Exogenous factors in pathology

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physical exogenous factors

a) occur naturally (UV radiation, warm, cold, noise, mechanical powers, natural radioactivity)

b) occur arteficially (laser, ultrasound, powerful magnetic field, ionizing radiation, AC - alternating current)

Physical factors - division

- mechanical factors
- nois, vibration, ultrasound
- high and low atmosheric pressure
- influence of high and low temperature
- influence of the light
- AC, DC
- ionizing radiation

Mechanical factors

- can evoke contusion, disruption of the tissue; infractions, fractures of the bone; distortion, luxation of the joints; disturbances of vessels ⟶ hemorrhage, disturbances of tissue perfusion
- in the places of disturbance ⟶ usually inflammatory reaction (it can occur also in sterile inflammation)
- injury of the myocardium, CNS ⟶ acute death possibility
- injury of CNS may be followed by brain oedema
  intracranial hemorrhage
  concussion, contusion of the spina
  contusion, interrruption of the peripheral nerves
- serious injury ⟶ traumatic shock

Traumatic shock

- evoking stimulation → pain, blood loss
- vasomotor centre → inhibition → vasodilation in periphery, disturbance of blood distribution, hypotension → reduction of coronary vessels perfusion
- trauma, hypotension, tissue hypoxia → stress reaction
- inflammatory reaction → activation of specific, non-specific defense mechanisms
- reaction of vessels → slow perfusion → creation of the microthrombi
- metabolic acidosis (catabolic stage)
- shock kidney – ATN
- air embolism, fat embolism

Crush syndrome

- traumatic shock connected with injury of the muscles
- release of myglobin and K^+
- myoglobin = m.w. 17.5 kDa, filtration in glomeruli ⟹ myoglobin casts obstruction in urine reflux
- resorbtion of myoglobin in tubuli → hemosiderin → tubular cell exfoliation
- lowering of the GFR (due to hypotension) + tubular function disturbance failure of the kidneys

Influence of the nois

- music and non-music tone perceived disturbingly = noise
- perception of the sound: most sensitively – middle frequention wawes, less sensitively – high and low tones
- influence: a) implicitly on CNS
  b) direct affection of hearing apparatus – **acustic trauma**
- excitation of the *n. acusticus* ⟶ hearing sensation
  in larger intensity – afferent stimulation – tactile treshold
  increases in intensity – pain treshold
- minimal adaptation – noise interrupted in short intervals
  high tones – larger damage of the acustic sysem then deep tones

Vibrations

in overrun of the treshold of mechanical cycles ⟶ perception also by other organs
vibrations evoke local and systemic changes
2000 – 20000 cycles/min ⟶ excitation of nerve endings in vessel wall (work with pneumatic hammer) ⟶ vasoconstriction, tissue hypoxia, disturbance of cartilages and bone

Ultrasound

used frequence about 1 MHz and higher – good convection in fluid and solid substances
thermic action – used in diathermia
large ultrasound beat – used in the crush of concrements
exploitation in many fields of medicine

Low atmospheric pressure

- decrease of partial pressure O_2, CO_2, N_2
- decrease of p_aO_2 ⟶ hypoxia
- deficient transport O_2 into CNS ⟶ several steps of consciouness disturbances
- increase in heart rate (80%), stroke volume (50%) = almost normal transport of O_2 to tissues
- decrease of O_2tissue pressure ⟶ larger production of erythropoietin
- respiretory system: V_T increases also respiratory rate, hyperventilation lowering of pCO_2 ⟶ respiratory alkalosis
- expansion of gases in GIT

High atmospheric pressure

- increase of partial pressure of gases in organism
- narcotic effect of N_2, toxic effect of O_2
- ogygen: inactivation of enzymes with SH- groups
  toxic effect on lung capillaries ⟶ lung oedema
  increase of p_aO_2, decrease of p_aCO_2 ⟶ vasoconstriction (brain!!)

