# PHYSICAL FACTORS AS CAUSES OF DISEASES AND HEALTH DAMAGE

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## 1. THE EFFECT OF MECHANICAL ENERGY

### 1.1. INJURIES AND WOUNDS

If the human body collides with another (human, living or nonliving) body, the kinetic energy of the collision can cause different **injuries (trauma), wounds (vulnus)** and in the worst case **sudden death.** Injuries are the most important cause of premature death and disability in young people in developed countries. One third of all deaths from injury are due to motor vehicle crashes, one third to other unintended causes (especially falls) and one third to intentional violence (suicide and homicide). As an example in the USA more than 150000 injury caused deaths are recorded each year and the consequences of nonfatal injuries causing permanent disability pose an even larger medical problem.

The main forms of wounds are listed in table 1. The consequences of these wounds vary considerable from negligible inconvenience to permanent disability and even death. The most common symptom of wounds is **pain** caused by irritations of extero- and interoreceptors, products of tissue destruction and later by inflammation. Almost every injury leads to some **blood loss**. If considerable amount (10 - 30 % of the total volume that is 0.5 - 1.5 l in average adults) is lost, arterial hypotension develops which in turn can contribute to the development of **traumatic shock**.

Into damaged blood vessels bubbles of air or droplets of fat from the surrounding tissues can get causing **air or fat embolism,** respectively. These bubbles and droplets obturate the small capillaries in remote organs and deteriorate their oxygen supply.

Tab 1

THE MAIN FORMS OF WOUNDS

| | |
|---|---|
| Contusio | bruise |
| Abrasio | graze |
| Laceratio | tear |
| Vulnus sectum | cut wound |
| Vulnus punctum | stabbed wound |
| Vulnus morsum | bite wound |

| | |
|---|---|
| Vulnus sclopetarium | bullet wound |
| Fractura | broken bone |
| Luxatio | dislocation of a joint |

Open wounds are **locus minoris resistentiae** where infection can enter the body. The most dangerous possibilities arise if the wounds are contaminated with anaerobic bacteria (mostly from soil) and not treated properly in time. In such cases life-threatening **gas gangrene** (necrosis of affected limbs with development of gas and sepsis) can develop. Gas gangrene was common in the pre-antibiotic era, namely in the wounded soldiers of World War I. In necrotic tissues around (even very small) wounds germs of Clostridium tetani can produce tetanotoxin - a protein of $M_r$ about 150 kD which is one of the most potent toxic substances. **Tetanus** is characterized by generalized painful muscle contractions. Vaccination and revaccination every 5 years completely prevent the danger of tetanus.

Every major injury triggers also the nonspecific adaptive reactions of the organism (**stress reaction**).

Blows of the head (even without fractures of the bones) often lead to brief loss of consciousness - **commotio cerebri** with consequences ranging from some hours or days (amnesia, vegetative symptoms as nausea and vomitus, nystagmus) up to such chronic complications as **posttraumatic epilepsy.** Repeated small injuries of the brain are characteristic features of boxing. The blows probably cause microscopical haemorrhages in the brain or lead to transient depression of neuronal and synaptic metabolism. Years after leaving the sport career the damage of the brain usually manifest as **extrapyramidal motor disturbance** and in some cases as serious deterioration of mental abilities - **dementia pugilica**. According to some studies injuries of the head are also a risk factor of **Alzheimer disease**

## 1.2. BLAST SYNDROME

This syndrome is caused by the shock wave of explosions. In fact after explosions several waves of increased and decreased pressure arise in very short time. These shock waves can damage the tympanic membrane and the tiny structures of the middle ear, disrupt the alveoles in the lung leading to lung haemorrhage and air embolism and compress the abdominal organs containing air (stomach, guts). Blast syndrome is usually combined with other types of injury (pushing the body against wall, splits of projectiles, flying objects, etc).

Properly targeted and focused underwater shock waves of appropriate energy are used to destroy gallstones and stones in the urinary tract **(extracorporeal lithotripsy).**

## 1.3. CRUSH SYNDROME

In people buried or partly buried under avalanches, in destroyed buildings (earthquakes) or crashed vehicles and similar situations the compression of soft tissues leads to their ischemisation. After rescue and decompression the perfusion is restored but mostly too late. If the endothel and the vessel wall is already irreversibly damaged, water and small molecules escape from the intravasal space and the fluid accumulates in extravasal space (**oedema**). This additional layer of fluid between vessels and cells further deteriorates the diffusion of oxygen to cells. Due to the fluid loss from the vessels the density and viscosity of blood increases and hypovolemia develops. Breakdown products of muscle and other substances released from the anoxic tissues (e.g. histamin) further worsen the circulation. If the compression is not released in time hypovolemic shock develops with prerenal kidney insufficiency resulting in oliguria or anuria. Crush syndrome may lead to death due to shock or uremia even without serious external injury and blood loss. In renal tubuli of the victims cylinders of precipitated myoglobin are present and according to an older theory this is the cause of the renal insufficiency. In fact the cylinder formation in crush syndrome is only a consequence of the renal failure.

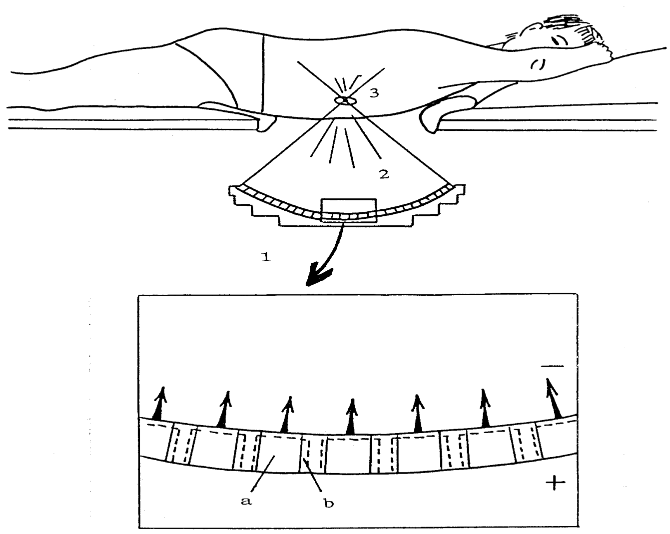



Fig 1

EXTRACORPOREAL PIEZOELECTRIC LITOTHRIPSY

1 – Piezoelectric ceramic crystals, changing shape with electric impulses.

2 – Focuses and concentrates pressure wave.

3 – gallbladder stone.

Insert: a,b – shape change of piezoelectric crystals.

The duration of pressure waves is in the millisecond and are repeated with 1 – 1,5 Hz frequency. 500 – 3000 impulses are necessary to disintegrate stones gallbladder or renal stones

## 1.4. VIBRATIONS, NOISE POLLUTION AND ULTRASOUND

Man perceives vibration in the range of 25 - 8200 Hz. People exposed repeatedly to vibrations (mostly as occupational damage) complain after months or years of exposure on pain of the spine and extremities. X-ray investigation can disclose severe osteoporosis. The regulation of the tone of small vessels of fingers is deficient. Vasospasms and the damaged local circulation lead to increased sensitivity of the fingers to cold and later to trophic changes of the skin and muscles. The symptoms are similar to those in Raynaud's syndrome which is a congenital disturbance of the vasomotor tone.

Chronic exposure to noise (noise is every sound which is perceived as disturbing and of intensity above 50 dB) leads to hearing loss and deafness and disturb the activity of the vegetative and central nervous system. 65 % of the European population is regularly exposed to noise intensities above 55 dB, which can cause annoyance, aggressive behaviour and sleep disturbance. 10 millions endure noise above 75 dB (the noisiest capital of Europe is Athens, Greece) which is a considerable stressor probable contributing to elevated blood pressure, heart disease and learning difficulties in children.

The relationship between the physical energy of acoustic vibrations and their perceiving as sounds or noises is logarithmical. The threshold of perceiving a sound is 0 dB and the physical energy of a 10 dB sound is 100 times more. The energy value of the 0 dB threshold varies with the frequency of the sound, its minimum is in the range of 2 - 3 kHz.

Ultrasound - frequency above 20 kHz, not perceived by human ear - of high intensity can lead to the same damage as vibration and noise and in addition it has also a thermal effect. The intensities employed in the diagnostic and therapeutic ultrasound devices are well below the dangerous threshold.

