Diseases of the immunity

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Diseases of the immunity

1) pathology of transplantations

2) autoimmune diseases

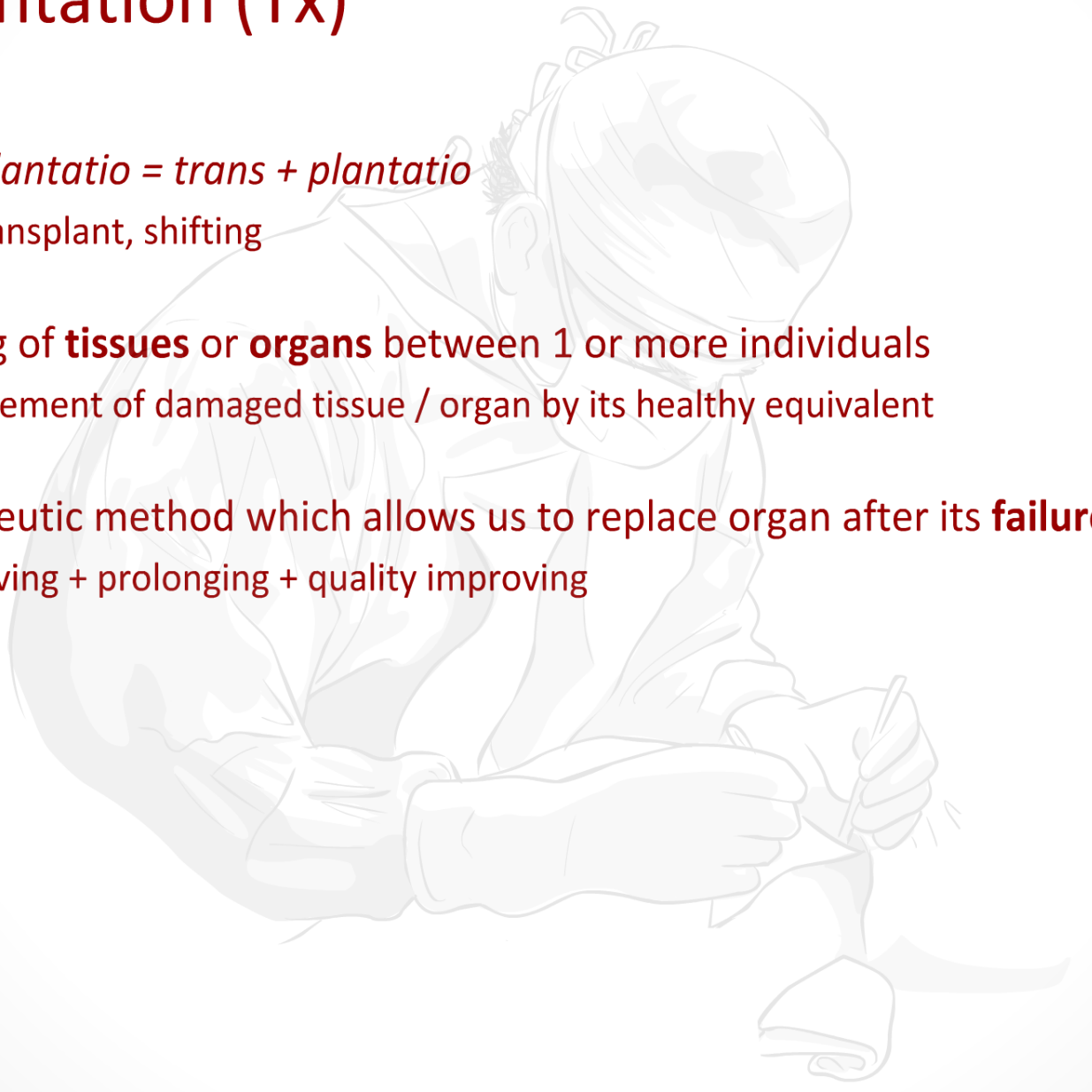
3) immunodeficiency

Transplantation (Tx)

- *transplantatio = trans + plantatio*
  - lat. transplant, shifting

- shifting of **tissues** or **organs** between 1 or more individuals
  - replacement of damaged tissue / organ by its healthy equivalent

- therapeutic method which allows us to replace organ after its **failure**
  - life saving + prolonging + quality improving



Transplantations - subtypes

- **autologous** (autotransplantation)
  - transplant of own tissues or organs

- **allogenous** (homogenous, allotransplantation)
  - tissues or organs of the same species (human)

- **xenogenous** (heterogennous heterotransplantation)
  - tissues or organs of another species (pigs, cattle)

- **isogenous** (syngenous, isotransplantation)
  - tissues or organs between identical twins

- **implantation**
  - using inorganic material

Transplantation - basic terms

- **graft** (implant)
  - transplantated tissue or organ (whole one / a part of it)

- **donor**
  - person who donates the graft
  - dead (cadaxerous) / alive

- **recipient**
  - patient who recieves the graft

- autologous transplant: donor = recipient

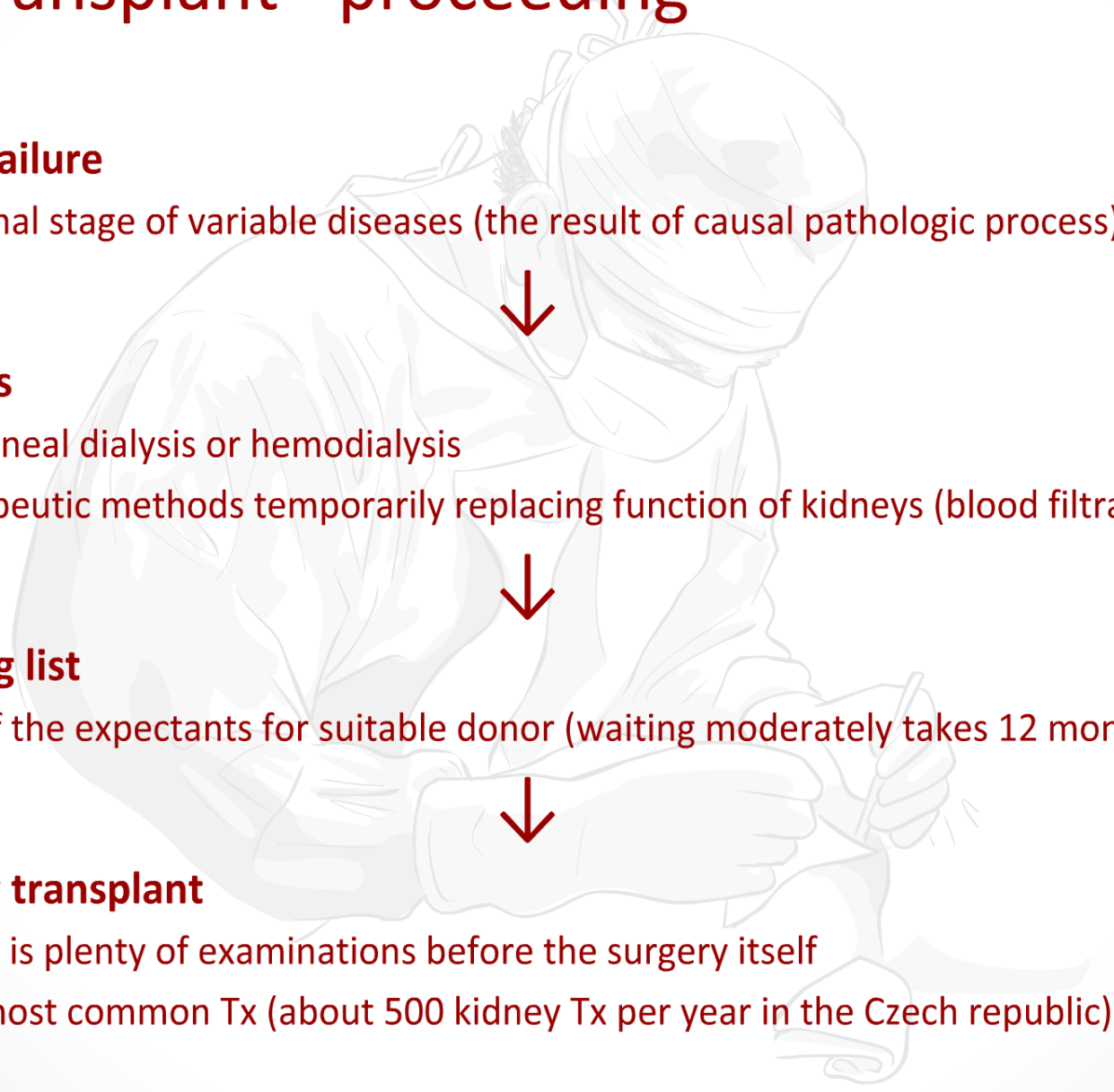
Transplantation - graft

- **organs**
  - kidneys
  - heart
  - lungs
  - liver
  - skin (and hair)
  - cornea
  - pancreas (the cells of Langerhans islets)
  - others (uterus, thymus, parathyroid, experimentally guts, stomach, testicles)

- **tissues**
  - bone marrow
  - blood (transfusion)
  - soft tissues (such as valves, tendons, nerves, vessels = bypass)
  - cartilage and bones

+ + experimental cases (extremities, face...), Tx of the stool...

