may be from the surrounding environment or other germ carriers

Pathogenicity: capacity of a pathogen species to cause disease

Virulence: sum of the disease-causing properties of a strain

of a pathogenic species

RESIDENT FLORA

- NO disease under normal conditions
- Includes bacteria, fungi, protozoa, viruses and arthropods (mites)
- Most areas of the body in contact with the outside environment harbor resident microbes; large intestine has the highest numbers of bacteria
- Internal organs, tissues, fluids microbe-free
- Bacterial flora benefit host by preventing overgrowth of harmful microbes

OPPORTUNISTIC FLORA

- Potentially pathogenic organisms that do not cause disease in their normal habitat in a healthy person
- Organisms that gain access into the tissue through broken skin or mucous membranes
- Host already weakened or compromised by infection.

Host involvement

Endogenous infection from the colonizing flora

Exogenous infection from invasion of host by microorganisms from external sources

Nosocomial infection acquired during hospitalization (urinary tract infections, infections of the respiratory organs, wound infection, sepsis)

Host involvement

Superinfection: occurrence of a second infection in the course of a first infection

Relapses: series of infections by the same pathogen

Reinfection: series of infections by different pathogens

Subclinical disease: No noticeable signs or symptoms (inapparent infection)

Host involvement

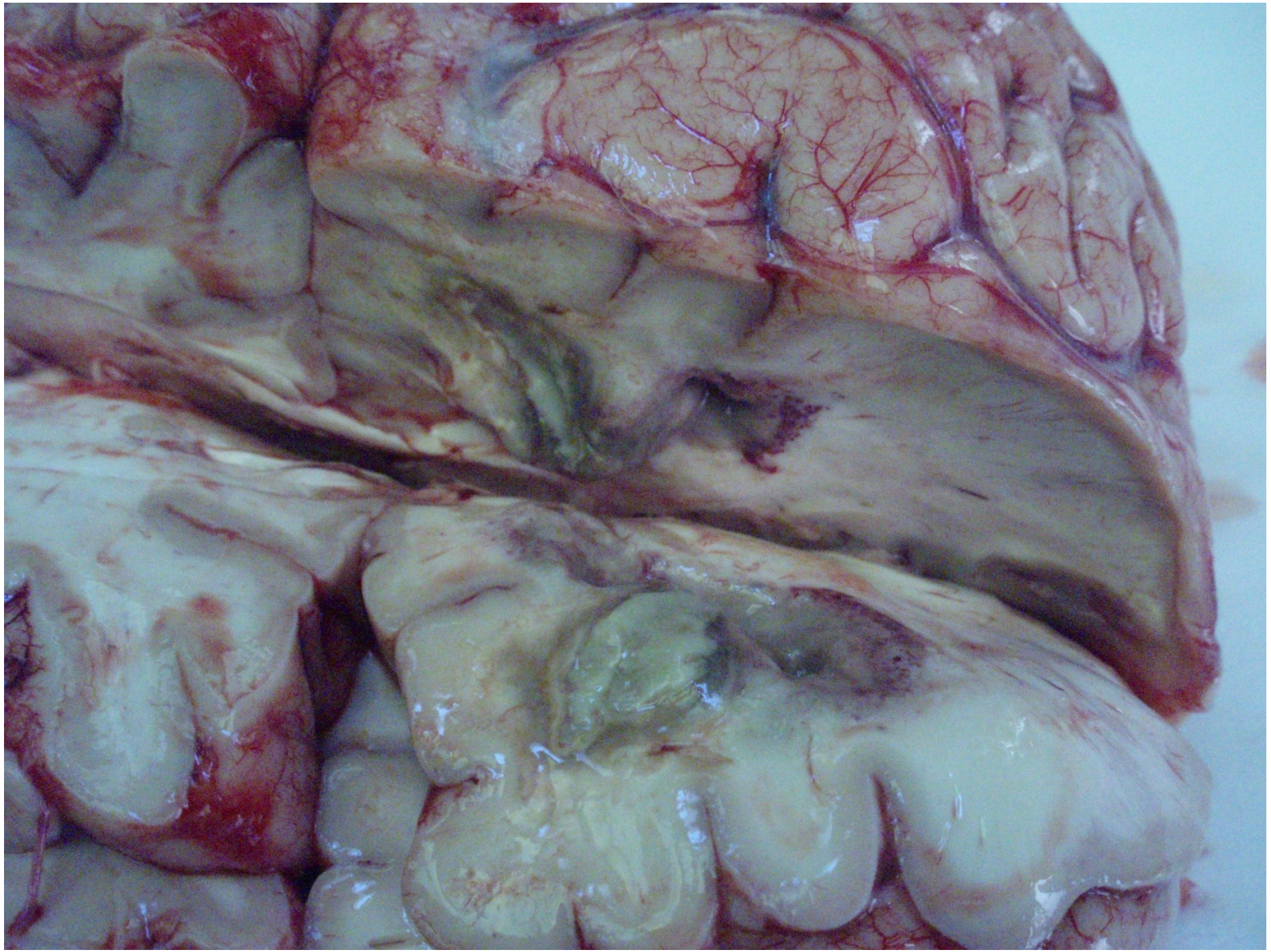
Local infection restricted to the portal of entry and surrounding area

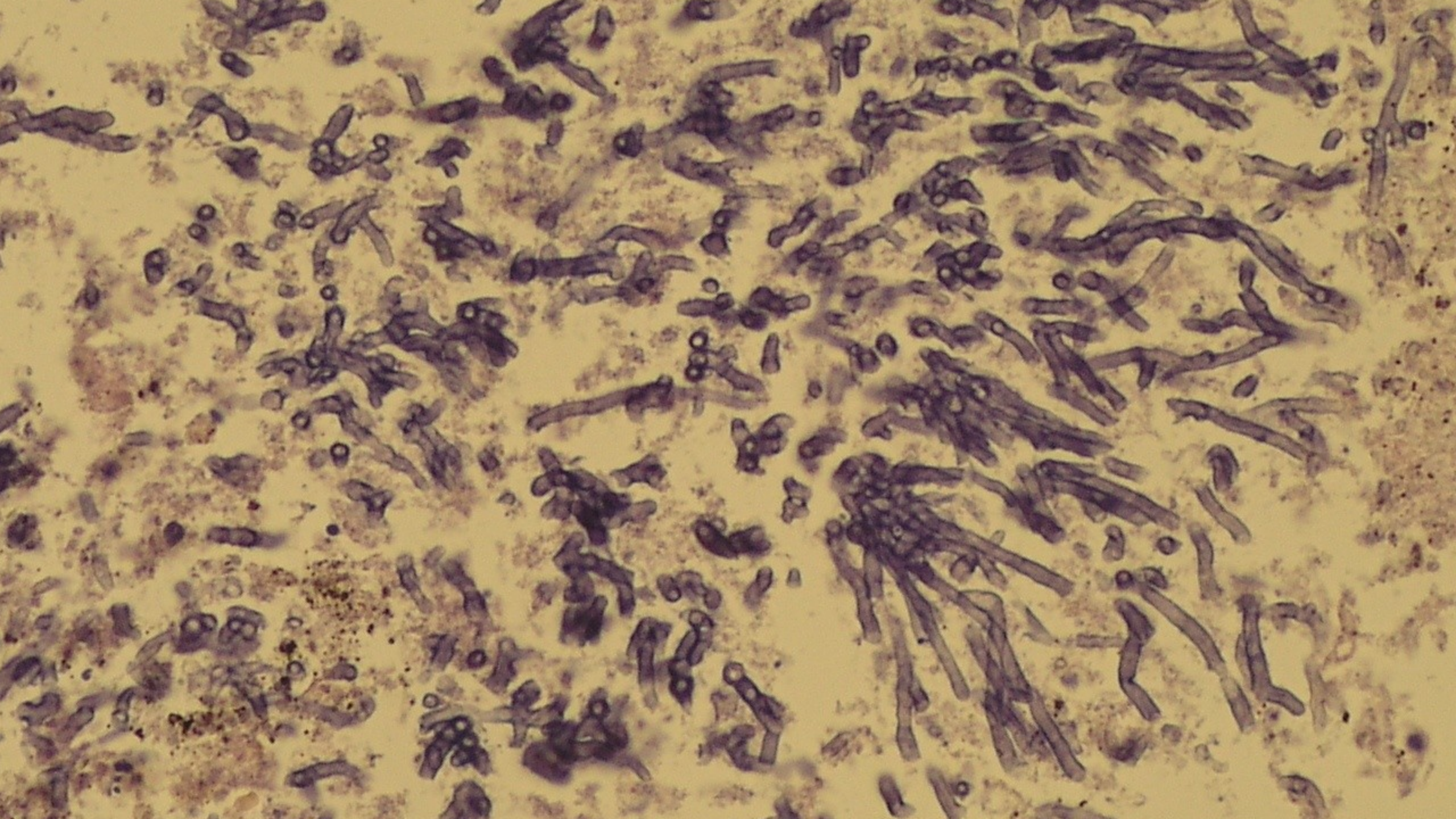
Generalized (systemic) infection Lymphogenous and/or haematogenous spread of pathogen from the portal of entry; organotropism; three stages: incubation, generalization, organ manifestation