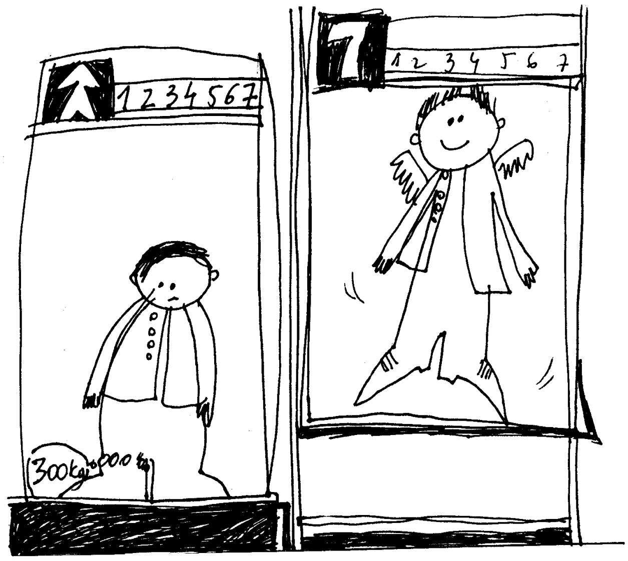
# 2. THE EFFECTS OF ACCELERATION AND GRAVITATION

## 2.1. ACCELERATION AND DECELERATION

Acceleration is the **change of movement** (characterized by its speed and direction). Moving at constant speed in one direction itself has no effect on the body (without visual control it is even impossible to perceive it) but if the speed or the direction of the movement changes the various parts of the body behave according the law of inertia - they tend to retain their original speed in the original direction. The vestibular apparatus of the inner ear works on this very principle and enables perceiving acceleration and deceleration. It is very important to recognize, that the forces arising from the change of movement act always in the opposite direction as compared with the acceleration.

The change of speed can occur in various directions, be of various intensity and duration. (Table 2). Let us consider some common examples (The first example is only for better understanding of basic terms – it has no harmful effects on the body):

**Acceleration and deceleration in an elevator:** In an elevator starting upward a short period of positive acceleration occurs (the weight of the body is perceived heavier than usual). After the start we do not feel anything strange - the speed is constant. At arrival at the top floor the change of speed is negative (deceleration) and the body becomes lighter than normal. On the way down the events occur in opposite direction (first acceleration downward, then slowing down the downward movement) and the feelings correspond to that.



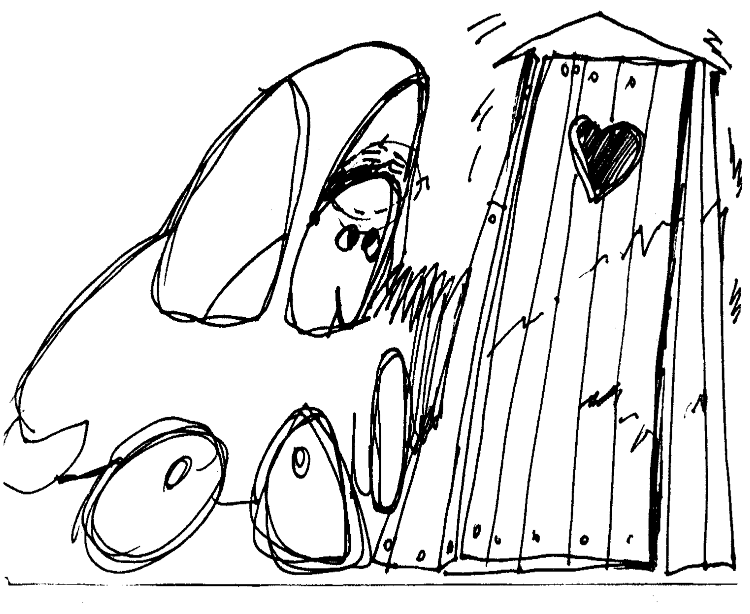
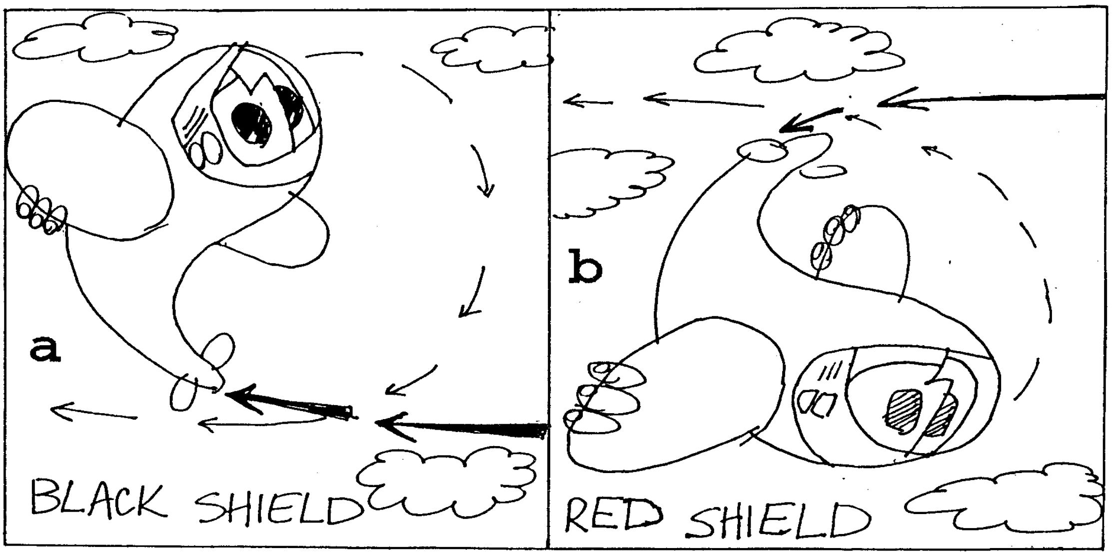



Fig 2

Acceleration and deceleration in elevators – a model situation to understand them

Fig 3

A very unpleasant and dangerous case of deceleration



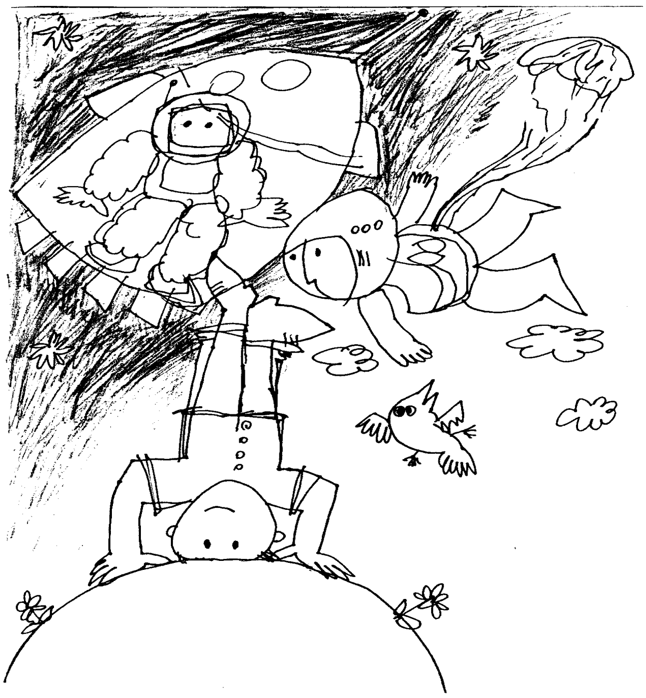



Fig 4

Black and red shield

Fig 5

Different forms of weightless state and –1 G negative acceleration during yoga exercise

**Acceleration and deceleration in traffic vehicles:** A racing car after start achieves in some seconds speed over 200 km/h. It is a strong positive acceleration in ventrodorsal direction, but this is relatively well tolerated. The pilot is pushed into his seat. Before the curves he needs to brake (negative acceleration or deceleration) and his body is held in the cockpit with the help of the safety belts. In the curves there are two possibilities: If the track is flat, the acceleration is lateral (the car and the pilot's body tend to proceed in the original direction). Some very fast tracks have tilted curves enabling the racers to take them with high speed. In this case the main force (arising from the combination of the vectors) is upward down and this in fact has the same effect as positive acceleration in craniocaudal direction.