- **hyperoxia** (therapeutic use of hyperbaric oxygen)
  intoxication by CO, anaerobic gangrene
  inherited defects of myocardium with cyanosis

Decompression sickness

- signs in persons working in high pressure atmosphere after fast decompression. Signs are evoked by bubbles of released gases in blood
- bubbles of O_2 and CO_2 disappear fast (good diffusion)
- bubbles of N (in air 80%) – slow diffusion, high solubility in fat tissue, also in myelin sheets
- signs: bubbles in vessels – disturbaces of tissue perfusion – embolism
  myelin sheets – disturbances of eff. and afferent system, CNS
- bubbles also in tissues with larger content of fats (adrenal cortex, bone marrow, dermis)

Barotrauma

- rises in sudden changes of atmospheric pressure
- at slow setting of difference atmospheric pressures in atmosphere and i organism can occur:
- mechanical disturbance of middle-ear cavity
- lung – very sensitive (divers, patients by using of breathing apparatus with positive end-expiratory pressure)
- in theese patients can rise pneumothorax, mediastinal emphysema, air-embolism

Action both of low and high temperature (physiology)

hypothalamus – thermoregulatory center,
central receptors – registration of temperature in *core* (blood in hypothalamus)
peripheral receptors in dermis, mucoses – registration of *shell* temperature (skin, dermis)

metabolism ⟹ warmth - body temperature
T_3, T_4, katecholamines
shivering thermogenesis
non-shivering thermogenesis – in newborns – thermal energy is created in brown fat tissue

body temperature is further controlled by:
- vessel activity – vasoconstriction, vasodilation
- relative air humidity

Cold

- cold ⟶ increase of sympathetic tone - vasoconstriction
- if it is not possible maintain body temperature ⟶ motor activity, shivering
- **hypothermia** – body temperature **< 35°C**
  deceleration of heart rate, disturbance of myocardium contractility
- **< 34°C** consciousness disturbance, **< 32°C** unconsciousnes
- **34°C – 27°C** – decline of metabolism, low oxygen uptake, vasodilation, fall of shivering
- **27°C – 24°C** – loss of all thermoregulatory mechanisms
- **24°C** – death – respiratory failure
  circulatory failure (arrhytmias, heart arrest)

Hypothermia in newborns and older persons

- newborns – thermogenesis in brown fat tissue (sympathetic activation – hormonsensitive lipase – fat splitting and resynthesis – release of thermal energy)
  thermoregulatory mechanisms – step by step development – in long term influence of cold ⟶ fall in *core* temperature ⟶ sleepiness, disturbance of consciousness

- during aging – decline of thermoregulatory mechanisms effectivity ⟶ easier rise of hypothermia in older persons ⟶ less intensive vasoconstriction, less intensive shivering)

Hypothermia in surgery

decline of *core* temperature ⟹ lowering of metabolism and oxygen uptake in tissues

controlled hypothermia is used prevalently in cardiosurgery and neurosurgery

programmed cooling of blood in extracorporal circulation

temperatures 32°C - 27°C are commonly used
in long-term surgery – body temperature can be lowered less then 25°C

after surgery – programmed relatively rapid blood rewarming

Systemic influence of the warm

if it is not possibility to releasing of warm into surroundings ⟶ **hyperthermia**
temperature of the *core* **>39°C**

increase in tissue oxygen uptake, catabolism, heart rate and respiratory rate
vasodilation – sweating – water and salt depletion – hypovolemia – increase of ECF osmolality
hypotension ⟶ collapse (due to vasodilation)
disturbance of skin perfusion ⟶ loss of sweating
total loss of thermoregulatory mechanisms – body temperature 42°C – 43°C
disturbances of CNS – unconsciousness, convulsions

influence of insolation on head:
primary: disturbances of CNS functions, headache, unconsciousness
secondary: hypertermia, ventricular fibrillation

Light

visible light – wavelenght 400 – 760 nm, <400 UV radiation, >760 IR

photochemical effect – in UV part of spectrum; aromatic and heterocyclic AA, nucleic acids ⟶ selective absorption ⟶ disturbances of proliferation - destruction of cell membranes, cell death

heat effect – increase with inreasing wavelenght

photosensibilization – excitation of photodynamic active substances with following O_2 activation (quinine, porphyrins, methylene blue)
result: erythema, local oedema, pustules, necrosis

photoalergy – light ⟶ allergen activation ⟶ hypersensitivity reaction
results: eczema, urtica (nettle rash)