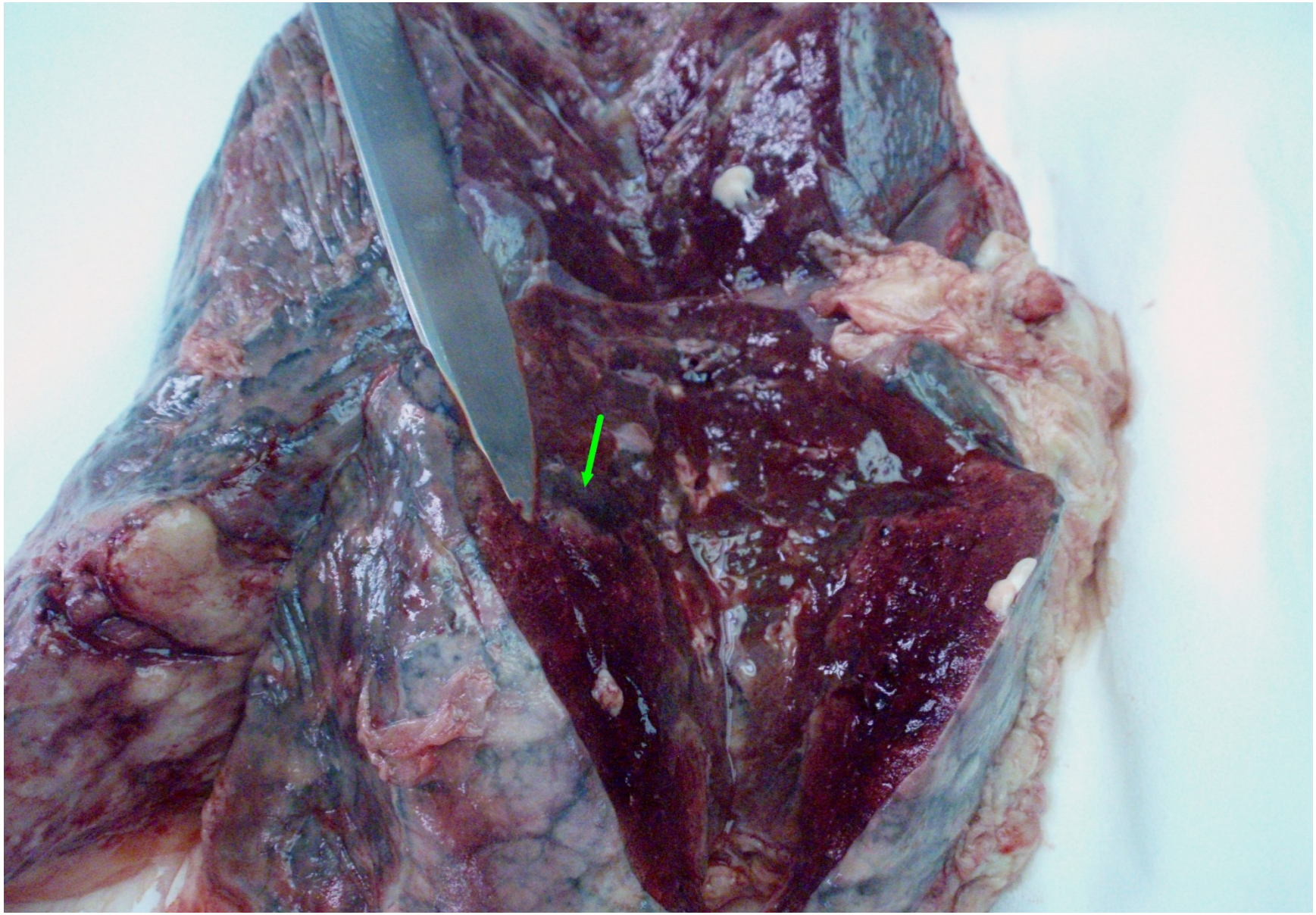
Systemic infection

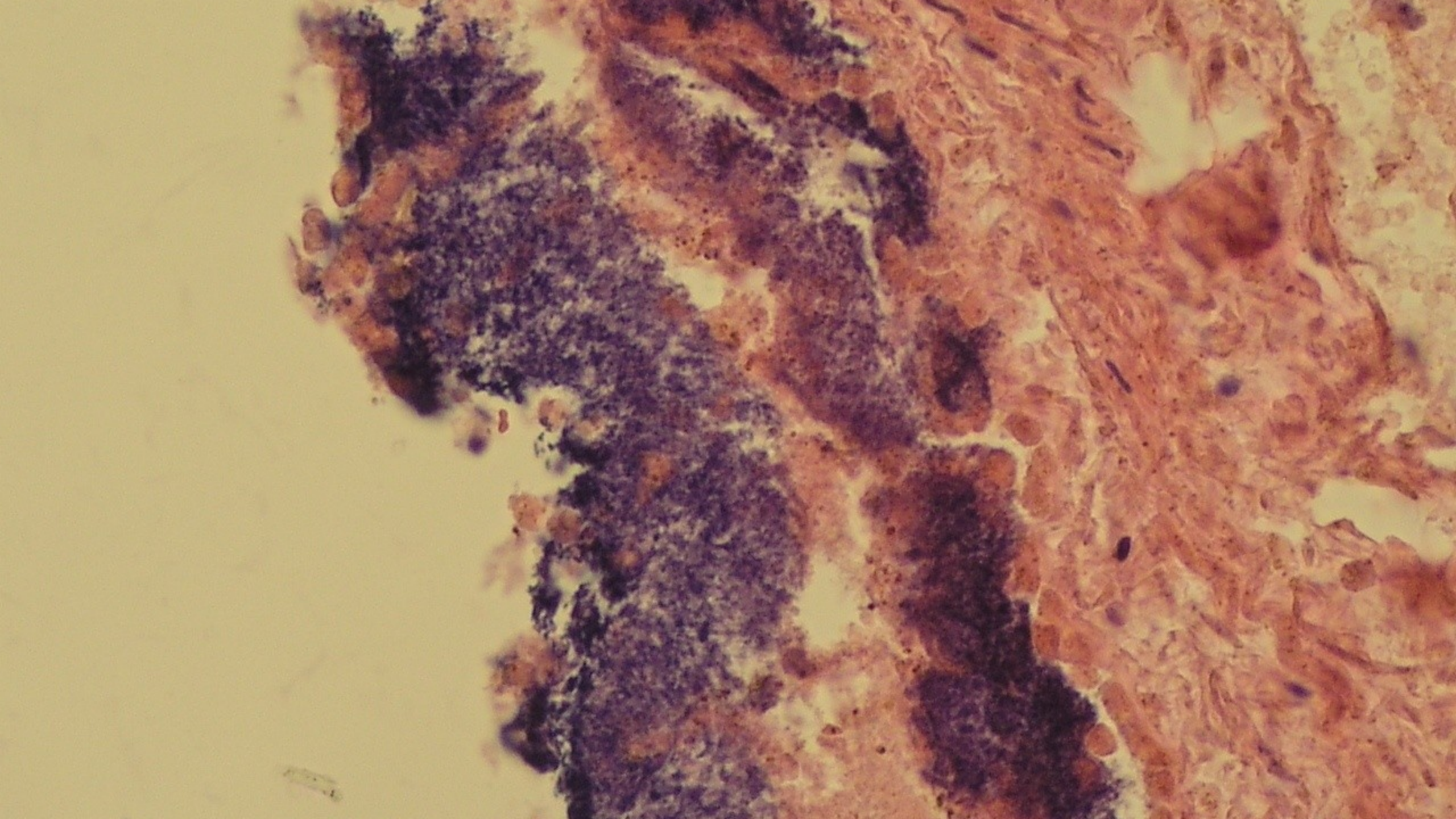
- example: immunocompromised host, mycotic infection, portal of entry – lung, skin
- generalisation - haematogenous
- organotropism – brain abscesses

  lung abscesses
- superinfection by bacteria









Host involvement

Sepsis Systemic disease by microorganisms and/or their toxic products; often a localized focus of infection from which pathogens or toxic products enter the bloodstream continuously or in intermittent phases, → shock

Septicemia Growth of (pathogenic) bacteria in the blood

Pyemia Bacteria in blood in aggregates (microemboli) + toxemia, → pyemic abscess, septic infarction

Transitory bacteremia/viremia/parasitemia Brief presence of microorganisms in the bloodstream

Epidemic process and epidemic factors of infectious disease

- **Source of infection** (basic conditions)

  Patients (acute, chronic), covert infection, carrier, infected animal

- **Route of transmission**

  Contact transmission (direct and indirect), blood-borne, soil- borne, food + water-borne, air-borne, insects, …

- **Susceptibility of population**
- **Factors of influencing epidemic process**