The worst case of deceleration occurs in a crash, when in a very short period of time extreme negative acceleration takes place. Proper construction of cars, their bumpers together with the safety belts and air bags help to absorb most of the kinetic energy of the crash and can avoid serious injuries and death in accidents).

**Acceleration in aviation and astronautics:** If a plane accelerates upward (looping) the blood accumulates in the lower parts of the body. If the force of acceleration overrides the compensatory mechanism of the circulatory system, the brain (and the retina) is suddenly deprived of blood supply - the pilot's sight is disturbed due to a **"black shield"** and even unconsciousness can occur. The same process occurs after launching a rocket.

If the pilot dives the nose of the plane downward (looping forward) the blood accumulates in his head and causing hyperemia of the retina and sight disturbance termed as **"red shield"**. Special suits designed for pilots of warplanes diminish the dangerous effects of sudden changes of speed and direction.

**Angular acceleration:** If a body rotates at constant speed, (e.g. the rotor of a centrifuge or a figure skater making a pirouette) acceleration arises from the change of the direction of the movement (centrifugal force). The particles in the test tubes in the centrifuge sediment and the skater should use force to pull his arms to his trump.

## 2.2 GRAVITATION AND WEIGHTLESS STATE

The forces of acceleration and deceleration have the same effect on the body as the gravitational force. (According to Einstein's theory of relativity it is impossible to decide between these two types of forces.) Our body (and every thing on the earth) is pulled to the earth with force equivalent to an acceleration 9.81 $m*s^{-2}$ = 1 G. Our mind and cardiovascular regulatory mechanism perceive this force as normal in upright, sitting or horizontal position. The gravitational force does not change if we are standing on the head but our body perceives it as a negative acceleration of -1 G (the overall change from +1 G to -1 G is -2 G).

On other planets the gravitational force may be much higher than on the Earth and on the Moon is only a sixth of it.

Tab 2

THE EFFECTS OF ACCELERATION ON HUMAN BODY

| ACCELERATION, G | TOLERANCE | EFFECTS |
|---|---|---|
| **+2** | ≈ 10 minutes | The weight of the body is increased, the body is pushed into the seat |
| **+2.5** | minutes | Impossible to stand up from the seat, breathing is difficult |
| **+3** | seconds | Pale, distorted face, sight disturbance (grey shield) |
| **+4** | seconds | Black shield, tachycardia, dyspnoe, loss of consciousness |
| **-1** | minutes | Discomfort |
| **-1.5** | minutes | Pressure in the head, red face |
| **-2** | ≈ 10 seconds | Strong pressure in the head, eyes, lacrimation, dizziness |
| **-2.5** | seconds | Pulsating pressure in the head, dyspnoe, red shield |
| **-4** | < 1 second | Acute pain in the head and eyes, red shield, disturbances of brain, function similar to commotio, loss of consciousness |

**Weightless state** is present in the case when the gravitational forces are counterweighted with acceleration. The most common case is the free fall (e.g. that of a parachutist before opening the parachute). Weightless state of long duration occurs in astronautics. If a space ship moves on an orbital trajectory round the earth, the gravitational force and the radial acceleration are in balance. The same is true for voyages between planets where the acceleration of the space ship is given by the gravitational forces of the surrounding celestial bodies and therefore its passengers are in weightless state. This is changed only when the rockets of the space ship are working or when the whole space ship is rotating around his axis (artificial gravitation).

**The effects of the space flights** on the human body are diverse. During launch strong acceleration occurs but the forces are far less intense than those imagined by the early science-fiction authors. On the orbit the weightless state disturbs first the function of the vestibular organ and symptoms similar to kinetosis can occur. The orientation in space is more difficult, the movements are less coordinated and precise than on the earth but in well-trained persons these changes are transient.

The lack of gravitation (or more precisely the **microgravitation)** leads to a shift of blood volume from legs to the upper part of the body, to changes of the heart rate (first to tachycardia, later to bradycardia) and to fluctuations of blood pressure. Interestingly, a similar shift in the distribution of blood does not occur in the lungs. The excretion of water and sodium is increased due to hormonal interactions - mainly those of antidiuretic hormone and atrial natriuretic factor.

In the course of long-term flights demineralization of the skeleton with concomitant rise of blood calcium and atrophy of postural muscles (mainly those of leg) develop. The muscular atrophy in the course of the longest flights (about 1 year) can reach as much as 40%. The loss of calcium may be a limiting factor of the long-term space flights because administration of calcitonin and D vitamin are ineffective measures against the steady calciuria. Fortunately, in the course of long flights the calcium loss stopped at 20 % of total body calcium but the occurrence of more profound losses during flights lasting more years are not excluded. With regular physical training and specially designed suits these changes are partially preventable.

An interesting feature of the space flights is the **cosmic anemia** - due to the decreased production of young red cells without apparent reason. The lifespan of the red cells is normal. During space flights the immune system is affected, too: the proliferative activity of lymphocytes and the activity of T-lymphocytes is decreased.

Space flights desynchronize the normal biorhythms of the human body and therefore the "day" and "night" of cosmonauts is timed from the space center on the earth.

The construction of the spacecrafts provides a good shield against the cosmic rays. However, the burden of ionizing radiation in long-term flights is near the upper limit of hygienic norms. Work in space suits outside the spacecraft is limited from the same reason. Serious danger of radiation will be a problem in the future voyages planned to reach Mars and other planets.

The body adapts quite well to the conditions of the weightless state but transient (mainly cardiovascular and postural) difficulties arise after landing because the regulatory systems are disaccustomed to the normal gravitational force of 1 G.

## 2.3. SEA SICKNESS (KINETOSIS)

Short changes of speed of different direction irritate the otolith apparatus of the inner ear. The chaotic signals from the utriculus are conveyed to the vegetative centers of medulla oblongata and the cerebellum together with signals from muscle spindle and tendon receptors. These parts of the nervous system are responsible for the symptoms of the sea sickness, namely nausea, hypersalivation, vomitus, changes of heart rate, pallor, faint and others. The sensitivity to kinetosis is individual. Some people do not suffer from travel on rough sea, others become sick during every trip by car or plane. Forced slow and deep breathing and visual control of the motion may be of some help against kinetosis.

# 3. HYPOBARIA AND HYPERBARIA

The atmospheric pressure on the surface of Earth is 101.3 kPa (760 torr or Hg mm or 1 ATA). Small fluctuations (± 3 - 4 kPa) of this pressure occur in connection with meteorological events and these exert certain influence on the physiological functions and health state. The study of meteorological and climatic effects on health and disease is the topic of **bioclimatology** and **meteoropathology.**

## 3.1 HYPOBARIA

The atmospheric pressure decreases parallel with the altitude (Table 3) and above 3 km **mountain disease** can develop due to the decreased partial pressure of oxygen. The main etiologic factor of mountain disease and other similar conditions is the lack of oxygen. All forms of **hypoxia** are described elsewhere.

In addition to lack of oxygen hypobaria threatens the body with damage due to distension of gases in hollow organs. Pain from middle ear and paranasal cavities can occur during flight in high altitudes in non-pressurized cabins if the communication of these cavities with the surrounding atmosphere is blocked. Gas pockets in carious or improperly filled teeth can also manifest with acute toothache in hypobaric conditions. The gases normally present in gastrointestinal tract expand, stimulate the stretch receptors in the intestinal wall, the peristalsis becomes more active and gut cramps may occur.

The ultimate limit of human tolerance to hypobaria is about 6.25 kPa which corresponds to an altitude of 20 km. This is the vapour pressure of water at 37 °C, and at this pressure the body fluids boil at body temperature causing death within a couple of seconds.

