UNIVERSITY of LIFE SCIENCES in Lublin
FACULTY OF VETERINARY MEDICINE

DEPARTMENT OF BIOCHEMISTRY
20-033 Lublin, Akademicka 12
Phone +48 81 445 66 08
www.biochwet.up.lublin.pl

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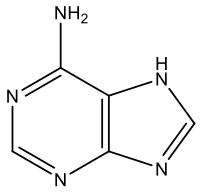
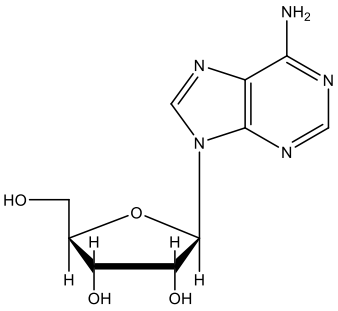
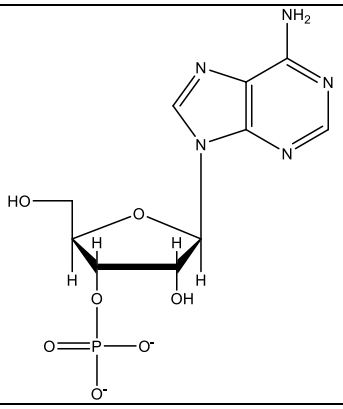
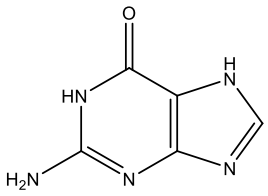
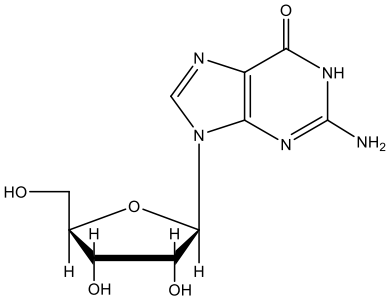
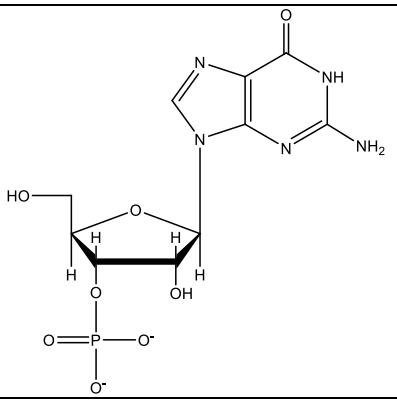
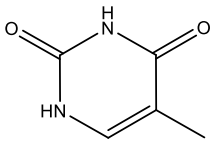
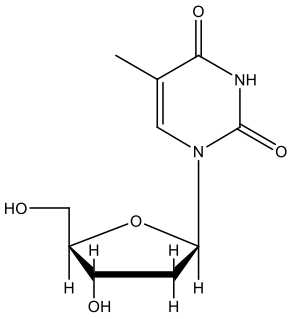
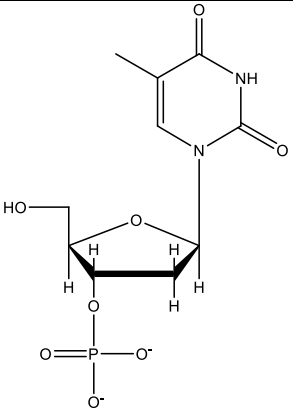
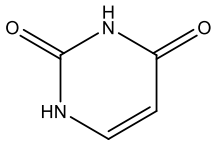
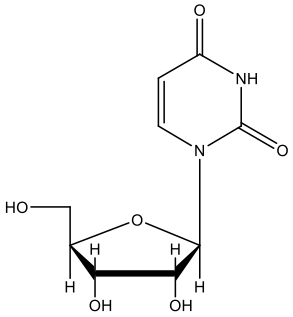
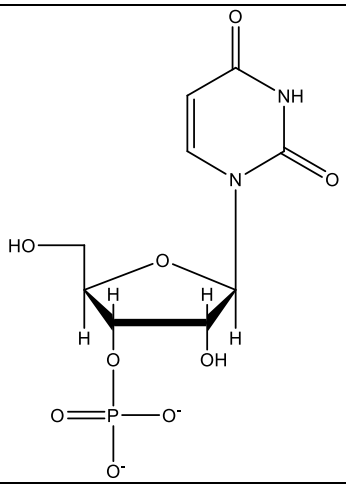
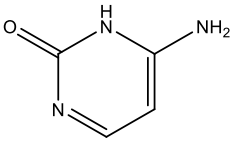
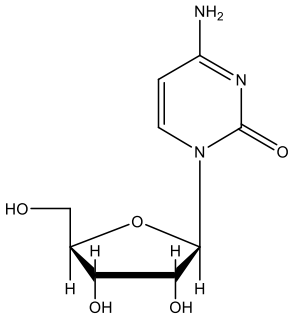
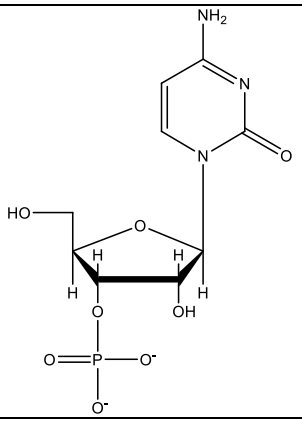
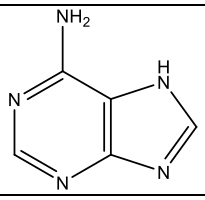
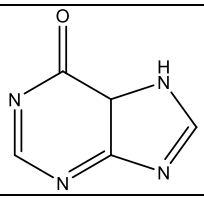
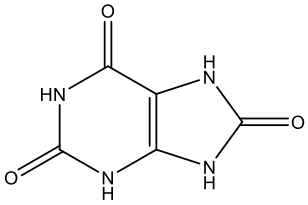
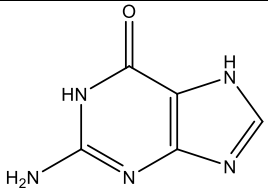
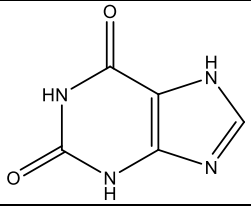
Nucleic acids