  nature factors, social factors

Reservoirs of infection

- **Continual sources of infection**
  - Human: COVID-19, AIDS, gonorrhea
    - **Carriers** may have inapparent (subclinical) infections or latent diseases
  - Animal: Rabies, Lyme disease
    - Some **zoonoses** may be transmitted to humans (COVID-19, zika, SARS, …)
  - Nonliving: Botulism, tetanus
    - Soil

CONTACT TRANSMISSION

- DIRECT CONTACT - reservoir to host
- INDIRECT CONTACT - reservoir to vehicle to host.
  - Vehicle – inanimate material, food, water, drugs, biological products, …
- DROPLET - reservoir to air (short distance) to host

  Airborne transmission - spread of agents by droplet nuclei or dust at a distance of more than 1 meter from the reservoir to host
- VECTOR

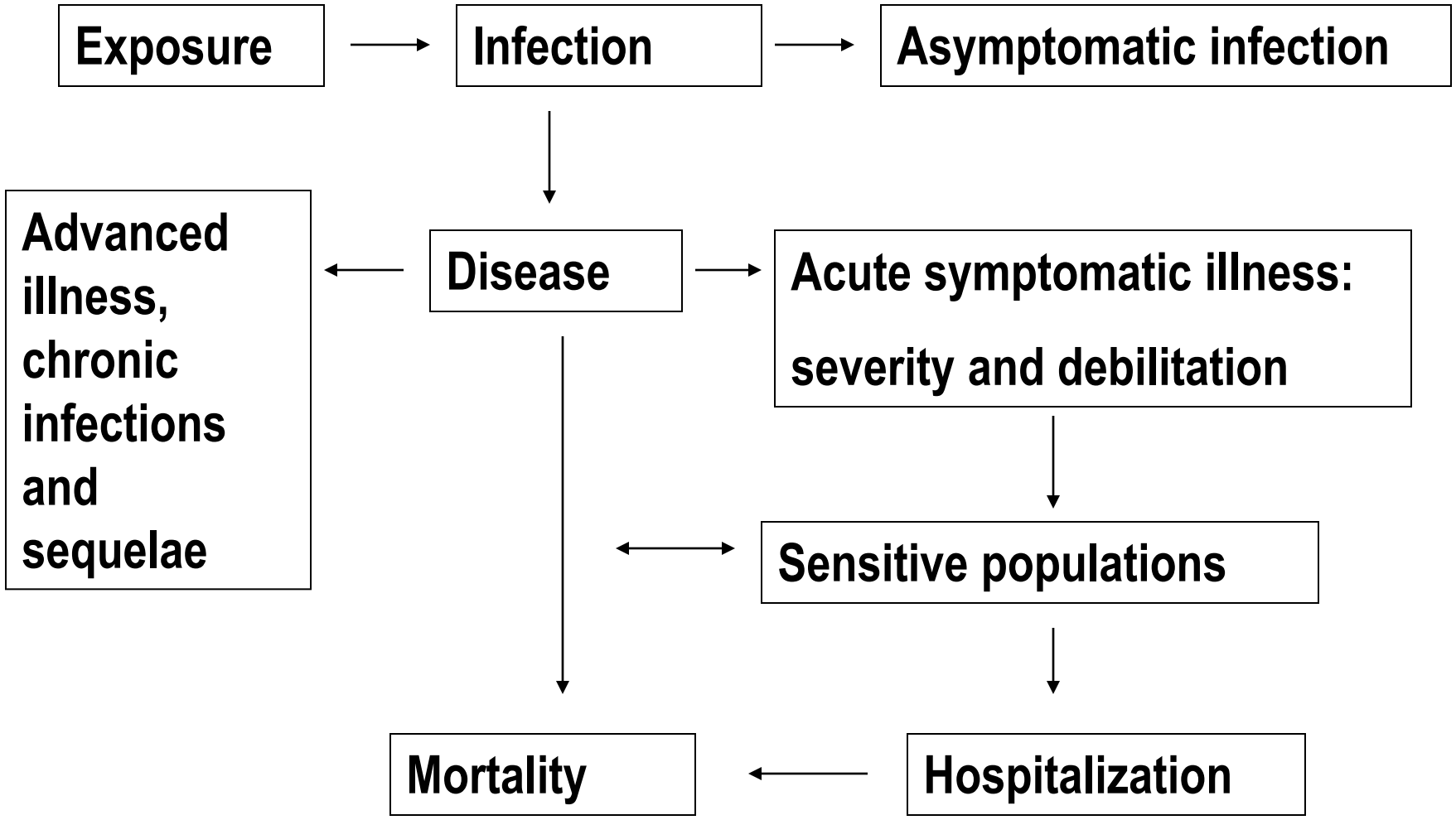
Host factors in pathogen transmission

- Age (old age, extreme youth – prematurity, infancy)
- Immune status (inborn and/or acquired defects, incl. immunosuppressive therapy, stress, etc.)
- Concurrent illness or infirmity
- Genetic background
- Pregnancy
- Nutritional status
- Demographics of the exposed population (density, etc.)
- Social and behavioral traits