Tab 3

THE RELATIONSHIP BETWEEN ALTITUDE AND AIR PRESSURE

| **Altitude**<br>**km** | **Air pressure**<br>**kPa** | **Air pressure**<br>**Torr** |
|---|---|---|
| 0 | 101,3 | 760 |
| 0,5 | 95,4 | 716 |
| 1 | 89,4 | 671 |
| 2 | 78,9 | 592 |
| 3 | 69,6 | 522 |
| 4 | 61,5 | 461 |
| 5 | 54,3 | 407 |
| 8 | 35,6 | 267 |
| 10 | 26,4 | 198 |

## 3.2 DECOMPRESSION SICKNESS (CAISSON OR DIVER'S DISEASE)

During diving the pressure increases by 101 kPa at every 10.3 meters of depth. The solubility of gases in fluids is pressure dependent and therefore in hyperbaric conditions more oxygen and nitrogen is dissolved in the blood, body fluids and cytosol of cells than at the surface of the earth. It is a physical phenomenon and the amount of oxygen bound to haemoglobin does not change. In addition to underwater diving hyperbaric conditions occur in diving-bells (caissons) and during building of underground constructions (in this case the increased pressure is achieved by compressors).

If sudden decrease of pressure occurs, the dissolved gases are released as bubbles which in turn damage cells and obturate small capillaries (**gas embolism**) deteriorating the perfusion of the organs. The bubbles do not form in the blood, but in the tissues and with predilection in the space between joint surfaces. The damage is caused more by nitrogen ($N_2$) than oxygen ($O_2$) because nitrogen is readily dissolved in lipids and its diffusion and elimination from the fat is slow. Bubbles occur already after a sudden decompression of 0.3 atm but these are small, asymptomatic and don't pose any harm.

The highest number of accidents occurs in connection with **scuba** diving (**s**elf **c**ontained **u**nderwater **b**reathing **a**pparatus, allowing diving to 40 m depth) – about one to five accidents for 10 000 diving. Proper training and sophisticated equipment are the best prevention of this condition.

The main symptoms of decompression disease are:

- joint and periarticular pain;
- itching, localized paresthesias, cyanotic mottles on the skin (bubbles in the skin);
- tachypnoe, dyspnoe, substernal pain, dry cough (bubbles in pulmonary capillaries cause pulmonary hypertension);
- variable signs of CNS dysfunction (motor and sensitive disorders, disturbed motility of the guts, etc.) up to delirium and loss of consciousness (bubbles in the brain capillaries, brain vasospasms);
- activation of the coagulation system.

After years of diving and repeated decompression sickness irreversible diffuse brain damage can develops. In people with foramen ovale patent (10-20% of the population) the possibility of arterial embolisation during decompression is an additional possible pathological condition.

The prevention of this disease is simple - slow decompression leaves enough time for the released gases to be eliminated without bubble formation. The first aid is based on the same principle: recompression in a pressure chamber and slow decompression thereafter.

In unexperienced and poorly trained divers the upholding of the breathing and the high pressure in the lungs can lead to **arterial air embolism** with severe neurological symptomatology (seizures, paralysis). This condition which can be fatal, is not related to the decompression.

Principially the same process as in divers' disease takes place when the decompression occurs at high altitudes, for example if the pressurized cabin of a high flying plane is damaged. The pressure falls in a split of second from normal to very low value (27 kPa at 10 km), **explosive decompression** occurs with air embolism, distension or rupture of the hollow organs combined with acute hypoxia. In these cases the altitude and the related time factor is of key importance.

### 3.3 HYPERBARIA

Elevated pressure in itself does not damage the body but physical work in these conditions is very exhausting. Well-trained healthy humans can live and work at pressures up to 50 ATA - 5000 kPa, equivalent to 500 m underwater depth.

Nitrogen from 400 kPa partial pressure exerts narcotic effect on the nervous systems and therefore in such conditions a mixture of helium and oxygen is employed instead of air. In helium atmosphere the forming of voice is distorted - a shift towards higher frequencies occurs making the human speech virtually unintelligible. Under 150 meters despite the use of helium **high-pressure nervous syndrome** develops with tremor, somnolency, vomiting and microsleep It can be prevented with other gas mixture formulas. For example a mixture of $H_2$ + He + 1 % $O_2$ enables to reach 400 meter depth. The amount of oxygen in these mixtures is very low but its due to the overall high pressure its partial pressure is high enough to keep the haemoglobin fully saturated. The pathogenesis of the depth narcosis and the high-pressure nervous syndrome is not fully understood but it is connected with the changes of biophysical properties of cell membranes.

Artificial hyperbaria with **hyperoxia** is used in the treatment of carbon monoxide poisoning and other conditions but in these cases increased oxygen concentration is the primary objective and not the increased pressure.

# 4. THERMAL INJURY

The effects of local high or very low temperatures on the body lead to **burns** or to **chilblains**, respectively.

Man survives at elevated or low ambient temperatures in a limited range by means of his thermoregulatory processes. If these are overridden, **hyperthermia and hypothermia** develop. **Sunstroke** is a special case of hyperthermia. On the other side **fever** is not a disturbance of thermoregulation, because in this case not external influences change the body temperature but the thermoregulatory center is set to a higher value.

Most enzymes function optimally at 37 °C and at temperatures above 42 °C they inactivate quickly (with the exception of the enzymes of thermophil bacteria living in hot springs). At 50 °C the cytosol of the cells coagulates. Low temperatures (above 0 °C) do not affect the structure of proteins but they simply stop working. At temperatures below 0 °C and during subsequent melting) crystals of ice can damage the subcellular structures.

## 4.1. BURNS (COMBUSTIO)

Local effect of temperature over 50 °C causes burn injury with overall effects on the organism according to its degree and area of damaged body surface (Tables 4 - 6). Small burns or scalds cause pain, leukocytosis and transient elevated body temperature. Burns of large area of body surface trigger the stress reaction. Through denuded body surface pathogen microorganism can enter the body and because the immune function is deteriorated, **sepsis** can develop.

Severe burn injury threats with **burn shock**, which is a special form of **hypovolemic shock**. The damaged skin allows uncontrolled loss of extracellular fluid and in addition the capillary permeability is increased due to direct damage of the capillary wall in the burned area, massive histamine and prostaglandin release and presence of toxic breakdown products of burned tissues in the circulation. The chemical mediators and toxins act not only in the site of injury, but in distant organs as well. The fluid loss and its translocation from the vessels into the extravasal space leads to decreased plasma volume, increased hematocrit and blood viscosity. If the fluid replacement is not sufficient, acute praerenal kidney failure can develop.

The metabolic response to severe burns is characterised by increased basal metabolic rate, protein catabolism with loss of lean body mass and raised core temperature. In addition hyperdynamic circulation, mild haemolysis and compromised immune function are usually present. Warm ambient temperature (32 °C) and pain relief are effective means of limiting the hypermetabolic state which otherwise can last some weeks.

Tab 4

SCALDING WITH HOT WATER

| **Temperature of water, °C** | **Time of action leading to serious injury** |
|---|---|
| 49 | > 5 min |
| 53 | ≈ 1 min |
| 56 | ≈ 15 sec |
| 60 | ≈ 5 sec |
| 65 | ≈ 2 sec |
| 69 | ≈ 1 sec |

Tab 5

FEATURES OF BURN INJURIES ACCORDING TO THEIR DEGREE

**1st DEGREE – COMBUSTIO ERYTHEMATOSA**

Only the epidermis is damaged. Characterised by necrosis of keratinocytes, vasodilatation in the dermis, red and aching skin. Heals without scars.

**2nd DEGREE – COMBUSTIO VESICULOSA**

**2a Superficial - only the epidermis is affected**

**2b Deep - both the epidermis and the dermis are damaged**

Necrosis of the epidermal (a) and (b) the dermal cells, intra- and extracellular oedema, subepidermal blisters and perivascular lymphocyte and neutrophil infiltration. Usually heals without scars but hyperpigmentation can be left over

**3rd DEGREE – COMBUSTIO ESCHAROTICA**

**3a Dermal - affecting only the skin**

**3b Subdermal - affecting the tissues under the skin (muscles, bones)**

Devastation of the skin and its adnexes, necrosis and damage of subepidermal structures, blisters, scabs, oedema, inflammatory infiltration.

Heal with scars. Skin transplantation and plastic surgery is usually necessary to prevent the forming of deforming hyperplastic scars

**4th DEGREE - CARBONISATIO**

Complete destroying, charring of tissues.