Structures of nitrogenous bases and respective nucleosides and nucleotides in DNA and RNA.

Nr	Base	Nucleoside	Nucleotide
1.	adenine	adenosine	adenylate
			
2.	guanine	guanosine	guanylate
			
3.	thymine	thymidine	deoxythymidylate
			

Nr	Base	Nucleoside	Nucleotide
4.	uracyl	urydine	urydilate
			
5.	cytosine	cytydine	cytydilate
			

Derivatives of adenine and guanine

Nr	Base	Derivative	
1.	adenine	hypoxantine	Uric acid
			
2.	guanine	xantine	
			

Maintaining the integrity of genetic material is at the core of life. It is stored in DNA and can be duplicated (replicated) and copied (transcribed). Genetic material consists of triplets of nitrogenous

bases that build the DNA chain. The DNA building block is a nucleotide containing a nitrogen-pyrimidine base (thymine, cytosine) or purine base(adenine, guanine) linked by a glycosidic bond with 5 carbon atoms containig sugar (deoxyribose) and an ester bond with the rest of phosphoric acid. The nucleotides in the chain are connected by a phosphodiester bond. Two complementary DNA strands form an alpha helix connected with hydrogen bonds in accordance with the complementarity rule. It involves the creation of complementary pairs only between the selected nitrogenous bases, ie adenine and thymine - two bonds (uracil in RNA) and guanine and cytosine - three bonds. The alpha helix creates a spatial structure in which 10 pairs of nitrogen bases are used per turn.
RNA is more diverse, it is distinguished by at least 3 types: **mRNA** created by transcribing information from DNA and constituting a matrix for protein biosynthesis, **tRNA**, which transports amino acids to the protein biosynthesis sites and **rRNA** necessary for the proper course of protein biosynthesis. It differs from DNA with sugar (ribose), the presence of uracil instead of thymine, single-stranded structure and function.

Copying, transcribing and translating genetic information is possible thanks to the complementarity rule. Errors in copying and rewriting or damage can occur at any time, hence all cells have mechanisms to repair damaged DNA.

The sources of DNA damage are:
- Endogenous damages caused by among others reactive oxygen species created during physiological cell metabolism especially oxidative deamination.
- Exogenous damages caused by:
  - Physical factors:
    - UV radiation,
    - Ionizing rays,
    - Temperature shock
  - Chemical factors:
    - Nitrous acid,
    - hydroperoxides,
    - hydroxyloamine,
    - alkalizing factors,
    - analogs of nitrogenous,
    - leki psychotropowe,
    - some antibiotics
  - biological factors:
    - some viruses

Endogenous factors can cause the following kinds of damage:
- oxidation of nitrogenous bases and breaking down DNA strands caused by reactive oyygen species,
- removal of complementary base during DNA replication,
- methylation of nitrogenous bases.