Sensitive populations – increased infectious disease risks

- **Infants and young children**
- **Elderly**
- **Immunocompromized**
  - **Persons with AIDS**
  - **Cancer patients**
  - **Transplant patients**
- **Pregnant**
- **Malnourished**

Outcomes of infection process



INFECTIOUS DISEASES

- **SYMPTOMS -** subjective evidence of disease as sensed by the patient.
- **SIGNS -** objective evidence of disease as noted by an observer.
- **SYNDROMES -** a specific group of symptoms or signs which accompany a particular disease.

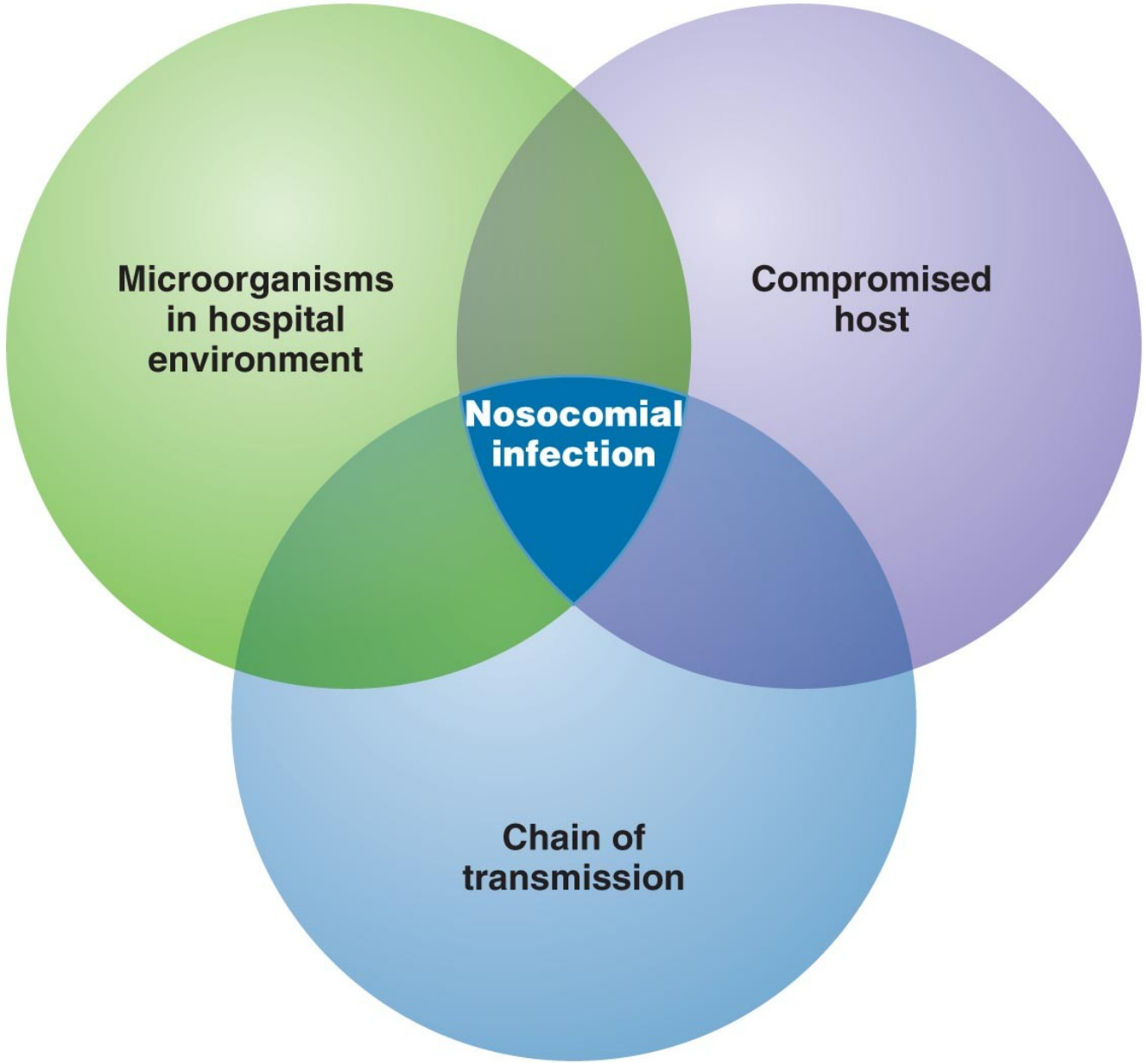
Common signs and symptoms

Signs	Symptoms
Fever	Chills
Septicemia	Fatigue, soreness
Skin eruptions	Itching
Chest sounds	Dyspnoea

Portals of entry

- Skin
- Gastrointestinal tract
- Respiratory
- Urogenital
- Via placenta
- Parenteral (injection, bite)

Nosocomial infections – health care-associated infections



Nosocomial infections

- ~ 10% of patients/clients acquire a clinically significant nosocomial infection
- 10-30% in developing countries

Nosocomial infections consequences

- Additional morbidity/mortality
- Prolonged hospitalisation
- Permanent damage possible
- Increased cost

Nosocomial infections

- Colonies of hospital bacterial strains develop on patient‘s skin, in respiratory and genitourinary tract within hours after admission
- **Risk factors**: patient related

  iatrogenic

  organisational

Iatrogenic risk factors

- Medical personnel hands as source
- Invasive procedures
- Antibiotics use + prophylaxis

Clinical implications

- Preventing of infection
- Control of transmission (airborne + droplet precaution, contact – hand hygiene, blood)
- Work restrictions for personnel with some infectious diseases

Emerging infectious diseases

- Diseases that are new, increasing in incidence, or showing a potential to increase in the near future (COVID-19, zika virus, Ebola)
- Newly recognised infectious causes of known diseases (Coronaviruses, Borrelia; hepatitis viruses – HEV; etc.)
- Opportunistic infections in immunocompromised patients (Mycobacterium-avium complex, Pneumocystis, HHV-8)

Emerging infectious diseases

- Geographic spread of known infections (West Nile virus, Plasmodium falciparum - malaria)
- Local spread – environmental changes (bats – rabies, COVID-19?; ticks – encephalitis, Lyme borreliosis; mosquitoes – dengue, zika)
- Crossing of interspecies barrier (coronaviruses, Ebola, BSE- bovine spongiform encephalopathy)
- Re-emerging infections, new strains event. resistant (TBC, Vibrio cholerae, influenza H5N1,H1N1)