Kidney transplant - proceeding



- **renal failure**
  - terminal stage of variable diseases (the result of causal pathologic process)

↓

- **dialysis**
  - peritoneal dialysis or hemodialysis
  - therapeutic methods temporarily replacing function of kidneys (blood filtration)

↓

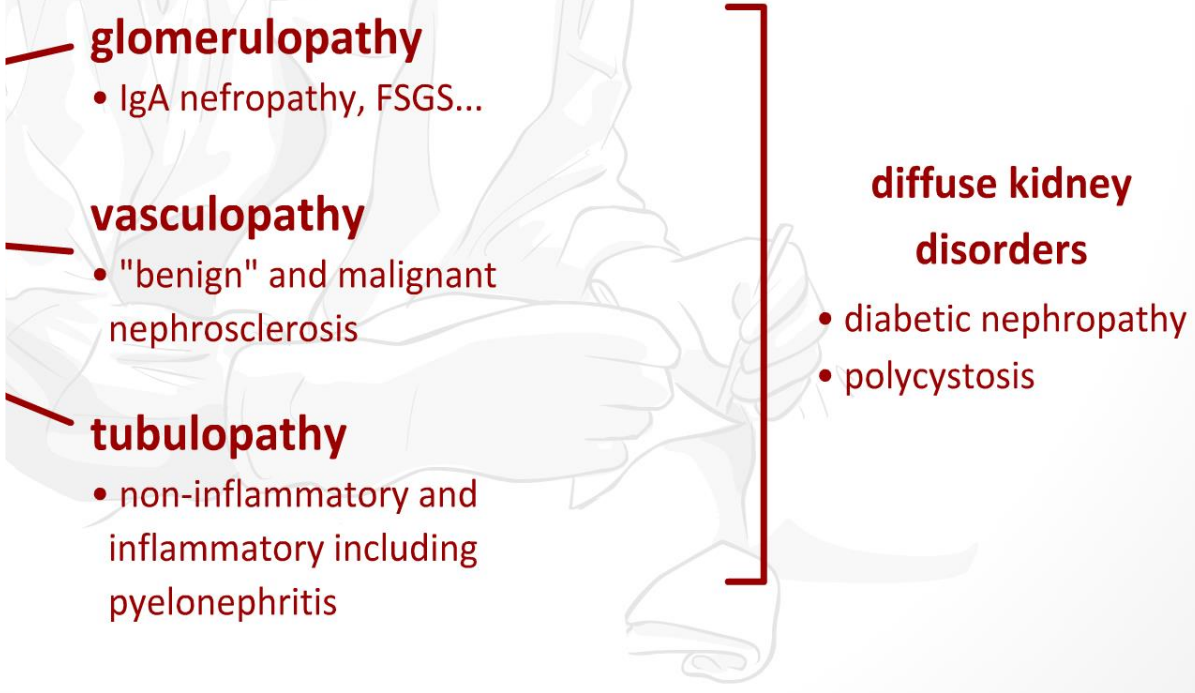
- **waiting list**
  - list of the expectants for suitable donor (waiting moderately takes 12 months)

↓

- **kidney transplant**
  - there is plenty of examinations before the surgery itself
  - the most common Tx (about 500 kidney Tx per year in the Czech republic)

Kidney transplant - indications

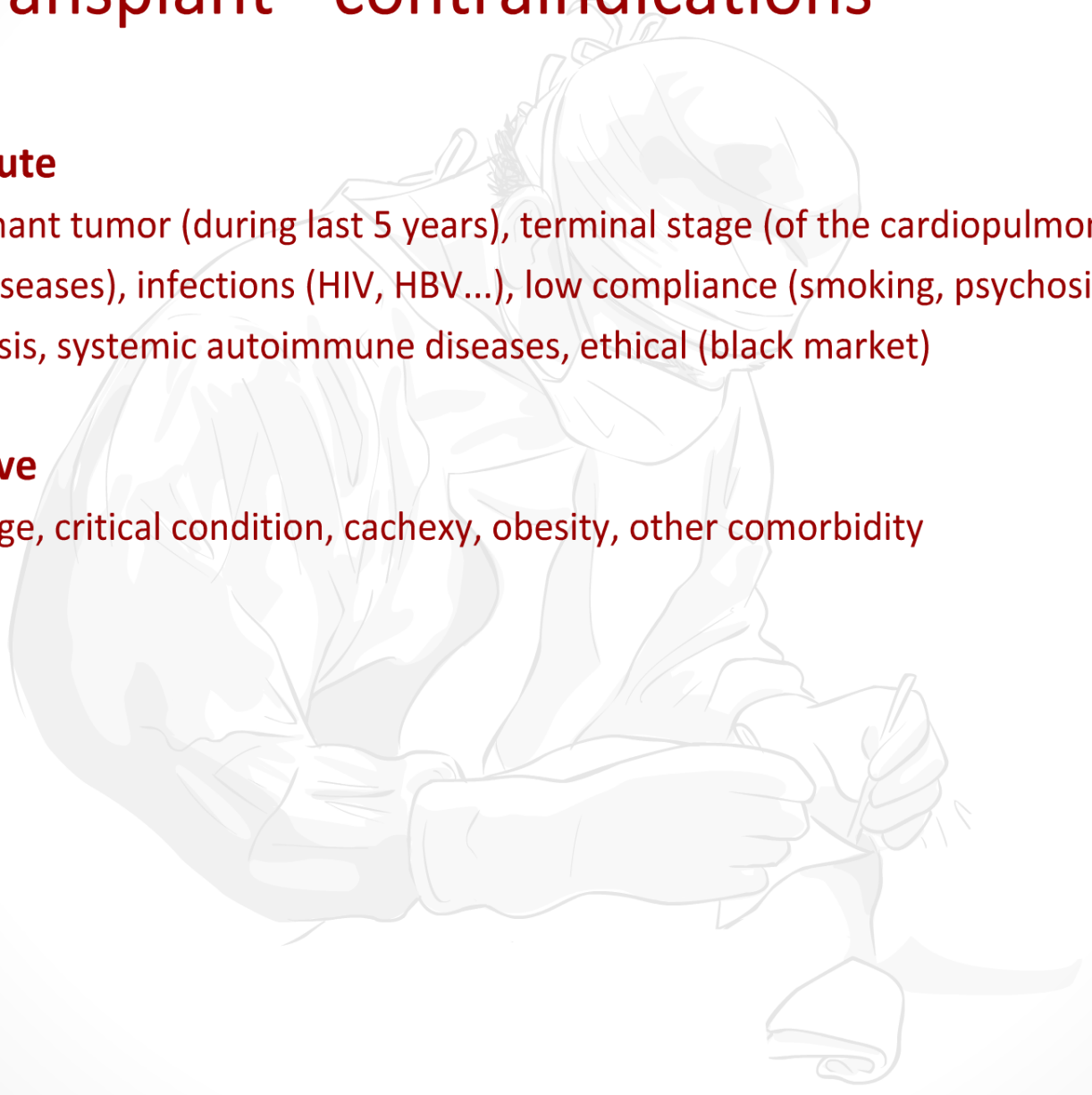
- **"end-stage kidney"** (renal failure)
  - renal **failure** develops after a period of renal insuficiency (the marker is GF)
- the **reasons** of the renal failure (acute and chronic) are various:



Kidney transplant - contraindications

- **contraindication** = a condition that serves as a reason to withhold a certain procedure
  - patient's condition doesn't allow Tx as a therapy of choice

