* **Free radical mediated cell injury**

Free radical are the species which have free electrons in the outer shell. These are highly reactive species and have autocatalytic effect. They bind to organic molecules and convert them into free radicals.

**Mechanism of formation of free radicals:**

* **Oxidative-reduction reaction:**

Redox reaction occurs inside the cell during respiration. Oxygen transfers 4 electrons to hydrogen during respiration resulting in formation of 2 water molecules. This is due to complete reduction of oxygen.

In some cases, oxygen is partially reduced and transfer 1 electron to hydrogen results in formation of superoxide ion.

If 2 electrons are transferred to hydrogen then hydrogen peroxide is formed.

If 3 electrons are given to hydrogen then hydroxyl free radicals are formed.

**In small amount:** These free radicals are produced in our body in minor amount and can be neutralized by reducing agent or by taking anti-oxidants agents like vitamin E.

**In large amount:** When they are produced in large amount, they cause cell death. These free radicals mediators cause cell death and this free-radical mediated cell death is known as ‘’oxidative burst’’.

* **Inflammatory cells:**

Leukocytes are responsible for production of free radicals either by redox or enzymes reaction.

* **UV radiations:**

 UV radiations cause lysis of water and generation of free radicals in the body.

* **Transition elements:**

Some transition elements e.g iron, copper that participate importantly in free radical production. These transition elements react with hydrogen peroxide and free radicals are produced.

* **Carbon tetrachloride**:

CCL4 enters into the body and metabolized by cytochrome P450 and results in CCL3 which acts as free-racical.

1. **Free-radical mediated cell injury**

These radicals cause cell injury by the following mechanisms: -

**Lipid peroxidation:**

Our membrane is composed of lipids which undergo oxidation by free radicals. These peroxides are unstable and take part in autocatalytic reaction that result in cell death.

**Protein oxidation:**

Mostly enzymes are protein in nature. Free radicals bind to sulfhydryl group of protein and cause oxidation of protein. As a result, the enzymatic activity become lose and misfolding of protein occur. The cells with misfolding protein do not perform its function.

**DNA damage:**

Free radicals bind with thymine nucleotide in DNA and cause single strand breakdown. This mutated DNA cause cell death.

1. **Chemical mediated cell injury**

Some chemicals directly cause cell injury by interacting with molecular constituents and cellular organelles.

**Mercuric poisoning:**In case of mercuric poisoning, mercury binds with cell membrane, proteins and inhibit ATP-dependent mechanism. It causes increase in membrane permeability by massive influx of Ca2+ ions.

**Anti-cancer drug:**

Anti-cancer drugs produce cytotoxic effect by covalently binding to proteins in the cell membrane.

**Exposure to chemicals:**

When we expose to some chemicals that are not toxic but, in our body, they are converted to toxic metabolites by mix function of oxidase enzyme in ER of liver. These toxic metabolites might be cause cell injury by covalently binding to proteins and lipids in the cell membrane.

**Carbon tetrachloride:**

In our body it is converted to CCl3. This free radical binds to the cell membrane and cause dissociation of ribosomes of ER and cause endoplasmic reticulum swelling. This results in reduced export of lipids from hepatocytes and result in their inability to synthesize apoproteins and to form complex with triglycerides. This will cause increased level of lipids in the liver that cause hepatotoxicity or fatty liver. e.g

Acetaminophen and its metabolite N-acetylbenzaminoquinine cause hepatotoxicity.