Respiratory tract infections

- **Viral**

  Rhinoviruses, Influenza, Coronaviruses

- **Bacterial**

  Str. pneumoniae, Haemophilus infl., Chlamydia, TB,

- **Fungal**

  Histoplasmosis, Coccidioimycosis, Pneumocystis

Lower respiratory tract

- Pneumonia – lobar (pneumococcus, Klebsiella); bronchopneumonia (variable pyogenic bacteria)

  atypical (interstitial): viral – SARS-CoV-2, influenza, herpetic viruses,

  small bacteria (Mycoplasma, Legionella, Chlamydia)

  fungal – Aspergillus, Pneumocystis, Cryptococcus, Candida,

  granulomatous: TB, MAC, Histoplasma

SARS-CoV-2 and COVID-19

- Spread: droplets, aerosol, contaminated surfaces, body secretions incl. faeces
- Incubation period: 2-14 days, usually approx. 5 days
- Commonly as respiratory disease
  - dry cough, sneezing and shortness of breath, sore throat, loss of smell/taste,
  - systemic signs: fever, chills, fatigue
- Non-respiratory symptoms
  - diarrhea, nausea, vomiting, headache and muscle pain, etc.
- Complications in acute stage
  - pneumonia incl. secondary bacterial, acute respiratory distress syndrome
  - septic shock, coagulation dysfunction incl. thrombosis/embolia; heart, liver, kidney injury, multiple organ failure

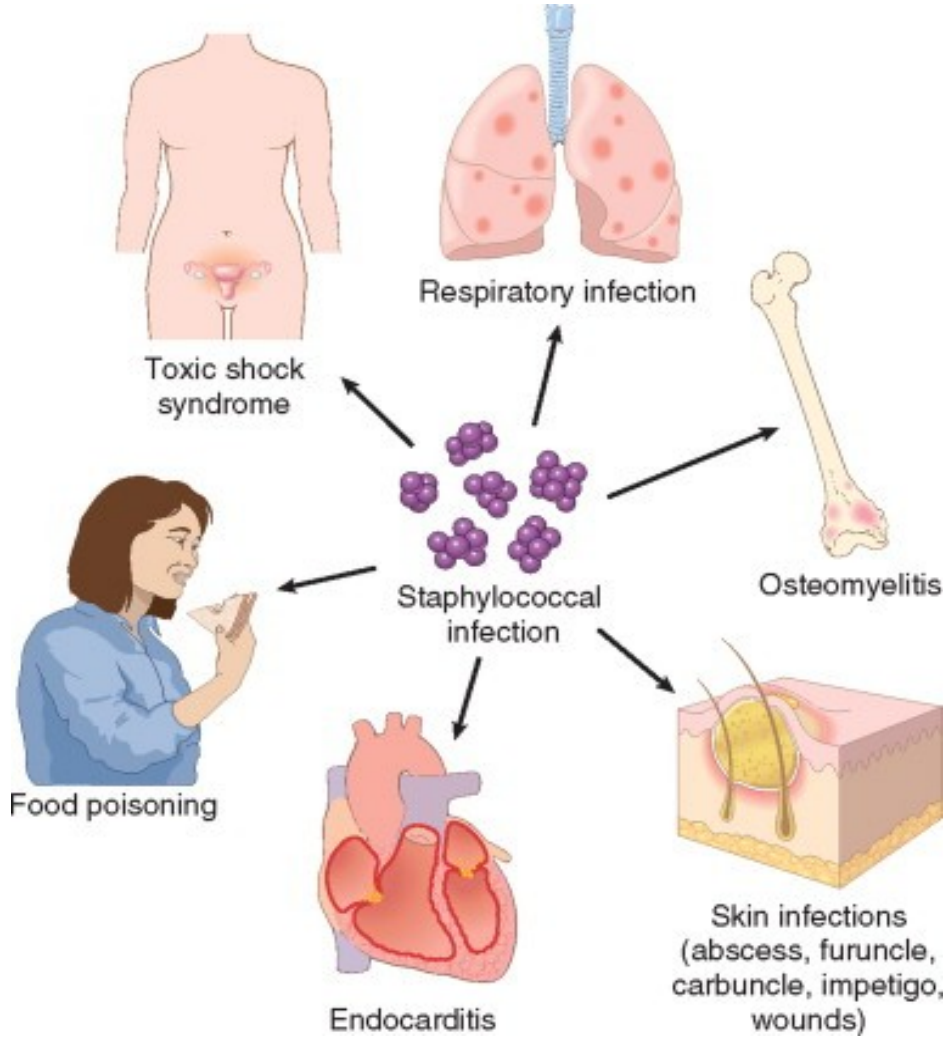
SARS-CoV-2 and COVID-19

- Later complications
  - „Long COVID“: fatigue, dyspnea, cough, anxiety, depression, inability to focus (ie, “brain fog”), gastrointestinal problems, sleep difficulties, joint pain, and chest pain lasting weeks to months after the acute illness.
  - most frequent symptoms after 6 months: fatigue, postexertional malaise, cognitive dysfunction. Nearly 50% were unable to return to work 6 months after infection.
  - lung and/or heart functional abnormalities
  - in children and teens possible COVID-associated multisystem inflammatory syndrome in children (MIS-C) with heart failure

Influenza

- Acute respiratory illness caused by influenza viruses.
- Typical symptoms-fever, chills, myalgia, headache, sore throat, cough.
- Serious cases in young children and elderly possible.