Kidney transplant - contraindications



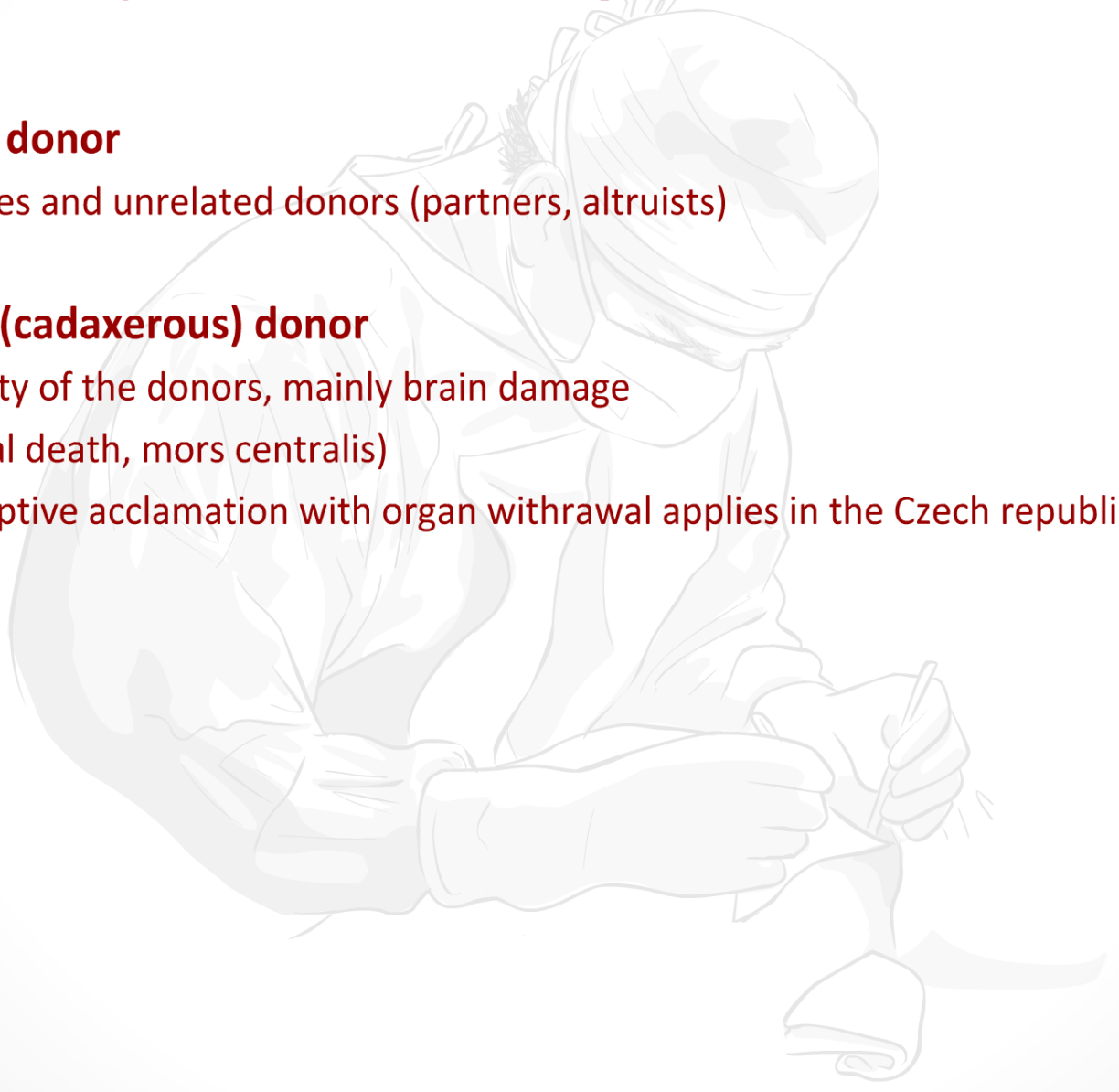
1) absolute

- malignant tumor (during last 5 years), terminal stage (of the cardiopulmonal and liver diseases), infections (HIV, HBV...), low compliance (smoking, psychosis...), prionosis, systemic autoimmune diseases, ethical (black market)

2) relative

- high age, critical condition, cachexy, obesity, other comorbidity

Kidney transplant - choosing of a donor



1) living donor

- relatives and unrelated donors (partners, altruists)

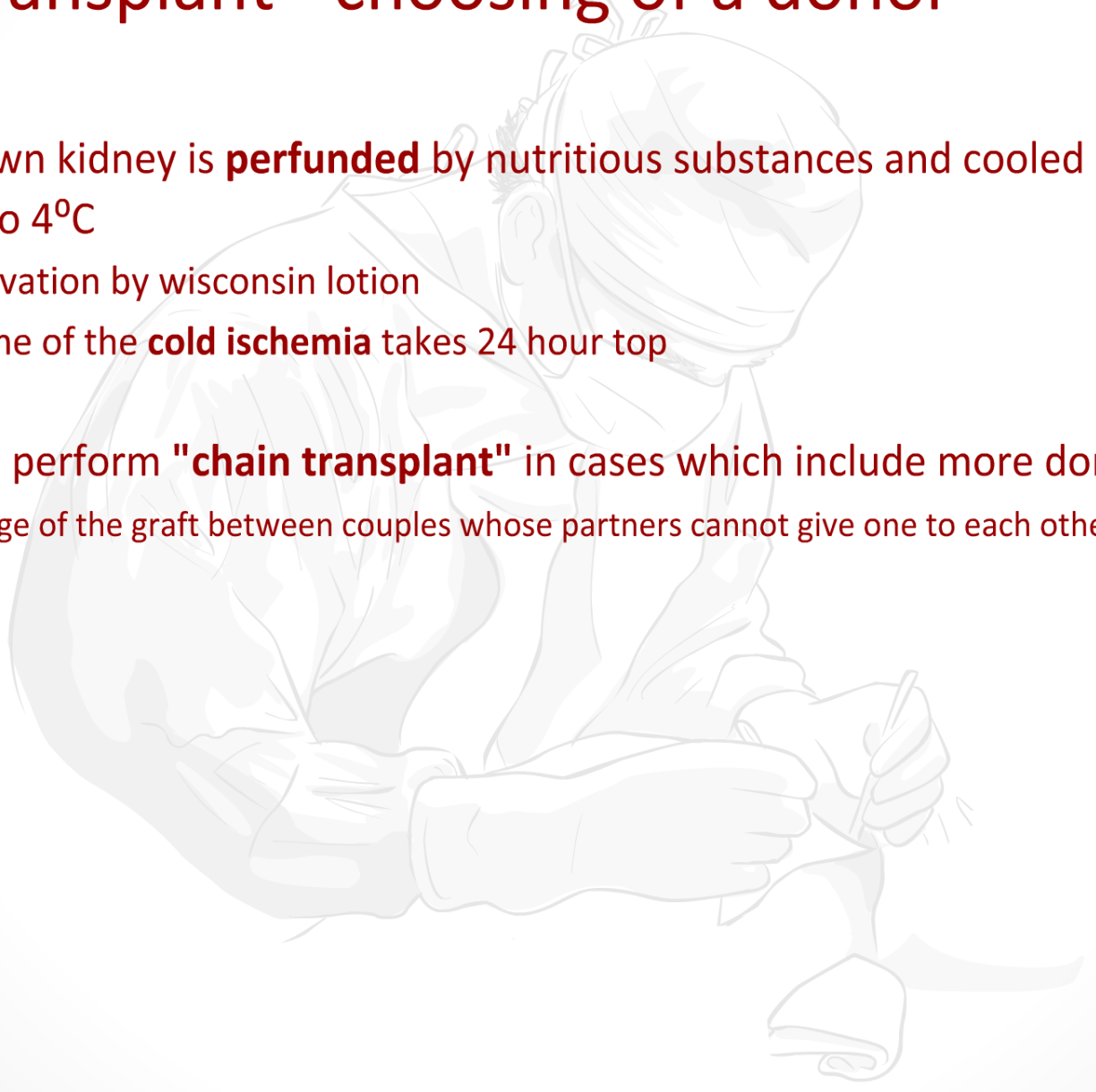
2) dead (cadaxerous) donor

- majority of the donors, mainly brain damage
  (central death, mors centralis)
- assumptive acclamation with organ withrawal applies in the Czech republic

Kidney transplant - choosing of a donor

- withrawn kidney is **perfunded** by nutritious substances and cooled down to $4^{o}C$
  - preservation by wisconsin lotion
  - the time of the **cold ischemia** takes 24 hour top