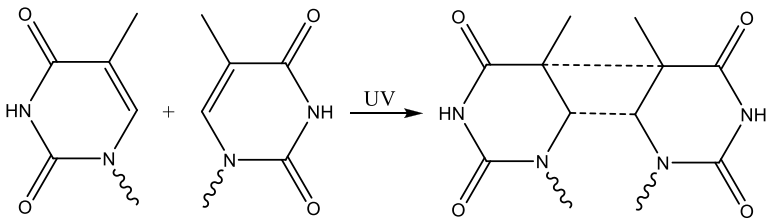
The types of damage caused by exogenous factors are:
• UV rays - cause changes in pyrimidine bases. Under their action, the pyrimidine dimers T-T, C-C, T-C are synthesized causing DNA disruption in replication. UV radiation triggers transitions and transversions.
• ionizing rays - their effect is tumor transformation.
• nitrous acid - causes deamination of nitrogenous bases. This reaction leads to the conversion of adenine to hypoxanthine, cytosine to uracil, and guanine to xanthine. The consequence of this is the replacement of the A-T pair with G-C pair. After DNA replication, transitions occur.
• nitrogen base analogs: 5-bromouracil, 2-aminopurine leads to transitions.

- hydroxylamine - modifies cytosine. This causes the C-G pair to pass into A-T pair.
  • improper food storage leads to the formation of fungus having carcinogenic activity (aflatoxins)
  • some food preservatives, eg nitrites, are mutagenic agents.
  • acridine dyes - penetrating the base pairs, they cause them to be dislodged and consequently errors in replication.

DNA damage usually consists of:
• breaking a single strand of DNA
• dimerization of the adjacent pyrimidine bases T = T
• deamidation of cytosine and its transformation into uracil.

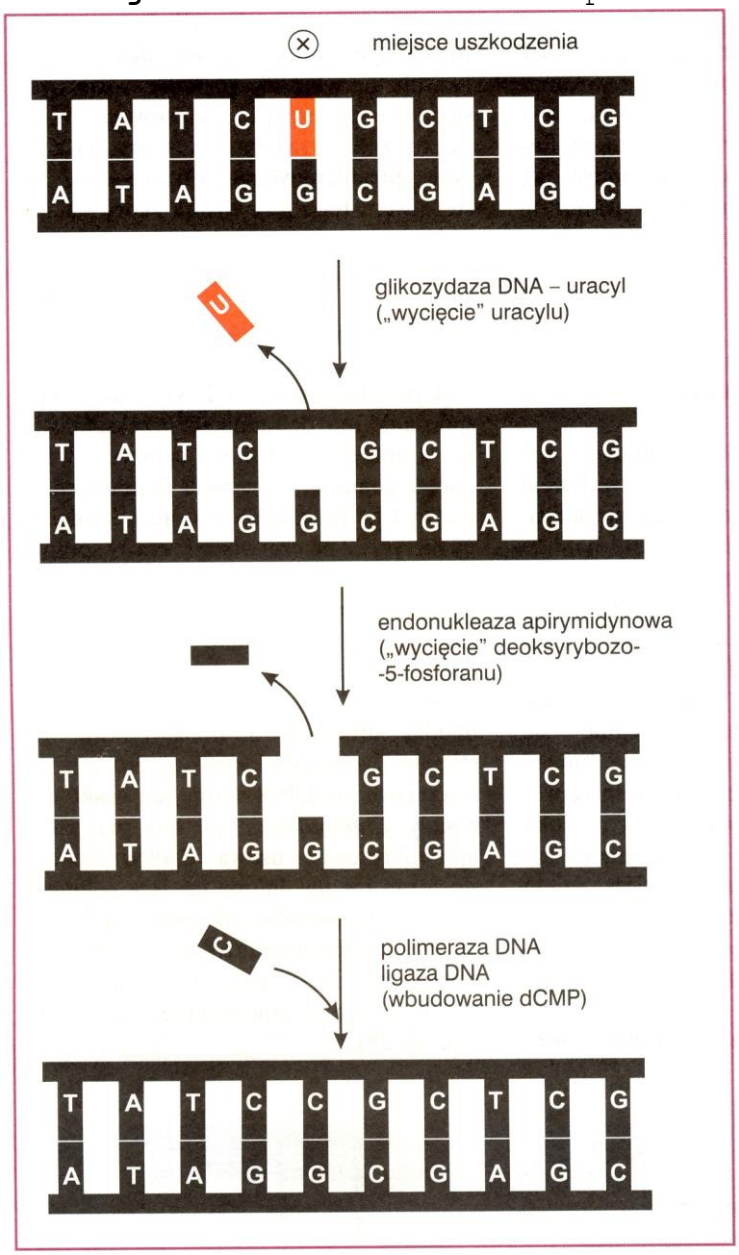
Breaking down of DNA stand can be caused by **endonuclease** action. The repair is based on the activity eg. **DNA ligase.**