Staphylococci



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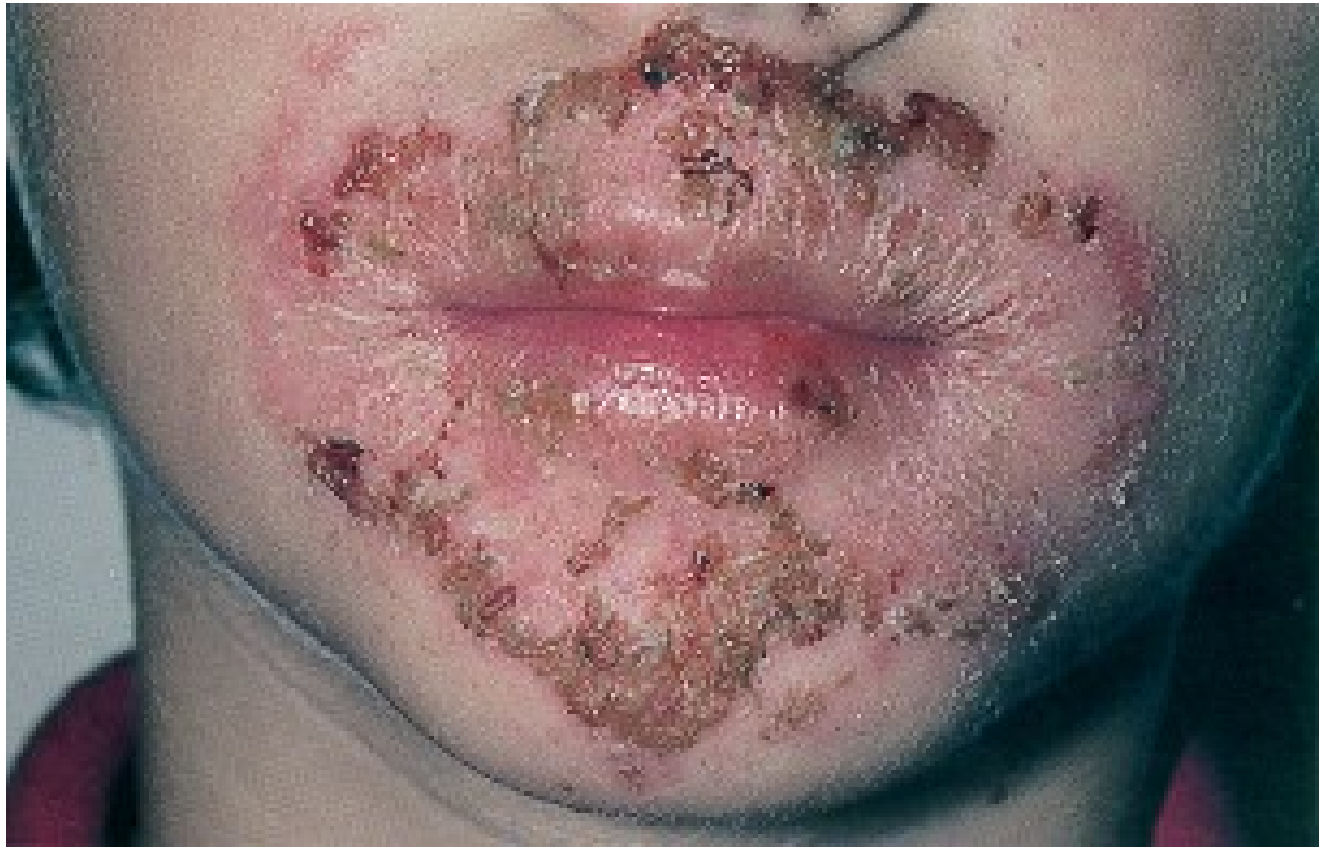
Staphylococci

- Destructive pyogenic inflammation
- Abscess, furuncle, impetigo
- **Carbuncle**: deeper suppurative infection spreading laterally beneath the deep subcutaneous fascia
- **Hidradenitis:** chronic suppurative infection of apocrine glands, most often in the axilla.

Impetigo



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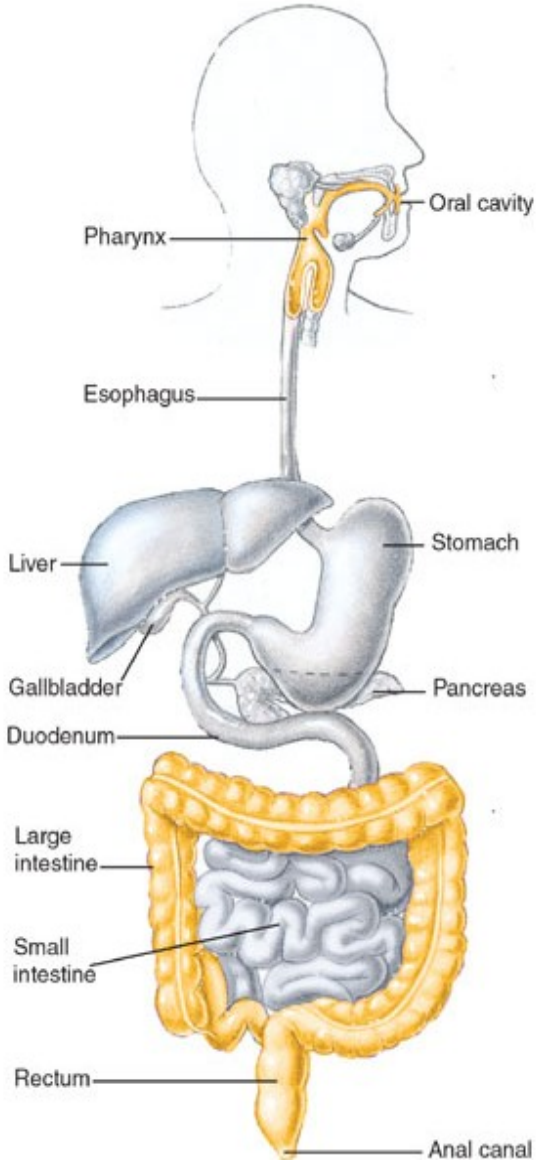
Streptococci

- Suppurative infections of the skin, oropharynx, lungs, heart valves.
- Post-infectious syndromes, incl. rheumatic fever, immune complex glomerulonephritis, erythema nodosum

GIT infections



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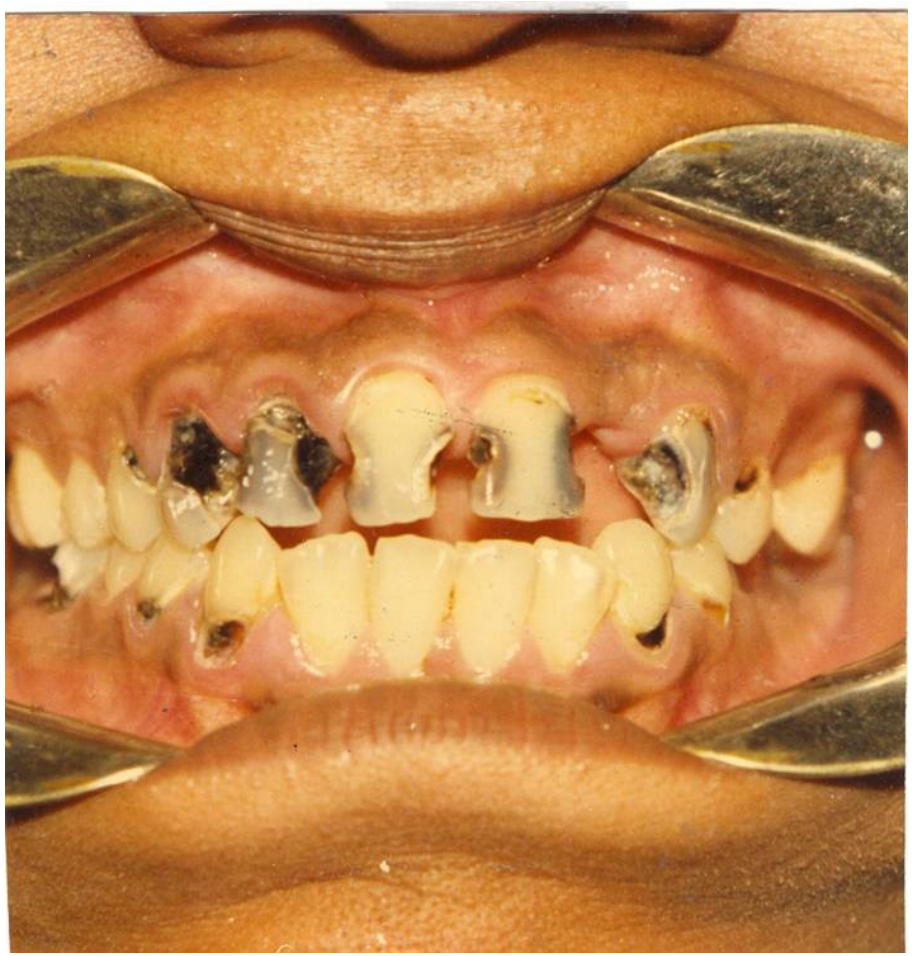
GIT infections

