Harper - Chop - Free radicals

* Tissue damage caused by free radical

→ DNA - Chemical change in DNA bases
If not repaired, may be inherited in daughter cell

Damage to

→ Lipid - Unsaturated fatty acid in cell membrane & plasma lipoprotein damage

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lipid peroxides formation

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Highly reactive dialdehydes formation

↓

Chemically modify protein & nucleic acid base

→ protein → Direct chemical modification by interactions with radicals

→ Damage to tyrosine residue in protein

↓

Dihydroxyphenylalanine formation

↓

Non enzymatic reaction

↓

formation of oxygen radicals

→ Radical damage effect :-

→ Mutations :- Radical damage to DNA in germline cell in ovaries & testes cause mutation

→ Cancer :- In somatic cell, radical damage to DNA cause initiation of cancer

→ Autoimmune disease :-

Direct radical action (or) reaction of products of radicals induced lipid peroxidation with amino acid in protein

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proteins - recognized as nonself by immune system

antibodies synthesis

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Cross-react with normal tissue protein

↓

autoimmune disease

→ Atherosclerosis :

modification of amino acid in apoprotein in LDL & lipids in LDL (peroxidation)

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Abnormal LDL synthesize

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Not recognized by liver LDL receptor

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Not cleared by liver

↓

LDL taken up by macrophage scavenger receptor

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lipid engorged macrophage infiltrates under blood vessel endothelium (damaged endothelium)

↓

killed by high content of unesterified cholesterol

↓

Atherosclerosis

↓

In extreme cases - completely occlude blood vessel