Tab 6

CLASSIFICATION OF BURN INJURIES ACCORDING TO SEVERITY AND RANGE

| | CLINICAL RATING | % TBSA TOTAL | % TBSA DEEP |
|---|---|---|---|
| 1 | SMALL[1] | < 20[3] | no |
| 2 | INTERMEDIATE | 20 – 25 | < 10 |
| 3 | HEAVY | 25 – 40 | 10 – 20 |
| 4 | CRITICAL[2] | > 40 | > 20 |

NOTES:

TBSA % = Percentage of **t**otal **b**ody **s**urface **a**rea affected.

[1]Only if injury of face, hands, feet and perineum is absent.

[2]Every burns in children under age 3 years and in people older than 60 years should be considered as critical. The same holds for burns combined with trauma, smoke intoxication and other aggravating conditions (e.g. cardiovascular disease, diabetes, etc.)

[3]In children the boundaries are 5 – 10 % lower

The mortality after burn injury depends on percentage of total body surface area burned (% TBSA), on the age and general health state of the injured and on the presence of complicating factors (trauma, smoke inhalation, infection, etc.). In the past 40 years considerable progress in treatment of burns took place. Now even patients with 70 - 90 % TBSA burned have good chances to survive the injury which is in striking contrast with the older data about high mortality after 33 - 50 % TBSA damage. The improvement is due to adequate fluid and electrolyte replacement, early excision of the damaged tissues, subsequent coating the wounds with natural or artificial skin preparations, auto- and allotransplantation of skin and appropriate antimicrobial pharmacotherapy.

### 4.2. CHILBLAIN (CONGELATIO)

Depending on the temperature and the time of action the skin is first pale (vasoconstriction) and aching, later cyanotic (vasodilatation), the pain ceases and parestheses or total anaesthesia develop. In the worst cases blisters, skin oedema and necrosis can occur with subsequent wet gangrene. The cold injury develops more rapidly and at relative higher temperatures if the circulation of the affected limb was deteriorated before the injury.

### 4.3. HYPERTHERMIA

There are four ways to lose excess heat produced by the body or absorbed from the environment:

1. **Radiation** is a simple physical phenomenon. Every object radiates energy according to its absolute temperature.
2. **Conduction** of heat to cooler things. A cold shower, contact with cold things or a cold drink cools the body in such way.
3. A breeze cools through **convection.**
4. The last but the most important way of thermoregulation is connected with sweating. The **evaporation** of every gram of water brought to the surface of skin by the sweat glands needs 2.4 kJ of energy. If the ambient temperature is higher than the temperature of the body, this is the only way to lose heat.

In warm and dry environment (e.g. in sauna, in ironworks and other similar workplaces) the blood perfusion of the skin and the excretion of sweat increases, and heat is lost through evaporation. This type of thermal burden is tolerated well until adequate replacement of lost fluid (which is slightly hypotonic) is maintained. Without fluid supply dehydratation develops with hypovolemia, blood hyperviscosity, low blood pressure with fainting. The first symptoms are muscle cramps and exhaustion (**heat cramps, heat exhaustion**). Inappropriate fluid replacement (pure water without electrolytes) can lead to dangerous hypokaliemia.

In warm humid environment, or if the evaporation of sweat is hampered by tight suit, this last thermoregulatory system is unable to function and hyperthermia develops. The body temperature rises together with the heart and respiration rate and the blood pressure falls. In this stage collapse can occur. As the core temperature reaches 40 °C fatigue, headache, buzzing in the ears and later vomitus and muscle seizures appear. (**heat stroke**). At 43 °C loss of consciousness ensues with subsequent failure of the circulation and irreversible damage of the nervous system. In general practice two types of heat stroke occur:

1. **Exertional heat stroke** typically affects military recruits, marathon runners, workers in foundries, etc. In its severe form it can be connected with lactic acidosis, decomposition of muscles (rhabdomyolysis) and acute tubular necrosis with kidney failure.
2. **Classic heat stroke** affects mainly children, older, obese and ill people. Due to hyperventilation respiratory alkalosis can develop.

### 4.4. SUNSTROKE (INSOLATIO)

If the thermal burden due to sunshine is concentrated on the uncovered, sometimes hairless head, (small children, old people) symptoms similar to hyperthermia can develop without dehydratation and without failure of the thermoregulatory systems. The symptoms are probably caused by local overheating of the nervous system and by meningeal and brain vasodilatation and hyperaemia.

### 4.5. HYPOTHERMIA

The body temperature of **poikilotherm** animals varies with the ambient temperature, whereas **homoiotherm** creatures maintain their core temperature within narrow range. Some mammals, called **hibernates** survive winter in a dormant state with decreased core temperature, metabolism, respiration and heart rate (e.g. bear, hedgehog, marmot). **Hypothermia in humans** is a pathological condition defined as core temperature of the human body below 35 °C.

In cold environment the perfusion of blood in the skin is diminished and piloerection appears (goose pimples). The skin and the immobilized layer of air on its surface act as thermal insulators. Man has lost his fur in the process of evolution and therefore he is forced to wear suit as additional thermal insulator.

In addition to the decreased heat loss in cold environment the production of the heat is increased by muscle work or by shivering. Fat has a dual role in thermoregulation. It acts as an insulator and can also produce heat through fat catabolism. This process is regulated by hormones (e.g. catecholamines and thyroid hormones).

**The adaptability to cold** varies with age, health status and other conditions. **People living in cold climate** (Eskimos) have better developed thermoregulatory adaptation against cold than people living in warmer parts of the Earth and individual adaptation to cold through inure is also possible. **Newborns babies** posses some brown body fat which safeguards them from hypothermia. The brown fat is used up in the first days of life and premature infants whose thermoregulatory system is not completely matured are prone to hypothermia. On the other hand newborns tolerate the consequences of hypothermia better than the adults. Thermoregulation and cold adaptability is deteriorated in the **elderly**. Fat is one of the best heat insulators and therefore obese people better bear cold than lean persons. People with strong muscles and vast energy reserves can produce more heat than their weak and undernourished counterparts. Patients with insufficient circulation, muscle weakness, diminished function of the thyroid gland and those suffering from Addison's disease are especially prone to hypothermia.

Striated muscles, the main producents of energy are able to produce enough heat only some hours because of fatigue and glycogen depletion. **Exhaustion** (e.g. in mountain-climbers without appropriate training and acclimatisation) therefore leads to rapid development of hypothermia. **Alcohol** and some drugs acting on the nervous system paralyze the thermoregulatory center. Alcohol in addition causes vasodilatation and a false feeling of warmth. This is the explanation of the well-known fact that drunk unconscious people can die from hypothermia even at moderate ambient temperatures.

If the adaptability range of the thermoregulatory system is overridden, the core temperature of the body begins to fall. At core temperature of 33 °C one becomes stuporous and muscular rigidity sets in. The heart and respiratory rate decline. At 30 C the shivering ceases and at 27 °C the muscles become flaccid and consciousness is lost. At this temperature fibrillation of the heart chambers can lead to sudden death. At lower temperature death due to circulation and respiration arrest ensues although individual cases of survival have been reported after core temperatures as low as 18 °C.

**Immersion cooling** is a special case of hypothermia. The skin is quickly cooled to the ambient water temperature and survival depends on the thickness of subcutaneous fat layer. Exercise (swimming) in cold water increases the heat loss. Death in very cold water can ensue within hours.

In cold weather the probability of viral and bacterial infections of the respiratory tract is increased for various reasons (the decreased blood flow deteriorates the defensive functions of skin and mucous membranes of the upper airways) and although bad weather is not the true etiologic agent of these diseases (it is probably only their triggering condition) the term **"common cold"** is widely used to date.

Hypothermia reduces the metabolic rate and the oxygen demand of the tissues. During controlled hypothermia or **artificial hibernation** the blood supply of the brain may be interrupted or the heart may be stopped for a few minutes without causing irreversible damage of brain cells. This technique was employed in the past in cardiac surgery but was already replaced by modern artificial heart and lung devices.

## 5. THE EFFECT OF ELECTRICAL CURRENT ON HUMAN BODY

The effect of electrical current on human body depends on various factors:

- the intensity and voltage of the current;
- the time of its action;
- the type of the current (alternating - A.C. or direct - D.C.);
- the frequency, if the current is A.C.;
- the resistance of the body;
- the path of the current within the body.