- we can perform **"chain transplant"** in cases which include more donors
  - exchange of the graft between couples whose partners cannot give one to each other



Kidney transplant - choosing of a donor

- **imunological compatibility** is required between recipient and donor
  - genetical equality cannot be found in allogenous and xenogenous Tx
  - various polymorphic Ag can play part in isogenous Tx even in cases with identical MHC

- **3 immunological criteria** must be granted:

Kidney transplant - choosing of a donor

1) compatibility in AB0 system

- donor and recipient must have identical **blood-group**
- nowadays there is a possibility to perform Tx even with different AB0 using plasmapheresis

2) at least partial compatibility in HLA system

- HLA (human leukocyte antigen) = MHC (major histocompatibility complex)
- **MHC class I** (HLA A-C) exposes intracellular epitopes (shows belonging to body)
- **MHC class II** (HLA D) APC exposes epitopes in lysosomes (foreign Ag)
- proved by **HLA typization**

3) negative cross-match test

- proves there are no natural **IgM** against donor MHC in the blood of recipient (these Ig can be created by **previous immunisation,** e.g. after transfusion)
- if the test is positive there is a risk of hyperacute rejection
- analogy of different groups of AB0 system

Kidney transplant - choosing of a donor

Zero-hour graft biopsy

- bioptic examination of the **donor kidney**
  - DIC must be excluded and other renal diseases must be identified

Kidney transplant - surgery

- several **examination** must be performed before the operation itself
  - internal, imaging, psychological...

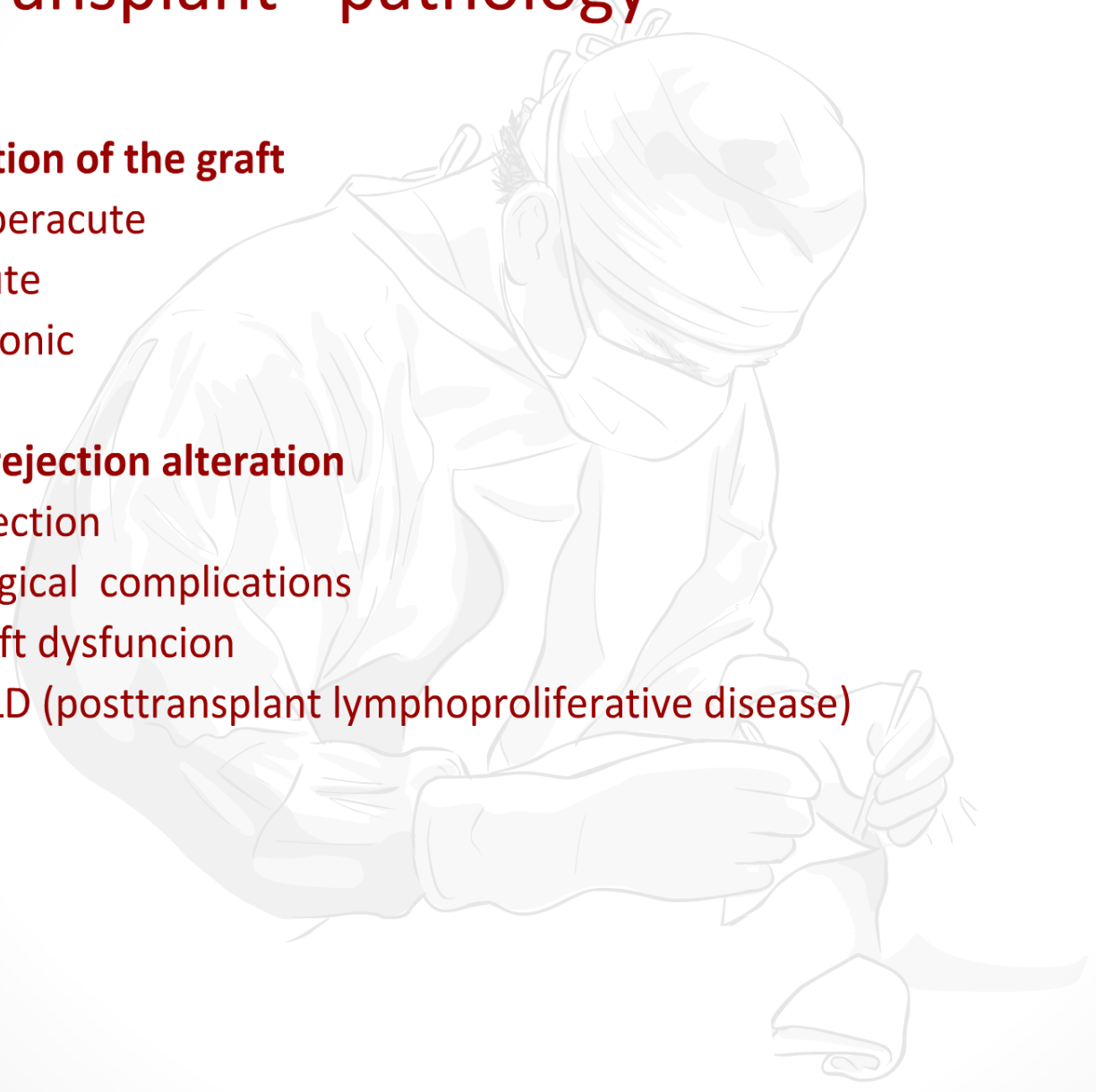
- graft is placed **heterotopically** (ectopically)
  - in contrast to **ortotopical** Tx (e.g. lungs, heart)
  - kindey is placed into right iliac region, vesels are connected to v. et a. iliaca and ureter must be connected to urinary bladder

- recipient's own kidneys are left in place
  - they shrink after some time (atrophy)
  - the only exception is renal polycystosis

Kidney transplant - postoperative period

- we need to repress **pathlogical changes** of the graft
  - to minimalize risks of **infection** and its antipole = **rejection**

Kidney transplant - pathology



1) rejection of the graft

1) hyperacute
2) acute
3) chronic

2) non-rejection alteration

1) infection
2) surgical complications
3) graft dysfuncion
4) PTLD (posttransplant lymphoproliferative disease)

Kidney transplant - pathology

1) rejection of the graft

- an issue mainly in alogenous tranplants
  - morphology of rejection corresponds to lymphocytic inflammation

- principle of the rejection is an **aloimmune reaction**
  - every individual has own genetical polymorphism ("there are not any 2 identical organisms in the world")
  - immune system of recipient identifies **donor Ag** and interprets them as foreign
  - in consequnce **immunity of the recipient** attacks the graft (recipient didn't develop any tolerance against graft tissues during thymic maturation)

- **MHC** represents the most important Ag of the rejection
  - in cases of the identical MHC of recipient and donor, the **non-MHC Ag** (minor histocompatibility complex) may play part in developing the rejection

Kidney transplant - pathology

1) rejection of the graft

- there are several **subtypes of the rejection**
  - these differ according to etiology, morphology and clinical manifestation

1) hyperacute

- humoral (antibody mediated)

2) acute

1) humoral (antibody mediated)

2) cellular (cellular mediated)

3) chronic

- immune as well as non-immune mechanisms take part in its developement

- there tend to be **mixation** of the cellular and humoral component

Kidney transplant - pathology

1) rejection of the graft

1) hyperacute (humoral) rejection

Etiology

- **humoral** (antibody mediated = Alo-Ig which activate complement)
- **preformed Allo-Ig** already present in blood, harming graft immediately
  - natural IgM or Ig created after transfusion, gravidity...
  - analogy of the incompetent blood-groups
  - reason to perform Alo-Ig **cross-match** test before Tx intself (positivity = CI Tx)

- there is also so called **accerlerated rejection** which is antibody mediated too, but the clinical course is slower
  - 3-5 days
  - Allo-Ig in these activates phagocytes and NK-cells instead of the complement

Kidney transplant - pathology

1) rejection of the graft

1) hyperacute (humoral) rejection

Morphology

- Allo-Ig activate **C4d** complement component resulting in **endothelial** damage with formation of **thrombi** within arteries (the 1st one in contact with C4d) → graft **ischemia**

Kidney transplant - pathology

1) rejection of the graft

1) hyperacute (humoral) rejection

Clinical manifestation

- results in an ischemical necrosis in matter of **minutes** ("out of blue")
  - developement of the **accelerated rejection** takes days
- increase of the **DSA** (donor-specific antibodies) in blood
- this type was **eradicated** thanks to the cross-match tests