- mostly by contaminated food or water
- ↓ local host defences (↓ gastric acidity, ↓ enzymatic and mucus secretion, loss of local defensins and IgA, loss of normal flora, obstruction)
- general immunodeficiency (→ fungal, CMV, MAC infection)
- resistant microorganisms (hepatitis A virus, rotavirus, H. pylori, protozoan cysts,…)

Dental caries



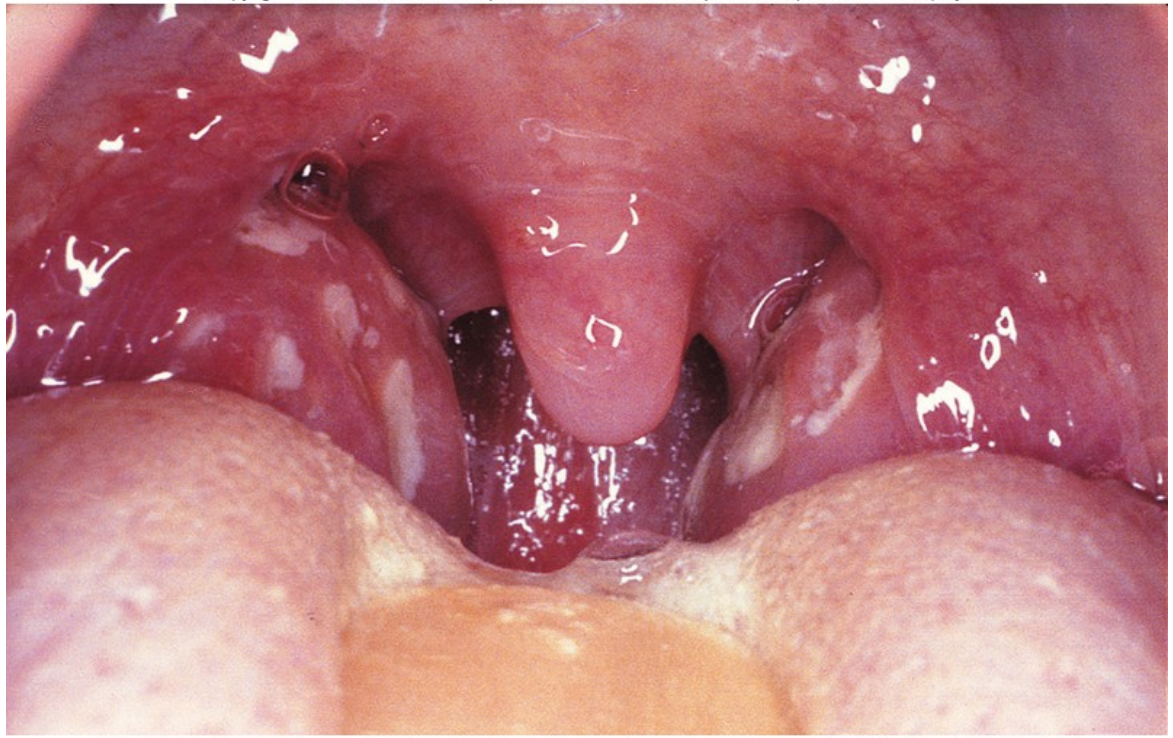
Dental caries

- Multifactorial dynamic process
- Involves the interaction of inborn or acquired host factors (tooth surface, saliva, acquired pellicle), diet (sugars), dental plaque (biofilm) – oral infection.
- Caries does not occur in the absence of either plaque or dietary fermentable carbohydrates.

Tonsillitis and pharyngitis

- bacterial (Streptococcus – 25%, Staphylococcus, dipthteria…)
- viral (EBV, influenza, adenoviruses, …)
- Clinical – sore throat, dysphagia, red + swollen tonsils + focal/confluent yellowish exudate, cervical lymhadenopathy, fever, malaise, …
- In viral + rhinitis, laryngitis

Tonsillitis



Intestinal infections

- Enterocolitis – usual manifestation as diarrhea, may be pseudomembranous, ulcerative, non-purulent
- worldwide more than 3 millions deaths annually, mainly children ≤ 5 yrs
- chronic or recurrent enterocolitis – parasites, protozoa

Infectious hepatitis

- Viral hepatitis – part of systemic disease (EBV, CMV, yellow fever, rarely rubella, herpesvirus, etc.
- Viral hepatitis – liver specific (hepatitis viruses HAV, HBV, HCV, HDV, HEV, …)
- Bacterial – abscess, chronic inflammation
- Parasitic – abscesses, cysts - Entamoeba, Echinococcus; malaria, schistosomiasis, cryptosporidiosis, etc.
- Fungal

Urogenital tract infections

- Ascending infection via urethra most usual (G- fecal bacteria – E. coli, Proteus,…)
- Anatomy – urethra 5 cm lenght in women, 20 cm in men
- Predisposing factors – obstruction, reflux, loss of protective vaginal flora, mucosal microtraumata

Sexually Transmitted Infections

- Sexually Transmitted Disease - STD
- Infection transmitted through vaginal, anal or oral sex
- Every sexually active individual is at risk
- Women acquire infections from men more than men from women
- 2/3 of STD occur in people under 25 yrs of age
- Infection by multiple agents common (↑ risk)
- Fetus or infants – vertical transplacental or perinatal transmission of STD → abortus, inborn defects, neonatal infection. Diagnosis + treatment!!

STI/STD

- **Viruses**: HSV, HPV, HIV, hepatitis B,C
- **Chlamydiae**: Ch. trachomatis
- **Mycoplasmas**: U. urealyticum
- **Bacteria**: Neisseria gonorrhoeae (clap), Treponema pallidum (syphilis), Haemophilus ducreyi (chancroid), Klebsiella granulomatis (granuloma inguinale)
- **Protozoa**: Trichomonas vaginalis (urethritis, balanitis, vaginitis)

Genital Warts

- Condyloma acuminatum - HPV
- Most HPV infections asymptomatic or unrecognized
- Mostly found in young, sexually active; associated with early onset of sexual activity, multiple sexual partners
- Transmitted by all types of sexual contact

Chlamydia: Manifestations

- In women often asymptomatic until uterus and tubes infected; may present with dysuria, urinary frequency, vaginal discharge
- 1/3 of men may be asymptomatic; dysuria, urethral discharge, testicular pain
- Patient infectious even if asymptomatic

Chlamydia: Complications

- May result in PID (pelvic inflammatory disease)
- Major cause of infertility, ectopic pregnancy in women; may cause stillbirth or spontaneous abortion (miscarriage)
- In men, may result in epididymitis, prostatitis, sterility, Reiter's syndrome
- In neonates, may cause blindness, pneumonia

Gonorrhea

- ‘clap’; one of the most common STDs (second only to Chlamydia)
- Caused by *Neisseria gonorrhoeae*; incubation period is 2-8 days
- Transmitted by sexual contact, during passage through the birth canal
- Usually targets the cervix, male urethra

Gonorrhea

- Female: mostly asymptomatic until advanced disease; dysuria, urinary frequency or abnormal vaginal discharge
- Male: dysuria, serous, milky or purulent urethral discharge; regional lymphadenopathy
- Complications: prostatitis, epididymitis, sterility;