As a rule of thumb one should remember that every current above intensity 0.1 A and voltage 50 V and of duration more than 1 second threatens the life. Alternating current is more dangerous than direct and the most dangerous frequencies are between 30 - 150 Hz.

The dry human skin is a good insulator but moisture decreases its resistance considerably. Ohm's law holds also in this case and therefore the intensity of the current flowing through the body will be much greater if one shuts the electric circuit with moist hands than if his skin is dry.

*Ohm's law*

*The higher is the voltage (U), and the lower is the resistance (R), the higher is the intensity (I)*

$$I = U/R$$

Within the body the current follows a path corresponding to the least resistance. Body fluids, muscles and nerves are the best conductors because they contain ions in high concentration. Putting two fingers into a current outlet leads therefore only to painful experience but if the current crosses the heart, sudden death can follow.

The electric current depolarizes the membranes of the cells. This is the cause of **muscle cramps, general seizures, respiratory arrest, loss of consciousness with amnesia and fibrillation of the heart chambers**. Heart fibrillation ensues when the electrical impulse crosses the chambers in the **vulnerable period** that is during the T wave. Ventricular fibrillation is the most serious consequence of electrical injuries because it is hemodynamically equivalent to cardiac arrest and without reanimation leads to death.

Within the cells the electrical current tranlocates the ions and disturbs the function of intracellular organelles. The energy of the electrical current transforms into heat and may cause burns. The production of the heat depends on the resistance of the tissue and therefore burns affect mostly the skin in the places where the current enters and leaves the body. The heat formed along the path of the current within the body coagulates the cytosol of the cells and can damage the vessel wall causing thromboses. High voltage electrical injury or injury by lightning can cause serious and large $3^{rd}$ degree burns.

The effect of the electrical current on the central nervous system is employed in the treatment of certain psychoses as electroshocks. Alternating currents of several hundred mA are applied transversely across the cerebrum causing transient loss of consciousness but after recovery the symptoms of the diseases are attenuated. This method was strongly criticized in the famous novel of Ken Kesey (Flying over cuckoo's nest, later filmed by Milos Forman) but its current mode of application is quite different from that depicted in the book and the movie.

Electrical current can cause heart fibrillation but on the other hand cardiac arrest can be successfully treated with short impulses of direct current - **defibrillation**. The energy of impulses is 200 - 360 Joule for adults. The same principle is employed in treatment of atrial fibrillation, but in this case (**cardioversion**) the electric impulse is very carefully timed not to reach the ventriculi in the vulnerable period. In **cardiac pacemakers** properly timed weak electrical impulses substitute for the missing function of the heart's own pacemakers. Weak A.C. currents are employed also in various procedures of **physical therapy** and **electroacupuncture**.

## 6. THE EFFECTS OF THE ELECTROMAGNETIC FIELD ON THE BODY

Between two electrically charged objects of opposite sign electric field and between two poles of a magnet magnetic field exists. Fluctuations of the intensity of either magnetic or electric field create electromagnetic waves. They are characterized by the frequency of the fluctuations and by the intensity of the electromagnetic field. All these waves propagate in vacuum with the speed of light ($3*10^8$ $m.s^{-1}$) and this value divided by the frequency (waves in one second, Hz) gives the wavelength of the radiation (Table 7). According to the quantum physics electromagnetic waves are at the same times small particles - photons. The energy of the radiation is in linear relationship with the frequency of the waves.

The range of the electromagnetic waves is extremely wide. Alternating electrical current (50 Hz) creates waves 6000 km long. The waves employed in broadcasting and television begin at kilometer (or kHz) and end somewhere in the centimetres (hundreds of MHz) range. Man and animal see waves between 760 nm and 380 nm as colours and green plants use the energy of this radiation to produce organic material and oxygen from water and carbon dioxide (photosynthesis). The artificially generated waves in X-ray devices, the gamma rays emitted from radioactive materials and arriving from the cosmos have wavelength below nanometres range and frequencies between $10^{16}$ - $10^{24}$ Hz and are carriers of dangerous amount of energy.

All these waves generated by natural (cosmos, sun, radioactive background radiation) or artificial (fire, light, radio, TV stations, electrical circuits) sources constantly bathes the earth and surrounds every object or living creature. Considering the biological and health effects of electromagnetic waves the basic but often neglected law is very simple:

| |
|---|
| *Only the absorbed radiation can exert an effect.* |

Tab 7

THE ELECTROMAGNETIC WAVES

| SOURCE | FREQUENCY | WAVELENGTH |
|---|---|---|
| Alternating electrical current | 16 – 50 Hz | 18000 – 6000 km |
| Radio and TV waves | | |
| long | 150 – 300 kHz | 2 – 1 km |
| middle | 500 – 2000 kHz | 600 – 150 m |
| short | 6 – 20 MHz | 50 – 15 m |
| UHF | 20 – 300 MHz | 15 – 1 m |
| Microwaves, radar | 0,3 – 1000 GHz | 1 m – 300 μm |
| Light | | |
| infrared | $10^{12}$ – $3{,}9 \cdot 10^{14}$ Hz | 300 μm – 760 nm |
| visible | $3{,}9 \cdot 10^{14}$ – $7{,}8 \cdot 10^{14}$ Hz | 760 – 380 nm |
| ultraviolet (A,B,C) | $7{,}8 \cdot 10^{14}$ – $3{,}0 \cdot 10^{16}$ Hz | 380 – 10 nm |
| Gamma and cosmic rays | > $3 \cdot 10^{16}$ Hz | < 10 nm |

NOTES

The energy of the radiation is directly related to its frequency according the equation $E = h\eta$, where "$\eta$" is the frequency of the radiation and "h" is the Planck's constant: ($h = 6.623 \cdot 10^{-34}$ Js).

One photon of a 100 MHz UHF radio signal carries therefore = $6.62 \cdot 10^{-26}$ J energy; a "red" photon of 760 nm wavelength = $2.6 \cdot 10^{-19}$ J and a 10 nm X-ray photon = $2 \cdot 10^{-17}$ J energy.

To warm 1 g water by 1 °C = 4.2 J is necessary, that is = $1.6 \cdot 10^{19}$ photons of red light or = $2.1 \cdot 10^{17}$ photons of absorbed X-ray radiation.

## 6.1. RADIO FREQENCIES

The human body is relatively transparent for these short waves. The absorbed portion of radiation has some heat effect which corresponds to the absorbed amount of energy. It is employed in physical therapy to treat painful muscles and joints (**short wave diathermy -** 40.68, 27.12 and 13.56 MHz).

In the history of medicine mystical beneficial (or harmful) effects were assigned to magnetic and electromagnetic fields and much pseudomedical quackery was based on these misbelieves. Serious research of these topics started only in the recent years. People living in the neighbourhood of radio, TV or radar stations or working close to emitters often complain on different diffuse symptoms (headache, psychic fatigability, etc.) and the results of some reports do not exclude the possibility that strong magnetic or radio frequency electromagnetic field can promote the proliferation of malignant cells and exert influence on the secretion of hormones and on the metabolism of calcium in the cell. The first such suspicion came in 1979 from Denver (USA) were children living close to high-voltage power lines had apparently elevated rates of leukaemia. Despite this and similar claims an expert panel of National Research Council in 1996 after 3 years of work (and reviewing more than 500 clinical and research studies) declared:

*No conclusive and consistent evidence that ordinary exposure to EMFs (electromagnetic field) causes cancer, neurobehavioral problems or reproductive and developmental disorders.*

Nevertheless, three members of the panel stated that: *It is still an open question whether EMFs threaten health.* Some researchers insist that at very high doses EMFs can have biological effects as disruption of chemical signalling between cells, inhibition of melatonin secretion and promotion of bone healing in animals and also that the effects of electrical blankets and video display terminals can harm the developing foetus.

New questions arise from the frequent use of mobile phones and their possible health hazard. Future research is necessary to give unambiguous answers for these open questions.

## 6.2. MICROWAVE AND INFRARED WAVES

Every warm object radiates infrared waves and recently special kitchen appliances (microwave owens) became widely used in households. Biological structures absorb this type of radiation and therefore they have thermal effect. This pose certain danger because much of the radiation passes the skin and is absorbed only in the deep structures lacking thermoreceptors. Overheating with concomitant tissue damage can occur because the nervous system is not alarmed through pain.