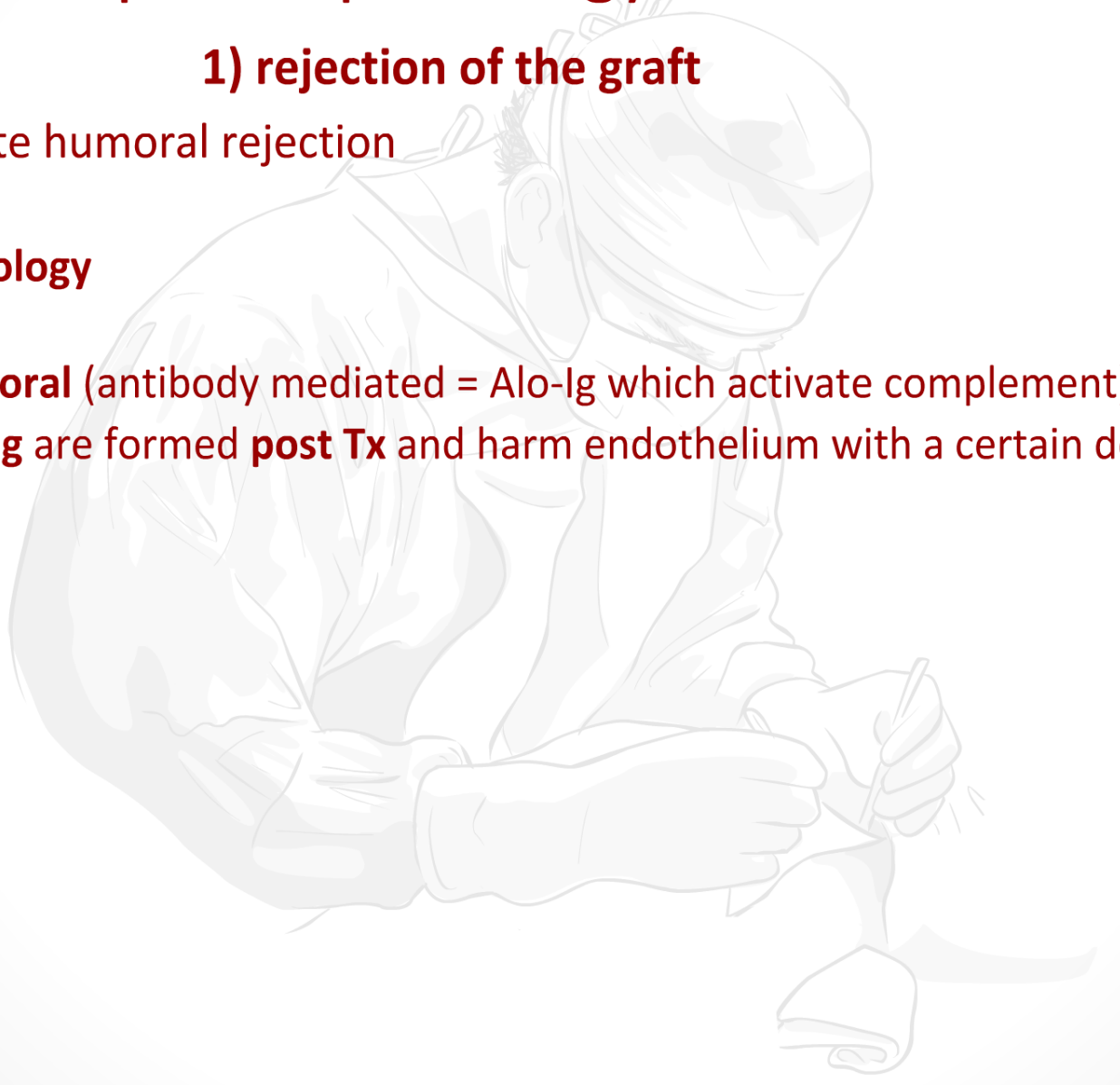
Kidney transplant - pathology

1) rejection of the graft

2a) acute humoral rejection

Etiology

- **humoral** (antibody mediated = Alo-Ig which activate complement)
- **Alo-Ig** are formed **post Tx** and harm endothelium with a certain delay



Kidney transplant - pathology

1) rejection of the graft

2a) acute humoral rejection

Morphology

- Allo-Ig activate **C4d** part of the complement and destroy **endothelium** giving rise to the **thrombi** (this time in peritubular capilaries → ATN can be developed)

Kidney transplant - pathology

1) rejection of the graft

2a) acute humoral rejection

Morphology

- **macroscopy** finding is subtle (possible to see ATN and thrombi)
- **microscopicaly** there is a various necrosis in the graft (**grading**)
  + confirmation of **C4d** part of the complement in capilaries (IHC or IF)

Grading

- **Grade I** ("ATN-like" = ATN with Cd4+ deposition)
- **Grade II** (Cd4+ in capilaries = capilaritis, glomerulitis or thrombi)
- **Grade III** (Cd4+ arteritis with fibrinoid necrosis)

- **diagnosis** requires DSA + micro changes + C4d in min. 50 % capillaries

Kidney transplant - pathology

1) rejection of the graft

2a) acute humoral rejection

Clinical manifestation

- clinical course takes **days or weeks**
  - may arise even years after transplantation and appear reapeatedly
- at first decrease of the **renal parameters** can be noticed (creatinin)
  - progression leads to the failure of the graft

Kidney transplant - pathology

1) rejection of the graft

2b) acute cellular rejection

Etiology

- **cellular** = mediated by specific cellular immunity

- **Tc-lymphocytes** (supported by **Th1-cells**) damage graft tissues
  - attacking interstitium and tubules of the kidney (**tubulointerstitial rejection**)

Kidney transplant - pathology

1) rejection of the graft

2b) acute cellular rejection

Morphology

- **macroscopy** finding is subtle (max. hyperemia + sparse necrosis)

- **microscopically** there are marks of rejection infiltrate within the sample
  - lymphocytes (CD8+, CD4+, + macrophages, plazmocytes, eosinophils

1) early infiltrate
- the cells tend to be around vessels in the interstitium

2) late infiltrate
- endothelitis appears (capilaritis = glomerulitis, arteritis and phlebitis)
- tubulitis occurs within parenchyma
- vascular damage can be noticed during acute humoral rejection too

Kidney transplant - pathology

1) rejection of the graft

2b) acute cellular rejection

Clinical manifestation

- same as acute humoral rejection (they often cooperate)
  - acute cellular rejection is the **most common** finding
- sometimes it's impossible to distinguish infection and allergy based TIN from the rejection
  - in such cases we need to perfom IHC, serology...

Kidney transplant - pathology

1) rejection of the graft

3) chronic rejection

Etiology

- participation of the **immune** and **non-immune** mechanisms

1) immune

- influence of repeated acute rejections + production of fibrogenic factors

2) non-immune

- alteration of the graft (denervation, lymphatic dysfunction, pre Tx ischemia, immunosuppression)

- **fibrosis / sclerosis** develops in the interstitium and the graft shrinks (**atrophy**)
  - interstitium as well as parenchyma are damaged
  - fibrosis develops also in the arteries (tunica intima) and causes ischemia

Kidney transplant - pathology

1) rejection of the graft

3) chronic rejection

Morphology

- **macroscopy** finding is renal atrophy

- **microscopically** there is a finding of the fibrosis in the interstitium and atrophy of the parenchyma (tubules and glomeruli)
  - sometimes **fibrotic endarteritis** can be seen (thickening of the tunica intima)

Kidney transplant - pathology

1) rejection of the graft

3) chronic rejection

Clinical manifestation

- developement takes **months or even years**
- gradual renal insufficiency leads to **chronic renal failure**
  - retransplantation can be performed