Skin and UV radiation

light erythema – app. 2 h. after irradiation – skin oedema, pustules, sometimes necrosis
cell proliferation is uncontrolled (skin thickening, change in number of mitoses)

in cells of epidermal *stratum basale* melanin is synthesised – 5 – 7 days after exposition
pigmental phenomenon – pigment in leukoform – brown colouring of the skin almost immediately

UV radiation and cancerogenesis

uncontrolled cell proliferation (similarly as after cancerogenic substances) ⟶
skin malignant tumors (*basalioma)*

Laser

concentrated rays of light, UV and IR radiation

effect is prevalently caloric

it is possible to evoke sharp bordered tissue coagulation

use in many fields of medicine

Electric current

alternating current AC – more dangerous then DC (direct current)

electric current at passage through organism evokes
- caloric changes
- functional disturbances of irritable structures – nerves, myocardium, skeletal muscles
- mechanical changes – disruption of tissues and organs

frequency – 50 – 60 Hz (in network system) – zone of dangerous frequentions (30 – 150 Hz)

current intensity – 25 mA ⟶ hypertension, convulsions
25 – 80 mA ⟶ arrhytmias
>80 mA ⟶ ventricular fibrillation

high intensity (3 A and more) – calorigenic influence

causes of death – ventricular fibrillation, convulsions of respiratory muscles, damage of spinal vasomotor centers

Electric current – therapeutical use

- **galvanotherapy, iontophoresis**
- electric discharge – **impulse** – short-term impulse contents all frequetions of AC, currents with hihgest intensity are used at **defibrillation**
- **AC** with weak intensity – use as **diathermia**
- **AC** high intensity - use in **electroshock therapy**
- high-frequency current - **electrocauterization**

Ionizing radiation

- part of electromagnetic spectrum

- rtg, γ-, neutron radiation – intersection through skin and tissues
- α-, β- radiation – intersection through skin negligible, dangerous is oral or paravenous administration of radionuclides

- value of absorbed dose is done in **Gy (**1 Gy = 1 Jkg^{-1})

- mechanisms of effects
  1) DNA breaks – chromosomal and gene mutations – probability of pathological cell clones creation
  2) free radical creation
  3) changes in ezyme activity

Influence of responsibility to irradiation

- **biological effect** – depends on the density of iradiated particles in the tissues
- **area and place of irradiation** – the larger irradiated area, the worse consequence
- radionuclides **are integrated** into metabolic pathways – consequently cumulation in some organs (iodine in thyroid gland, phosphorus, strontium in bones, in liver)
- **cumulation of the effects** – the larger, the shorters intervals among expositions
- **tissue sensitivity** – most sensitive – proliferating cells (germ cells, enterocytes, hemopoitic stem cells, epidermal cells)
  in non-proliferating cells/tissues – changes of function
  in tissues with slow cell turnover (thyroid gland, lens) – consequence after several years

Clinical picture after irradiation

- acute syndrome
- local effects of ionizing radiation
- late sequelae of irradiation

Acute syndrome

- after whole-body irradiation 1 – 10 Gy (LD_{50} for humans is 4 Gy)
- till 48 hours – non-specific signs: lassitude, weakness, anorexia, nausea, vomiting
- hematopoiesis – arrest of stem cell proliferation
  lymphopenia – till 48 hours
  granulocytopenia - till 2 – 3 days
  anemia after 2 – 3 weeks
- GIT – hemorrhagic diarhoea (!!!)
  nausea, vomiting
  anorexia
- CNS – after several hours - excitatory state, hyperreflexia,
  then sleepiness, disturbances of consciousness
- respiratory system – oedema of bronchioli (dyspnoea, cough)

Local effects of irradiation

skin involvement: erythema, epilation, dermatitis

Late sequelae

latency several month or years

epidermis – atrophy, lasting epilation

CNS – disturbances of myelin sheets – involvement of afferent, efferent, cognitive functions
GIT – chronic diarrhoea, malabsorption

respiratory system – inflammation – lung fibrosis (!)

several types of malignant tumors (esp. leukemias)

Ionizing irradiation – malignant tumors

possibility of origination of functionally significant mutation ⟶ cancerogenesis
most frequently LEUKEMIAS – latency 8 – 12 years

significantly high frequention carcinomas in
thyroid gland, breast, lung,
malignant tumors in bones