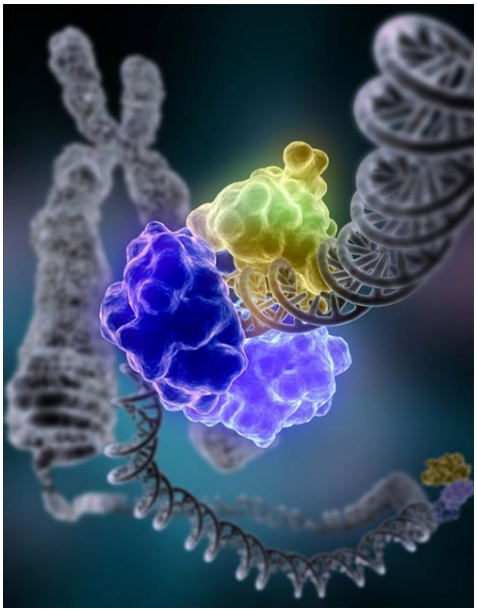
Under the influence of ultraviolet light, adjacent T = T dimerize. The resulting dimer must be cut out because it inhibits replication. In the immediate vicinity of the dimer or next to it, the phosphodiester bond is disrupted by endonuclease. The defective dimer "deflects" allowing the second strand to perform the matrix function. The biosynthesis of the correct 5'-3 'strand of DNA is performed by **DNA polymerase.** The defective dimer is removed by **polymerase I. Ligase** combines the newly formed strand of DNA. The innate lack of endonuclease is the cause of the metabolic defect - **xeroderma.** This defect is manifested by hypersensitivity of the skin to the radiant sunlight, which results in skin atrophy and a tendency to skin cancer.



Ryc. 1 The formation of dimer between two molecules of thymine

Cytosine forms a pair with guanine C = G correctly. As a result of deamination, uracil is formed giving an incorrect U = G pair. The repair system consists in the hydrolysis of the N-beta-glycosidic bond between uracil and deoxy-ribose by specific DNA-uracil glycosidase. At the site of the missing base, a specific endonuclease breaks the DNA strand and then removes the deoxyriboso-5-phosphate. The appropriate nucleotide dCMP is added to the released site, which is complementary to dGMP by **DNA polymerase**. The **DNA ligase** will connect the repaired ends.

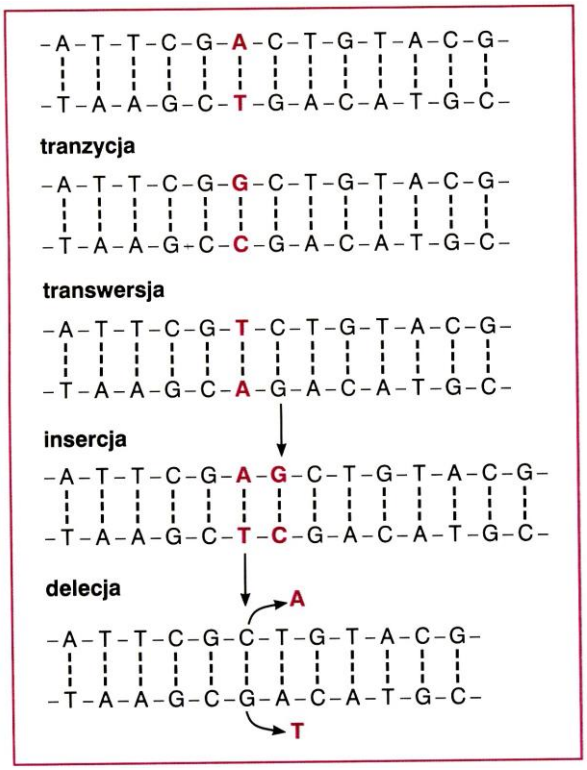




Ryc. 2 DNA Ligase during repair of damaged chromosome (USA National Institute of General Medical Science (NIGMS))

Changes in the nucleotide sequence of DNA are **mutations** among which we differ:

- transitions - replacement of one purine base with a second purine or one pyrimidine with other pyrimidine base,
- transversions - replacing the purine base with pyrimidine and reverse,
- deletions - loss of nucleotide pair,
- additions (insertions) - incorporation of additional nucleotide pair



Mutations can be:
- spontaneous
- caused by analogs of nitrogenous bases
- caused by DNA base modifiers

It has been established that the causes of such inherited diseases as phenylketonuria, albinism, alkaptonuria, hemophilia are mutations that cause the synthesis of modified polypeptides that are part of the respective enzymes. Modification of these enzymes causes disruption of biochemical processes and clinical symptoms.

A certain variety of anemia called sickle cell anemia is characterized by a difference in the composition of beta chain of hemoglobin. This chain contains 146 amino acids, and the sixth amino acid of the chain - glutamic acid is substituted with valine. Another example of the pathological effects of mutations is the innate bone fragility. This disease is caused by a change in the amino acid sequence of the type I tropocolagen chain. The consequence of this disease is the reduced mechanical resistance of collagen fibers.

References:

1. Ryc. 2 originates from collection: Courtesy of Tom Ellenberger, Washington University School of Medicine in St. Louis, USA, Biomedical Beat National Institute of General Medical Science (NIGMS) Cool Image Gallery