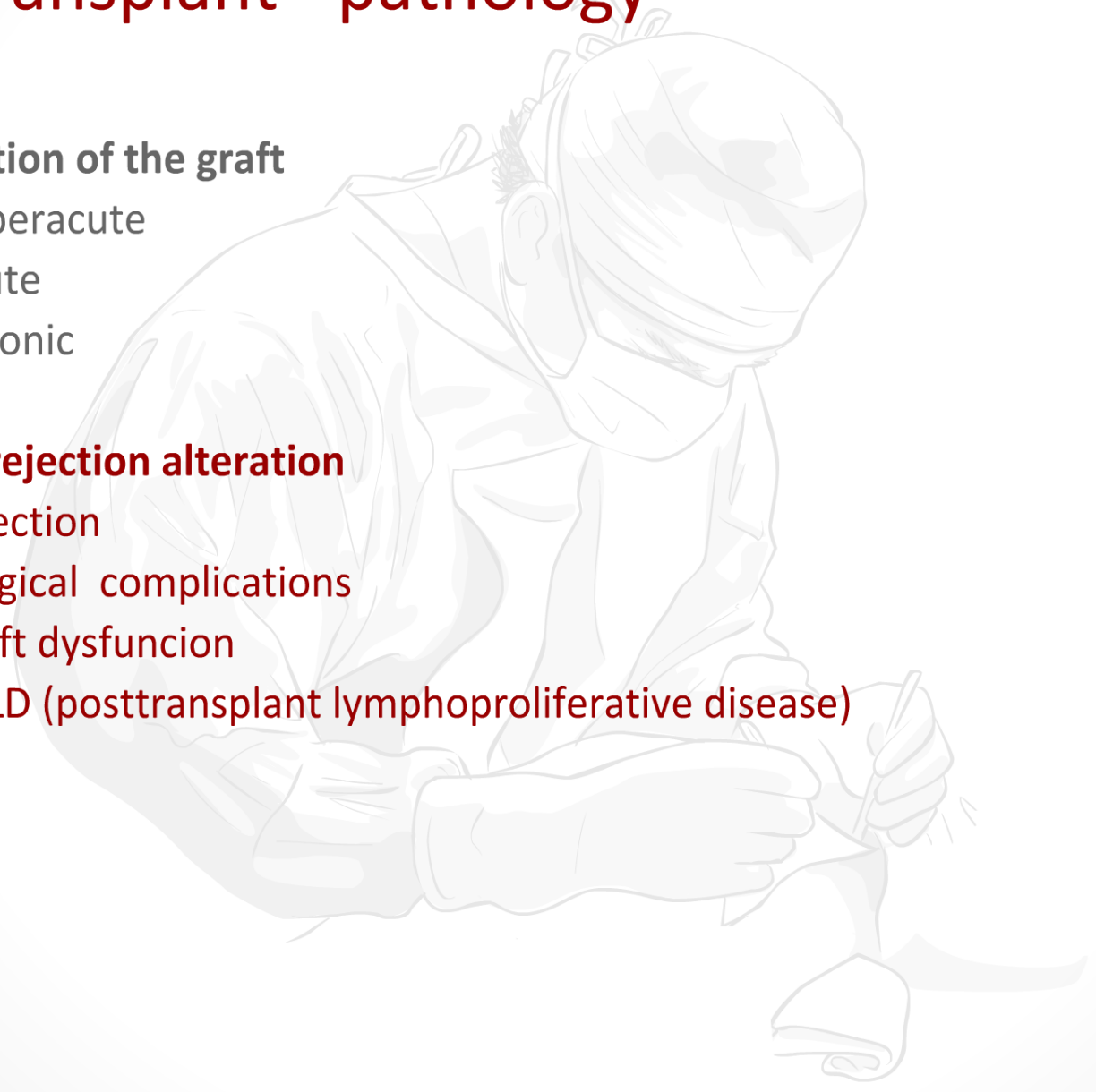
Kidney transplant - pathology

1) rejection of the graft

- therapy of choice is **immunosuppression**
  - corticosteroids (Solumedrol), cyclosporin, sirolismus, azathioprim...
  - the main point is to **repress** immune activation (on the other hand this weakenes organism's defence against infections)

- we need to consider the risk of **rejection** as well as **infection**
  - + there is toxicity of the therapy

Kidney transplant - pathology



1) rejection of the graft

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4) PTLD (posttransplant lymphoproliferative disease)

Kidney transplant - pathology

2) non-rejection alterations

1) infections

- pacient is prone to infections because of **immunosuppression**
- bacterial, viral, mycotic a parasitic infection can develop (mainly **viral**)

Kidney transplant - pathology

2) non-rejection alterations

1) infections

1) bacterial
- mainly ascendent pyelonephritis (purulent)

2) viral
- mainly **CMV**, EBV, HPV and **BKV** infection

BK virus
- human polyomavirus (*Papovaviridae*)
- transmission is idiopathic, tropism to urothelium a renal tubules
- the most severe one, TIN or even ATN can develop

3) mycotic
4) parasitic

] rare

Kidney transplant - pathology

2) non-rejection alterations

2) surgical complications

- pathological changes related to surgical procedure

Kidney transplant - pathology

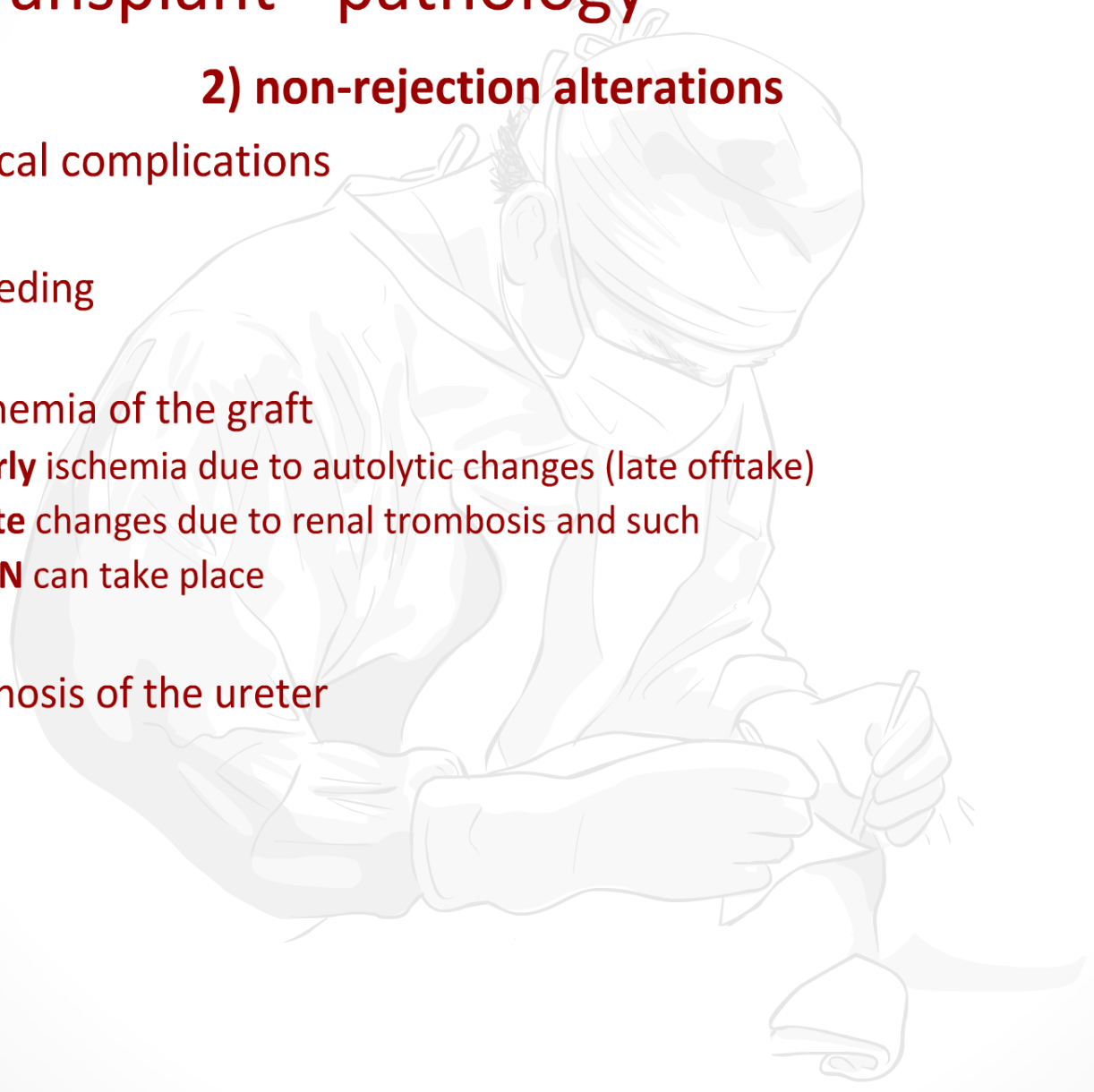
2) non-rejection alterations

2) surgical complications

1) bleeding

2) ischemia of the graft
- **early** ischemia due to autolytic changes (late offtake)
- **late** changes due to renal trombosis and such
- **ATN** can take place

