Mutagenic and teratogenic environmental factors

Mutagens = factors capable of causing mutations.

Physical mutagens

1. Ionizing Radiation
2. electromagnetic radiation with a shorter wavelength and greater energy than visible radiation: Ultraviolet radiation (biophysics)
3. increased body temperature

Ionizing radiation

- X-rays (RTG), gamma rays, cosmic rays
- It has high energy and passes through tissues
- When passing through tissues, collisions with atoms and the release of their electrons occur, free radicals and ions (H^+, OH^-) are formed along the beam track, which can react with other molecules of the cellular structure, including DNA. DNA atoms can also be directly affected by radiation. Ionizing radiation causes, in particular, the oxidation of bases and breaks the pentose-phosphate bond in the DNA chain; mutagenic effect of irradiation depends on the amount of ions produced.
- *Absorbed dose of radiation* is given in units of *gray* [Gy = J/kg]
- The mutagenic effect depends on the dose, the time of exposure, the phase of the cell cycle and the quality of the repair mechanisms
- Mainly causes chromosomal breaks and subsequently chromosomal rearrangements; event gene mutations
- There is no threshold dose for radiation, and even individual quanta can induce mutation
- The magnitude of the radiation dose, which doubles the frequency of mutations in humans, is important in genetics for risk prediction - especially in the etiology of neoplasia

Ultraviolet radiation (UV)

- has significantly less energy than ionizing radiation, but even UV radiation is able to increase the energy of the electron of the affected atom (excitation)
- is absorbed by many organic molecules, especially purines and pyrimidines
- is a strong mutagen for unicellular organisms; in multicellular organisms it damages only their surface cells → in humans it can cause neoplasia of the skin (carcinomas, melanomas)
- the risk of UV radiation now increases as the ozone content of the atmosphere decreases
- causes mutations mainly through the formation of purine hydrates and pyrimidine dimers (especially '*thymine dimers*)
- **thymine dimers** cause mutations in two ways:
  - 1. disrupts the structure of the DNA double helix and makes it impossible for DNA polymerase to follow the template and thereby interrupt DNA replication
  - 2. when repairing them, bases may be incorrectly included
- repeated interruption of thymine dimer replication without repair of the resulting gap in the newly synthesized chains causes a chromosome break; other manifestations are caused by base substitutions and deletions

Chemomutagens

- chemical substances with a mutagenic effect
- food dyes of acridine nature, smoking products (cyclic hydrocarbons), components of flue gas and exhaust gases, components of plastic materials (PCB-polychlorinated biphenyls)

According to the mechanism of action of chemomutagens:

1. substances causing mutations only during replication: base analogues and acridine dyes

Base analogs = substances structurally related to nucleotide bases and incorporated into DNA during replication, deviations in their structure then cause incorrect base pairing and, as a result, mutations

- are important primarily in the experimental study of mutagenesis processes
- the most widely used analogues of the bases: 2-aminouracil and 5-bromouracil (5-BU = thymine analogue; the bromine atom replaces the methyl at C5 of the pyrimidine and increases the probability of tautomeric shift; in the enol form, 5-BU is paired with guanine; upon incorporation of the enol 5- BU into the new chain during subsequent replication, the keto form of 5-BU is paired with adenine and thus the transition G:C – A:T)

Acridine dyes - ex. proflavine, acridine blue

- induce a reading frame shift; base molecules intersperse between base pairs during replication and change the conformation of the DNA double helix; replication then results in a deletion or insertion of one or more bases with all the phenotypic consequences

2. **substances mutagenic when acting even on non-replicating DNA:** substances causing alkylation, deamination and hydroxylation of bases

Alkylating substances = chemical substances that can be donors of alkyl groups

- the first described mutagen was mustard gas, or its nitrogen derivative
- the most effective mutagens from this group include nitrosoguanidine
- the action of alkylating agents induces a change in base pairing by linking a methyl or ethyl group with thymine
- alkylating agents can cause all known types of mutations, incl. chromosomal breaks and chromosomal rearrangements

Deaminating agents

- cause oxidative deamination of the amino group of adenine, guanine and cytosine
- classic representatives are nitric acid and nitrites
- the amino group of the bases is changed to a keto group by their action
- deamination changes the ability of a base to form hydrogen bonds
- hypoxanthine pairs with cytosine, uracil pairs with adenine
- deamination of bases causes transitions in both directions (C-G to A-T and A-T to C-G)

Nitrogen oxides

- arise from the burning of fossil fuels; the main sources of emissions are electric power plants and automobile transport

Nitrites

- are used to preserve sausages → they threaten mutations, especially of the cells of the digestive tract

Hydroxylating agents

- can change cytosine to hydroxylaminocytosine, which pairs with adenine → thus causing a unidirectional C-G to A-T transition

Links

Related articles

- Mutation
- Mutagens and mutagenesis
- Teratogens
- Teratogenesis
- Congenital developmental defects

Reference

- ŠTEFÁNEK, Jiří. *Medicína, nemoci, studium na 1. LF UK* [online]. [cit. 11. 2. 2010]. <https://www.stefajir.cz/>.