  PID, endometritis, salpingitis, peritonitis;

  in neonates gonorrhea can infect the eyes, nose or anorectal region

Syphilis

- Spirochete *Treponema pallidum*
- Transmitted from open lesions during sexual contact
- Organism can survive days in fluids
- May also be transmitted by infected blood, body fluids, including saliva
- Average incubation is 20-30 days
- Spreads through blood, lymphatic system
- Congenital syphilis - transplacental

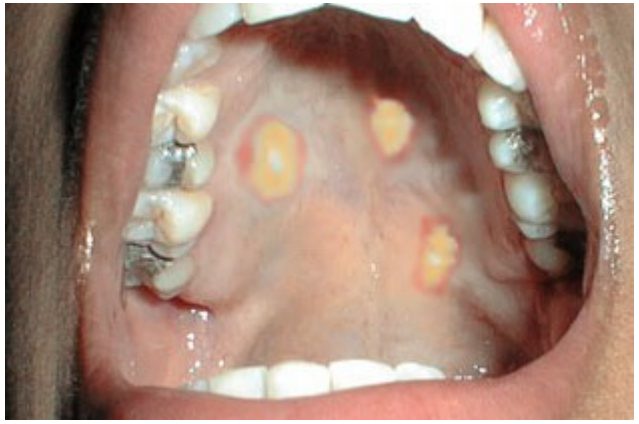
Syphilis: Primary stage

- **Chancre:** painless ulcer in the site of innoculation; regional lymphadenopathy
- chancre appears 3-4 weeks after infectious contact, disappears within 4-6 weeks
- Chancre may go unnoticed in women
- Highly infectious during primary stage even if no symptoms are present

Syphilis: Secondary stage

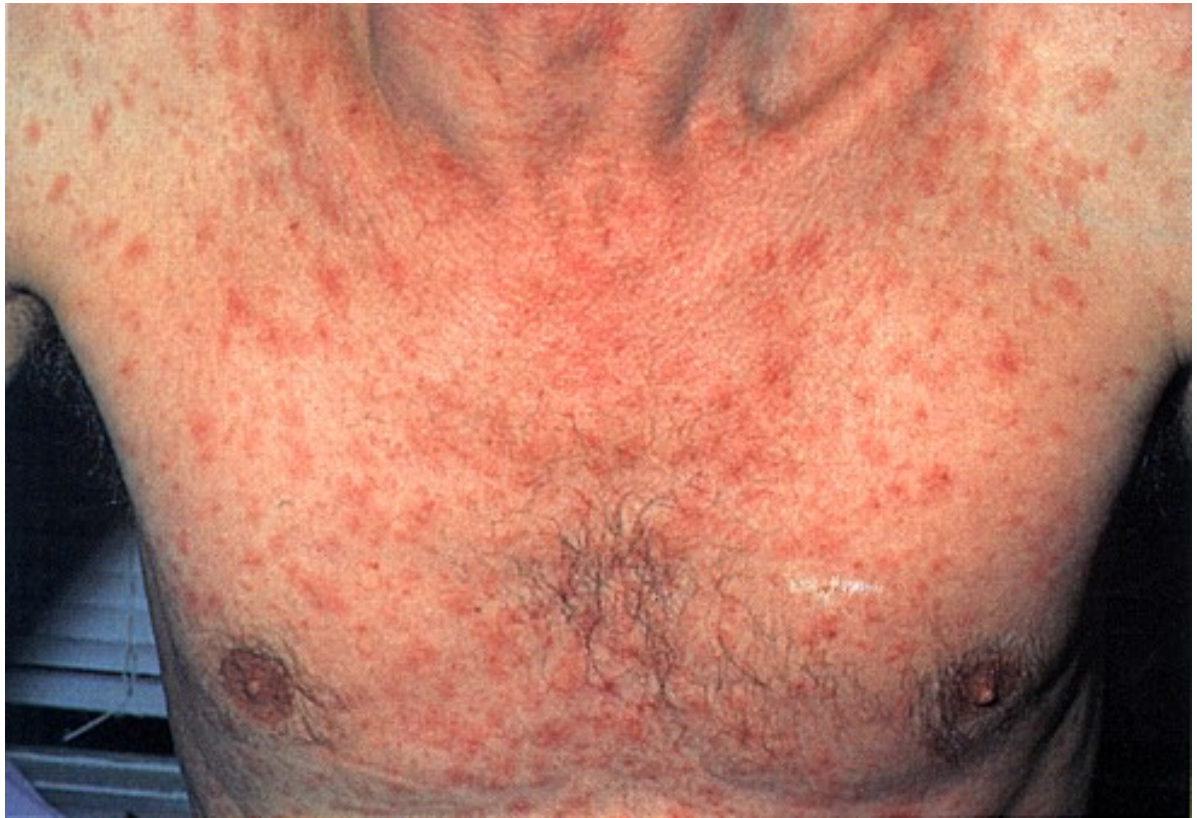
- Symptoms of secondary syphilis appear any time from 2 weeks to 6 months after initial chancre disappears, in 75% of untreated people
- **Primary generalisation**, flu-like symptoms, sore throat; generalized lymphadenopathy
- **Skin rash** (especially on palms of hands and soles of feet) maculopapular, pustular;
- **condylomata lata** - mucus patches + erosions in oral cavity; flat, broad-based wart-like papules on labia, anus or corner of mouth, **highly infectious**; secondary alopecia
- Disappear within 2-6 weeks

Syphilis - secondary



Condylomata lata

Syphilitic rash



Skin infections

- The dense, keratinized outer layer of skin - natural barrier to infection. Low pH of the skin (5.5) and the presence of fatty acids inhibit growth of microorganisms other than residents of the normal flora.
- Potential opportunists, such as *S. epidermidis* and *Candida albicans*.
- Few microorganisms able to traverse the unbroken skin
- *Most microorganisms penetrate through breaks in the skin*

Skin infections

- Viral exanthematic inflammations – HSV, varicella-zoster, etc.
- Viral pseudotumorous lesions – warts (HPV), molluscum contagiosum (poxvirus)
- Bacterial infections – superficial (impetigo – Stph. aureus, blisters + neutrophils), deep (panniculitis, phlegmona)
- Fungal inf. – superficial (Tinea – dermatophytes)
- Parasitic inf. – scabies etc.

Fungal infections

- Superficial infections by dermatophytes : skin, hair, nails.
- The term “tinea” + the area of the body affected (e.g., tinea pedis, “athlete's foot”; tinea capitis, “ringworm of the scalp”).
- Certain fungal species invade the subcutaneous tissue, causing abscesses or granulomas (e.g., sporotrichosis and tropical mycoses).

Common childhood viral infections

- Measles (rubeola, red measles)
- Rubella (German measles)
- *Erythema infectiosum* (Fifth disease)
- Mumps
- Varicella-Zoster (Chickenpox)
- Coxsackievirus and Echovirus associated infections (hand-foot-and-mouth disease)

CNS infections

- Meningitis

  acute pyogenic (bacterial)

  aseptic (acute viral)

  chronic (+ encephalitis; tbc, borrelia,

  T. pallidum, cryptococcus)

- Brain abscess (bacterial, Naegleria)
- Viral encephalitis (+ meningitis) acute (arboviruses, herpetic, CMV, poliomyelitis, rabies, HIV), persistent (progressive multifocal leukoencephalopathy – JC virus, subacute sclerosing panencephalitis – measles)
- Fungal (cryptococcus etc.), parasitic (Toxoplasma)