3) stenosis of the ureter



Kidney transplant - pathology

2) non-rejection alterations

3) graft dysfunction

- various renal illness of the donor kidney

1) recurrence of the original disease
   - Ig-A and diabetic nephropathy recure nearly everytime
   - glomerulopathy of the systemic diseases recure commonly
   - combination of renal-pancreas Tx can stop recurrence of diabetic nephropathy

2) progression of the donor's diseases
   - e.g. nephrosclerosis (therefore optimal donor age should by under 50 years)

3) de novo glomerulopathy
   - completely different glomerulopathy can occur

Kidney transplant - pathology

2) non-rejection alterations

4) PTLD

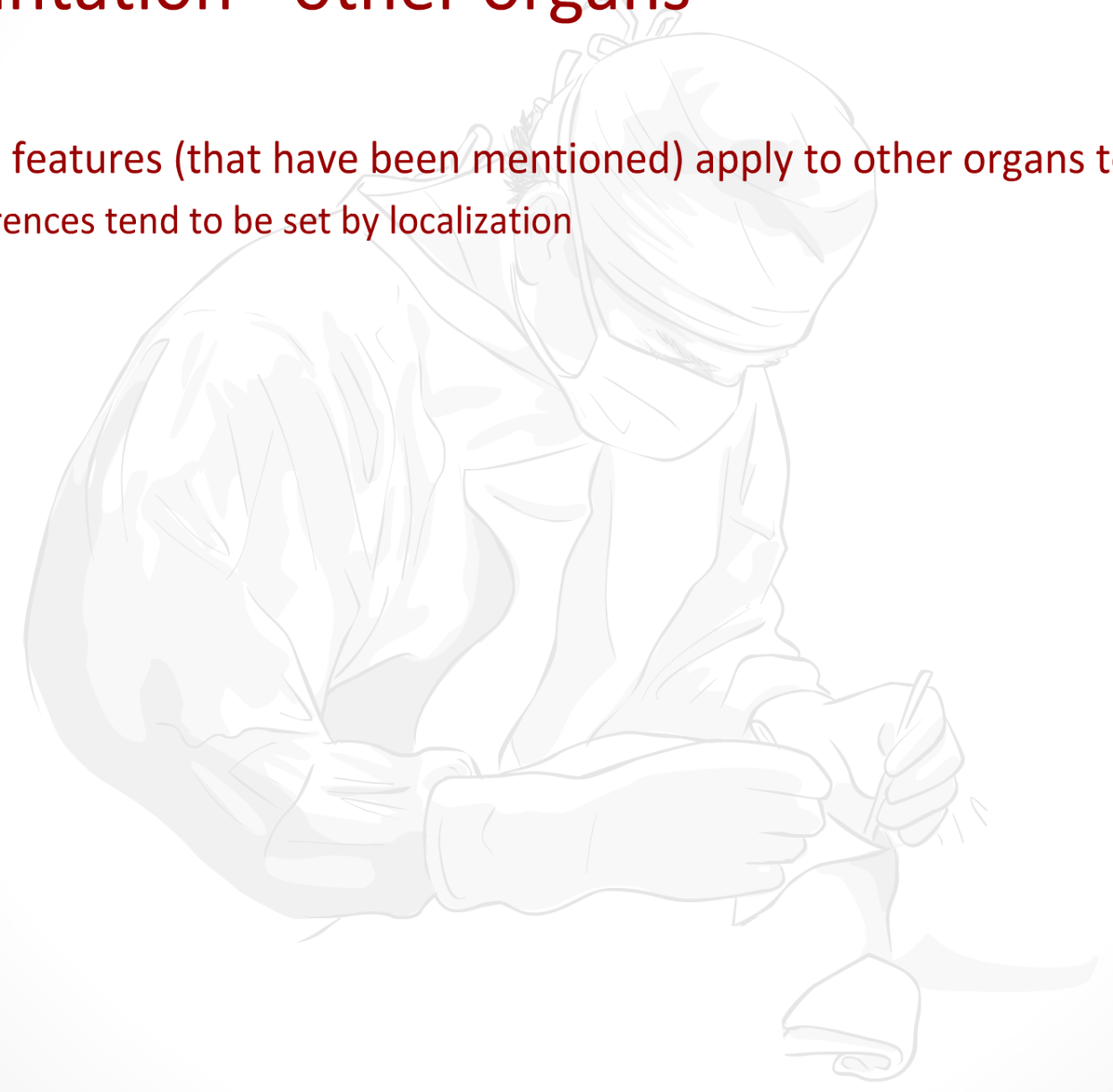
- posttransplant lymphoproliferative disease
- **tumors** arising in connection to transplantation

- **immunosuppression** + **EBV** are the causal factors
- B-**lymphomas** can develop approximately 1 years after Tx
  - in lymphatic nodes, tonsils and extranodaly too (even in the graft itself)
  - arising from the recipient!s lymphocytes

- other malignancies are possible too (skin carcinomas, sarcomas...)

Transplantation - other organs

- all the features (that have been mentioned) apply to other organs too
  - differences tend to be set by localization



Transplantation - other organs

- Tx of heart
  - **indications** include malformations (HLTx), CMP, IHD...
  - **rejection** ISHLT grading (ACR grade 0-3R, AMR grade 0-3)

- Tx of lung(s)
  - **indications** include ILDs, CF, COPD, EAA, PAH...
  - rejection ACR (grade A0-4, B1-2R), AMR, CLAD (BOS, RAS, NRAD, D)

- Tx of liver
  - **indications** include cirrhosis (6 months abstience), cholestasis, poison...
  - **rejekce** Banff classification

Hematopoietic stem cell transplant

- transplantation of **hematopoetic** stem cells to restore blood production
  - HSC may be delivered from bone marrow, peripheral blood and umbilical cord blood

- term **myeloablation** means destroying hematopoiesis (radiation, drugs) → i. v. HSC injection → bone marrow colonisation **(engraftment)** and maturation

Indications

- hematopoiesis malfunction (immunodef.), metabolic disorders, leukemia

GvH

- graft vs. host disease
- pathogenetic mechanism is quite **inverse** compared to the rejection
  - donor cells attack tissues and organs of the recipient
- **clinical manifestation** can be acute (skin, gut, liver disorders) → chronic (similar to autoimmune diseases)
- **GvL** (graft vs. leukemia) is desirable form as for it destroys cancer cells

Autoimmune diseases

Autoimmune diseases

Etiology

- wide spectrum of diseases based on **autoaggression** of the immune system
  - cca 80 clinical units (affecting 2-5 % of population)
- chronic destruction of own tissues by own immunity focused **against auto-Ag**
  - auto-Ig or autoreactive T-lymphocytes

- **idiopatic** mechanisms based on inner and outer factors
  - **genetic predispositions** = FA, mainly ♀, role of HLA and cytokine polymorfisms
  - **enviroment** = microbial (streptococci, viruses), tissue damage, stress, drugs, UV
  - causing **disturbing of autotoleration** (destruction of a- and autoreactive clones)

Autoimmune diseases

Pathogenesis

- understanding requires knowledge of mechanisms of autotoleration

Autoimmune diseases

Pathogenesis

1) central autotoleration

- primary organs of immune system (thymus, BM)

- **negative selection** = induction of apoptosis in T-cells affine to MHC I (clonal deletion)
- **positive selection** = saving the cells with low affinity to MHC I + receptor editing of B-lymphocytes and maturation of Treg-lymphocytes

2) peripheral autotolerantion

- secondary organs of immune system (LN, tonsills, spleen MALT)

- **clonal deletion** = elimination of autoreactive clones with apoptosis (negative selection)
- **anergy** = inactivations of lymphocytes, not retrieving costimulating signal from APC
- **ignorance** = subliminal expression of AutoAg without activation of receptors
- **supression** = inhibition of autoagression with cytokines, Ig, Treg/NK-T-cells, APCs...

3) immunologic privileges

- organ bariers (brain, testicles, thymus, cornea...)