Chronic exposure to infrared radiation can cause cataract of the eye lens (**glass-blower's cataract**).

## 6.3. VISIBLE LIGHT

The eye is an optical device which focuses the light on the retina. Visible light of high intensity (sun observed through telescope, the light of lasers and nuclear blasts) can cause retinal burns with blind spots as a consequence. On the other side laser treatment in ophthalmology can save the sight of many patients with diabetic retinopathy, glaucoma or retinal tears.

## 6.4. ULTRAVIOLET LIGHT

The range of the ultraviolet (UV) light is divided into three components:

- UV-C : 100 - 280 nm;
- UV-B : 280 - 315 nm and
- UV-A : 315 - 380 nm.

This high-energy radiation coming from the sun is invisible but it is absorbed well in biological structures. It can disrupt (UV-C) even covalent chemical bonds - damage nucleic acids, proteins and other macromolecules. Oxygen absorbs waves shorter than 240 nm and the ozone layer in the ionosphere those shorter than 290 nm. Vapours of water and dust in the various layers of atmosphere absorb a great part of the remaining UV light. The surpassing small amount of UV-A and UV-B is sufficient to convert provitamin to vitamin D in the skin and irritate the skin to produce melanin and attain a healthy suntan.

Too much sunshine (the sensibility depends on the colour of the skin) can cause **sunburn** which begins with painful erythema and discomfort lasting 8 - 24 hours. Sometimes vesiculation (actually it is a 2$^{nd}$ degree superficial burn) and massive desquamation occur. Gradually increasing doses of UV light enable adaptation of the skin and do not cause such problems. Repeated sunburns or too much sun-bathing after many years lead to degeneration of the skin, to its accelerated aging and can foster the development of skin cancer.

All these dangers became augmented in the past few years. Due to the continuing ozone depletion more short-wavelength UV radiation reaches the surface of the earth (the most at the poles, in spring and summer and at noon). The situation threatens with increasing number of melanoma, skin cancer and cataract not only in humans (who are able to defend themselves) but mainly in the animal kingdom. The first reports on blind sheep and kangaroos from Australia are alarming. Other possible effects may arise in the future, e.g. disturbances of the immune system in humans and animals or the increased number of mutations in plants if the destruction of the ozone will continue.

# 7. THE INFLUENCE OF IONIZING RADIATION ON HUMAN BODY

From physical point of view the important forms of radiation are divided into corpuscular and electromagnetic radiation (Tab.1). Radiation penetrating either living or nonliving matter is partly absorbed and the radiation energy is delivered mainly by means of ionization of atoms and molecules and free radical formation*. The basic units of radioactivity and those employed in radiobiology are given in Tab.2.

* From physical point of view free radical formation and ionization can arise as a result of collision of the accelerated particles with electrons (e.g. alfa and beta particles) or with atomic nuclei (e.g. neutrons). Photons can also hit and excite electrons of atomic or molecular orbits or interact with nuclei of heavy atoms and give rise to electron-positron pairs. The excited particles are sources of secondary, mostly gamma radiation.

Tab.1. The main forms of ionizing radiation

| ELECTROMAGNETIC WAVES - INDIRECT IONIZING EFFECT* |
|---|
| **X – rays**<br>Electromagnetic waves (photos) from X-ray tubes.<br>Penetrate soft tissues, absorb well in bones<br><br>**gamma rays**<br>Electromagnetic waves (photons) a part of cosmic radiation or from decay of radioactive elements. |
| CORPUSCULAR RADIATION<br>CHARGED PARTICLES - DIRECT IONIZING EFFECT |
| **protons ($p^+$)**<br>Exist in great amount in the Van Allen belts surrounding the earth and are produced by solar flares. Absorbed in the highest layers of atmosphere, may be dangerous for space travellers.<br><br>**alpha particles ($\alpha^{2+}$)**<br>Identical with nuclei of helium - two protons and two neutrons.<br>Produced spontaneously in the process of radio - active decay of heavy elements. Enormous ionizing power but short tange of action and low penetrating ability.<br><br>**beta particles ($\beta^-$, $\beta^+$)**<br>High energy electrons or positrons produced by nucle-ar transfor-mation or in accelerating devices. When decelerated can produce high energy electromagnetic waves (electrons in X-ray tube). The only difference between electrons and positrons is in their charge. Positrons interacting with elec - trons annihilate and release great amount of gamma rays. |
| WITHOUT CHARGE - INDIRECT IONIZING EFFECT |
| **neutrons ($n^0$)**<br>Neutrons can interact with matter only when collide with it. Ionization is an indirect consequence of these colisions. |

*The other types (light, thermal radiation, radiowaves) ofelectromagnetic radiation are nonionizing.

Tab. 2. Basic units of radiobiology

| UNIT | SYMBOL | DEFINITION | EXPLANATION, OLD UNITS |
|---|---|---|---|
| ACTIVITY | BECQUEREL, Bq | $s^{-1}$ | 1 Bq = 1 radioactive decay in 1se-cond<br>Old unit: Curie, Ci<br>1 Bq = $2.7*10^{-11}$ Ci |
| RADIATION DOSE | | C/kg | Coulomb/kg<br>The dose of radiation which in 1 kg of air forms 1 coloumb of negative and 1 C of positively charged particles<br>Old unit: Röntgen, R<br>1 C/kg = 3876 R |
| ENERGY | JOULE, J | $m^2*kg*s^{-2}$ | Unit often used in radioacti vity: eV (electronvolt) or MeV<br>1 J = $6.242*10^{12}$ MeV |
| ABSORBED DOSE | GRAY, G | J/kg | Old unit: rad<br>1 Gy = 100 rad |
| EQUIVALENT DOSE | SIEVERT, Sv | | RBE=relative biological efe-ctivity. Its value form some common types of radiation x, gama and beta rays = 1<br>alpha particles = 20<br>neutrons = 2 – 10<br>Old unit: rem 1 Sv = 100 rem |

## THE RADIATION BACKGROUND, PROFESSIONAL AND OTHER EXPOSURE

It is important to take into consideration that we live in an environment with a certain natural radiation level **(radiation background)** which penetrates here both from the space **(cosmic radiation)** and from the soil (**terrestrial radiation)**. To this natural radiation in this century man-made sources of ionizing radiation were added. The average dose of natural background radiation is about 0.5 - $1*10^{-3}$ Gy yearly. However, there is a great geographic variability in the value of the terrestrial radiation. For an example in the inland of state Denver (USA) the mean value of absorbed radiation is more than $10^{-3}$ Gy/year but on the coastal area of Cape Kennedy only a tenth of it. Furthermore different building materials have different level of natural radioactivity. Personsliving in stone buildings are exposed to a higher risk of cumulative radiation damage (due to radon emission) than inhabitants in wooden buildings.

A further source of ionizing radiation in the living organism is the **potassium isotope $^{40}$K, an emittor of β-radiation.** $^{40}$K constitutes 0.0012 % of potassium in the nature and has a half-time of $1.3*10^9$ years. From $^{40}K$ our body receives approximately a dose of another $10^{-3}$ Gy per year. In a lifetime of 70 years it presents 0.07 Gy of cumulated radiation dose.

For different professions it is necessary to add further radiation doses to the background radiation. It concerns namely health workers dealing with diagnostic or curative X-ray and other radiation sources. The introduction of effective safety measurements and modern equipment with low radiation level led to substantial reduction of this type of radiation exposure. It exceeds now the yearly dose of 0.01 Gy only exceptionally. Principially the same is true for patients undergoing X-ray investigations.

In some cases the radiation exposure can exceed the background level considerably. Atomic bombs (thrown to Hiroshima and Nagasaki in 1945), tests of atomic and hydrogen bombs, accidents in nuclear plants (Tchernobyl, 1986) exert twofold effects: Near the epicentre of the blast or the accident the radiation dose usually reach deadly levels, and in remote regions the radioactive fallout and the elevated background radiation can do harm to large number of people. Elevated radiation exposure restricted to individuals occur furthermore in uran mines, during nuclear laboratory accidents and in patients undergoing tumor radiotherapy. The handling and storage of radioactive waste materials (especially those with long half-life) poses a very important ecological problem.

## THE EFFECTS OF IONIZING RADIATION ON LIVING MATTER

The biological effects of ionizing radiation are extensive. There is no part of the body not affected by it but it is evident that there are different functional changes in every tissue originating from absorption of radiation energy. From biological point of view it is significant that the slower is the movement of the radioactive particle, the bigger is its ionization effect. (A single alfa particle can give rise to 20 - 60 thousand ion pairs while penetrating a 1 cm layer of water, whereas the energetically more powerful gamma radiation is far less effective from this pont of view.) This property of radiation is expressed in the factor termed "Relative Biological Effectivity (RBE)" and in the sievert (Sv) unit (Tab. 2).

The effect of ionizing radiation on living organism is at present explained by two theories which are not mutually exclusive:

* **The shot theory** (**direct effect**) states that radiation damages sensitive parts of biomolecules directly while handing over energy to the target molecule.
* According to **the radical theory** (**indirect effect**) radiation penetrates into the molecules of water, causing radiolysis of water and creating highly reactive free radicals which enter into reactions with biologically important macromolecules. (These free radicals are usually ions at the same time but the two terms are not synonyms).

Free radicals have a high affinity to biologically significant molecules and can damage nucleic acids, proteins, lipids and polysaccharides. On the other side due their high reactivity they are soon inactivated by the surrounding molecules with redox ability or neutralized by the different mechanims of **antioxidant defense system** present in all cells, tissues and in the body fluids.

For better understanding the effects of radiation can be divided into four stages:

* **physical** - the radiation hits an atom or molecule;
* **physicochemical** - free radical formation and ionization;
* **chemical** - reactions of free radicals, damage of biological macromolecules and
* **biological** - subcellular, cellular and tissue damage, radiation disease or late genetic consequences (carcinogenesis, mutations).

## CELL AND TISSUE DAMAGE CAUSED BY RADIATION

At the **cell level** radiation leads to functional and structural alterations of biological membranes, proteins and nucleic acids. From lysosomes hydrolytic enzymes are released and the ATP synthesis in mitochondria is decreased. The cells are, however, able to repair this type of damage during relatively short time

One of the crucial effects of ionizing radiation is the damage of the genetic code, particularly of chromosomes during the mitotic cycle with successive suppression of cell mitotic activity and other consequences. Single-strand breaks can be repaired but double-strand damage leads usually to irreperable chromosome damage.

According to its consequences the damage can be divided into three types:

* **pure somatic damage** (at cell level loss of mitotic capacity, membrane, mitochondrial and other organelle damage)
* **genetic damage restricted to the somatic cells** of the given individual (possible consequence: carcinogenesis)
* **genetic damage of the gametes** witch can be handed over to the next generations (new mutations manifesting in the next generations).

The first type of injury requires relatively high doses of radiation (above 2 Gy) whereas a few, otherwise harmless quantums of absorbed energy can change the genetic information (2nd and 3rd type of damage) with the possibility of severe late consequences.

The range of tissue damage caused by ionizing radiation depends on the kind and dose of radiation, on the total condition of the organism and on the length of radiation. A given dose divided into small portions exerts lesser somatic effects than the same dose absorbed at once because less cells are killed and the others have time to regenerate. On the other side, the probability of genetic damage is higher in the case of repeated doses. The effect of radiation is furthermore different depending on the fact whether the radiation is local or affects the whole body.

Single tissues and organs have different sensitivity to ionizing radiation. In general cells with high mitotic rate are very sensitive to radiation whereas postmitotic cells are usually resistant. The sensitivity of tissues furthermore depends on their metabolic intensity and grade of differentiation. According to this aspect we divide the tissues of human body into:

* **radiosensitive** (bone marrow, lymphatic tissue, mucosa of small intestine, bone marrow, gonads)
* **radioresistant** (muscle, kidney, liver, endocrine organs except gonads).

A specific case of extreme sensitivity towards radiation injury is the **developing fetus** especially in the first weeks of intrauterine life.

In addition to external radiation injury the body can be contaminated with radioactive materials through inhalation, ingestion or directly (through injuries or in the case of surgical implantation of radioactive sources).

## DOSE-RESPONSE RELATIONSHIP

Despite intensive research discussion is going on about the problem whether the effect of ionizing radiation has got a quantitatively determinable threshold or any small dose of ionizing radiation has its own harmful, though tiny effect. In such case it would mean a non-threshold effect. The problem is probably unresolved because small doses cumulate during a lifetime and their effect manifest only after a long latency.

There might be another possibility, namely that very low doses of ionizing radiation may have a stimulating effect on some biological functions. In such cases one cannot speak about a direct relation of the dose and its effect which could be rather expressed by a **"J" shaped curve.** The plausibility of this model seems to be supported by experiments and the results of a study, which states that employees of nuclear laboratories live longer than the comparable controls. In this study a significant difference was found between qualified staff exposed to higher doses of radiation and manual workers with lower expositions. In the second group an inverse correlation of tumour occurence and absorbed doses was found. It shows a controversial situation, where the radiation apparently stimulates the biological resistance of organism.

# RADIATION DISEASE

Radiation disease (morbus ex irradiatione) can be initiated either by external radiation or by internal contamination of organism and according its course can manifest as acute or chronic form.

**Acute disease from radiation** develops after a single irradiation of the whole body with high doses of ionizing radiation. We distinguish four stages of acute radiation disease and three types according to the main symptoms:

**1. The stage - primary reaction**

Nausea and vomiting (after dose 2-3 Gy these may be the only symptoms), lassitude, irritability, higher temperature, accelerated breathing.

**2. Latent stage**

No clinical symptoms but apparent changes of blood count as a result of hemopoiesis inhibition (leukopenia, thrombocytopenia, reticulopenia)

**3. Stage of evident clinical symptoms**

Manifestation of hemorrhagic diathesis, further inhibition of hemopoiesis, increased permeability of cell membranes, decreased immunity with bacteremia or sepsis - for further details see the description of the radiation syndromes.

**4. stage - reconvalescence or transition into the chronic form of the disease or death.**

According the main clinical symptomes three forms of radiation disease can occur:

**1. Bone marrow (or hematological) syndrome**

It occurs after radiation with doses in the range of about 2-10 Gy. The symptoms of the primary stage subside after one day but 2 - 3 weeks later purpura, petechiae and signs of deteriorated immunity (infections) manifest. The symptoms correlate well with the changes in red and white cell count.

**2. Gastrointestinal syndrome**

If the dose of absorbed radiation is between 10 - 30 Gy the intestinal mucosa gets rid of its epithelial cells, stops absorbing nutrients and water. From clinical point of view after a short asymptomatic period severe diarrhea and fluid loss occur together with hematological symptoms and infection. Doses around 100 Gy lead to immediate manifestation of gastrointestinal symptoms. This type of radiation disease is usually fatal despite modern treatment techniques (bone marrow transplantation).

**3. central nervous syndrome**

After 20 - 50 Gy the immediate gastrointestinal symptoms are followed with ataxia, sweating, prostration and shock. Huge doses (300 - 500 Gy) can cause immediate death due to CNS dysfunction.

**Chronic disease from radiation** originates either after a single radiaction with subletal dose or after repeated radiation with low doses or after internal contamination by radionucleids. Clinical symptoms include weakness, exhaustion and irritability. Significant are changes in blood count - permanent leukopenia, thrombocytopenia, anemia and hypoplasia of bone marrow. Months or years after irradiation hepatopathy with portal hypertension, renal injury with proteinuria, headache and decrease of mental abilities can occur. Repeated intermediate doses of radiation lead to premature aging.

The symptoms after **local or regional irradiation** are in general less pronounced and depend largely on the sensitivity and properties of the affected organs.

**Late effects of low-leve ionizing radiation** manifest with genetic and carcinogenic consequences. The estimated risk of carcinogenesis and birth defects is around 1000 events in million people after 1 Sv of exposure per year.

The average time of latency between radiation exposure and tumor manifestation is about 10 - 15 years. This fact, however, can be modified by various other circumstances favouring carcinogenesis. In actual fact in the surroundings of nuclear experimental centres in Semipalatinsk (Kazahstan) and Lop Nor (China) there is an extraordinarily high occurence of malignant tumours (in all age groups) and also of birth defects and inborn diseases in children.