Autoimmune diseases

Pathogenesis

- mechanisms of disturbing the **autotoleration**:

1) modification of Ag
- remodeling of Ag structure also changes the character of Ag

2) crossed reactivity
- between AutoAg (MHC I) which can be similar to foreign Ag (MHC II)

3) polyclonal activation of B-lymphocytes
- defect targeting to the epitopes of Ag

4) revealing of cryptogenic AutoAg
- tissue damage can reveal AutoAg, against which there is no autotoleration

5) monogenetic diseases
- rare inherent autoimmune diseases
- defect of developement of Treg-lymphocytes (FoxP3 protein, IPEX syndrome), apoptosis of lymphocytes (ALPS)

Autoimmune diseases

Clinical manifestation

- **monoorgan** illnesses (nosological units of organ specific = **special pathology**)

1) thyroid
- Hashimoto thyreoitis, Graves-Basedow disease

2) hematopoetic system
- ITP, autoimmune hemolytic anemia, agranulocytosis...

3) muscles
- myasthenia gravis, IMNM...

4) GIT
- atrophic gastritis (anemia perniciosa), autoimmune hepatitis, PBC, PSC, DM I, IBD?

5) urinary system
- membranous glomerulopathy, IgA glomerulopathy, Goodpastuer syndrome...

6) skin
- psoriasis, pefigus vulgaris, bulous pemfigoid, dermatitis herpetiformis...

7) kcardiovascular system
- autoimmune myocarditis...

8) CNS
- multiple sclerosis, Guillain-Barré syndrome, ADEN...

Autoimmune diseases

Clinical manifestation

- **systemic diseases** (affecting several organs = **general pathology**)

1) collagenoses (mixed connective tissue diseases)
1) SLE (+ antiphospholipid syndrome, Sjögren syndrome)
2) sclerodermia
3) dermatomyositis / polymyositis **(prof. Zámečník)**

2) autoimmune "arthritis" **(prof. Kodet)**
1) RA
2) Seronegative arthritis
   - Bechterew disease, Reiter syndrome
3) chronic Lyme disease

3) revmatic fever **(prof. Kodet)**

4) IgG4 disease **(Dr. Chmelová)**

5) systemic ANCA+ vaskulitis **(Dr. Soukup)**

SLE

Etiology

- **multisystemic** autoimmune inflammatory disease
  - used to be lethal within 2 years, nowadays 95 % 5 year survival

- developement of widely reacting **Auto-Ig**
  - anti- nuclear (ANA), DNA (dsDNA), histons, erythrocytes, lymphocytes, platelets...

- inner and outer factors
  - **genetic predispositions** = mainly ♀, African Americans, Asian people
  - **environment** = drugs (Isoniazid, Hydralazin, Penicilamin), UV

SLE

Pathogenesis

- **2nd** (cytotoxic) and **3rd** (immunocomplex) immunopathologic reaction
  - hyperreactivity of B-cells with ADCC and accumulation of immunocomplexes (activation of PMN)
  - **interstitial fibrinous** inflammation

SLE

Clinical manifestation

- multiorgan disorder with huge **diversity** of symptomps
  - **acute** (even fulminant), or **chronic** manifestation

1) general
- fever, fatigue, weight loss, weakness
  - serology positive for Ig

SLE

Clinical manifestation

2) local (organ specific)

- **skin** = malar ("butterfly rash"), photosensitivity various rashes (mainly chronic)
- **musculosceletal** = arthritis, aseptic necroses, myositis
- **renal** = 80 % patients affected (6 classes of manifestation)
- **serous membranes** = lymphocytic (poly)serositis
- **heart** = Libman-Sacks endokarditis (verrucous), vasculitis, myo- a pericarditis
- **GIT** = autoimmune "lupus hepatitis", pancreatitis, enteritis
- **hematopoetic** = ***cytopenia***, coagulopathy, lymphadenopathy
  + **antiphospholipid syndrome** = trombophilia (venous and arterial trombi)
- **respiratory** = ***lung fibrosis***, pneumonitis
- **CNS** = variabile, neurologic symptoms, ***stroke***

SLE

Clinical manifestation

2) local (organ specific)

Sjögren syndrome

- autoimmune inflammation of **tear** and **salivary** glands
  - **primary** = isolated
  - **secondary** = association with SLE, RA (more often)
  - AutoIg against ribonucleoproteins Ag SS-A(Ro) and SS-B(La)
- clinically **sicca syndrome** → organ damage (kidneys, TG, pancreas) → lymphoma
  - keratoconjunctivitis sicca with failure to produce tears (**xerophtalmia**) leading to corneal damage
  - destructive dryness of oral mucosa (**xerostomia**) with erosions, fissures, ulcers

SLE

Morphology

1) skin

- degeneration of **epidermis** (atrophy, hyperkeratosis, vacuolisation, vesicles...)
- **dermis** contains lymphocytic inflammation, fibrinoid dystrophy and až necrosis, scars
  - **IF** shows IgG deposits in degenerated BM (immunocomplexes)

2) organ

- **intersticium** shows lymphocytic infiltrate, fibrinoid dystrophy and až necrosis, scars
  - vasculitis apparent (arteriolo- až arteritis)
  - **LE cells** (micro- i macrophagocytes with fuzzy chromatin due to ANA damage)
  - **LE bodies** (remains of caryorhectic nuclei in intersticium)
- **kidneys** contain deposits of IgG in BL of glomeruli ("fingerprint")
  - **IF** shows Ig, C3, **c1q** (immunocomplexes)

Sclerodermia

Etiology

- **multisystemic** autoimmune inflamatory disease
  - prognosis based on visceral organ affection

- **idiopatic** mechanism of developement of immune dysregulation
  - results in **fibrotic changes** of skin +/- visceral organs

- inner and outer factors
  - **genetic predisposition** = mainly ♀, African Americans
  - **environment** = chemical exposition

Sclerodermia

Pathogenesis

- includes **3 basic disorders**:
  - **vasculopathy** = alteration of endothelium, vessels fibrosis and ischemia
  - **activation of immunity** = Ig against DNA-topoisomerase, anticentromeric Ig...
  - **extensive fibrosis** = activation of fibroblasts and fibrosis / sclerotisation

Sclerodermia

Clinical manifestation

- terms "sclerodermia" reflects typical skin disorder
  - **inflammation** (erythema) → **sclerosis** (relatively abundant collagen fibres)
    → **atrophy** of epidermis (thickening of the skin, resembles scroll paper)

Sclerodermia

Clinical manifestation

1) localised type (*sclerodermia circumscripta, morphea*)

- fibrosis of the **skin** distally (extremities and face)
  - "skin thickening", facial deformity, hypomimia, acroosteolysis (ulceration, amputation), Raynaud's phenomenon, depigmentation...

- developement of lung hypertension is possible

Sclerodermia

Clinical manifestation

2) diffuse type (*sclerodermia diffusa*)

- fibrosis of the **skin** proximally (gridles, trunk) + **visceral** disorders
  - **skin** affection is extensive (shortness of breath)
  - **visceral** affection is variable (mainly kidneys, myocardium, esophagus and ***lungs***)

- sometimes a group of symptoms called **CREST syndrome**
  - **C** = calcinosis (deposition of calcium in the skin and other organs)
  - **R** = Raynaud's phenomenon (finger vasoneurosis: pale → red → blue transition)
  - **E** = esophageal dysmotility
  - **S** = sclerodaktyly (contraction)
  - **T** = teleangiectasis

Sclerodermia

Morphology

1) skin

- atrophy of **epidermis**
- **dermis** is swollen and contains lymphocytic infiltrate + hyalinization + atrophy of the skin adnexa

2) organ

- **fibrosis** + **lymphocytic** inflammation
  - "onion-like" thickening of the vessel wall (fibrosis of tunica intima)
  - lung fibrosis, submucosal fibrosis of esophagus, "nephrosclerotic" kidney changes (even fibrinoid necrosis), myocarditis

Immunodeficiency

Immunodeficiency

Etiology

- **increased** reactivity of immunity to Ag

- **primary** or **secondary** causes
  - primary = **inherited** defects of non-specific and specific immunity
  - secondary = **acquired** defects (CHT, aging, malnourishment, HIV, DM disease...)

Immunodeficiency

Pathogenesis

- **primary** ones have symptomes based on defective type of immunity
- there are **100 clinical units** (stated in the book):
  - isolated IgA deficiency, CVID, X-linked Bruton's agammaglobulinemia, hyper IgM syndrome, DiGeorge syndrome, complement deficiency, SCID

Immunodeficiency

Clinical manifestation

- manifestation starts during **childhood** (newborns, infants)
  - only mild types are recognized lately or in adulthood

- prone to **infections**
  - reccurent infections including opportune pathogens and malnourishment
  - risks od developement of autoimmune diseases and allergies

- variable **severity**
  - **light** cases are common (1 / 500 newborns)
  - **severe** cases are rare

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