FARMAKOTERAPI ANTIOKSIDAN

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RADIKAL BEBAS

- Radikal bebas = atom atau molekul (kumpulan atom) yg memiliki elektron yang tak berpasangan (*unpaired electron)* pada lapisan luarnya.
- e-yang tak berpasangan cenderung utk membentuk pasangan, dan ini terjadi dg menarik elektron dari senyawa lain shg terbentuk radikal baru :
- **X:H + $^{\bullet}$O–H → X$^{\bullet}$ + H–O–H**

  radikal hidroksil radikal baru
- radikal bebas memiliki dua sifat, yaitu :
  - Reaktivitas tinggi, karena kecenderungan menarik elektron.
  - Dapat mengubah suatu molekul menjadi suatu radikal

Pembentukan Radikal Bebas

Radikal bebas terbentuk dari :

1. Pemecahan 1 molk normal sec homolitik menjadi 2, mis. akibat pemanasan tinggi, radiasi ion, atau sinar u.v **A:B → A˚ + ˚B**
2. Kehilangan satu elektron dari molk normal

   $A \rightarrow A^{+}{}^{\circ} + e^{-}$
3. Penambahan 1 elektron pada molk normal

   $A + e^{-} \rightarrow A^{-}{}^{\circ}$

Pembentukan Radikal Bebas

Inisiasi :

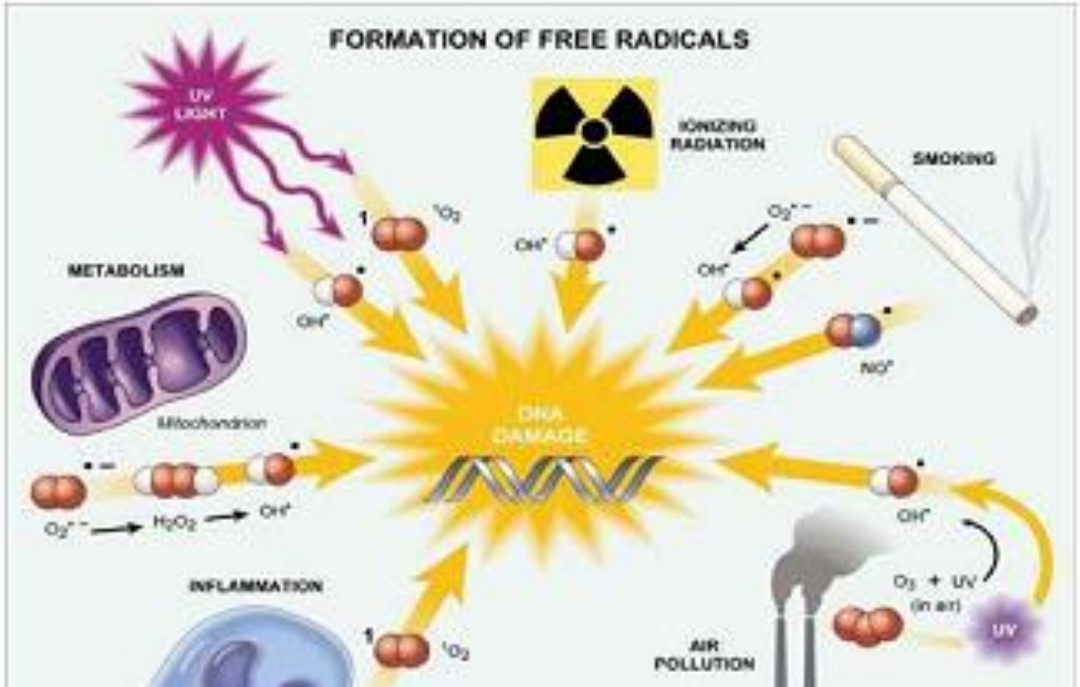
$$ZH \longrightarrow Z^{\bullet} + H^{\bullet}$$

Propagasi :

$$Z^{\bullet} + R-\underset{\displaystyle HO}{\underset{|}{C}}=\underset{\displaystyle OH}{\underset{|}{C}}-R' \longrightarrow ZH + R-\underset{\displaystyle HO}{\underset{|}{C}}=\underset{\displaystyle O^{\bullet}}{\underset{|}{C}}-R'$$

Terminasi :

$$Z^{\bullet} + R-\underset{\displaystyle HO}{\underset{|}{C}}=\underset{\displaystyle O^{\bullet}}{\underset{|}{C}}-R' \longrightarrow ZH + R-\underset{\displaystyle O}{\underset{||}{C}}-\underset{\displaystyle O}{\underset{||}{C}}-R'$$



Radikal Bebas termasuk Oksidan

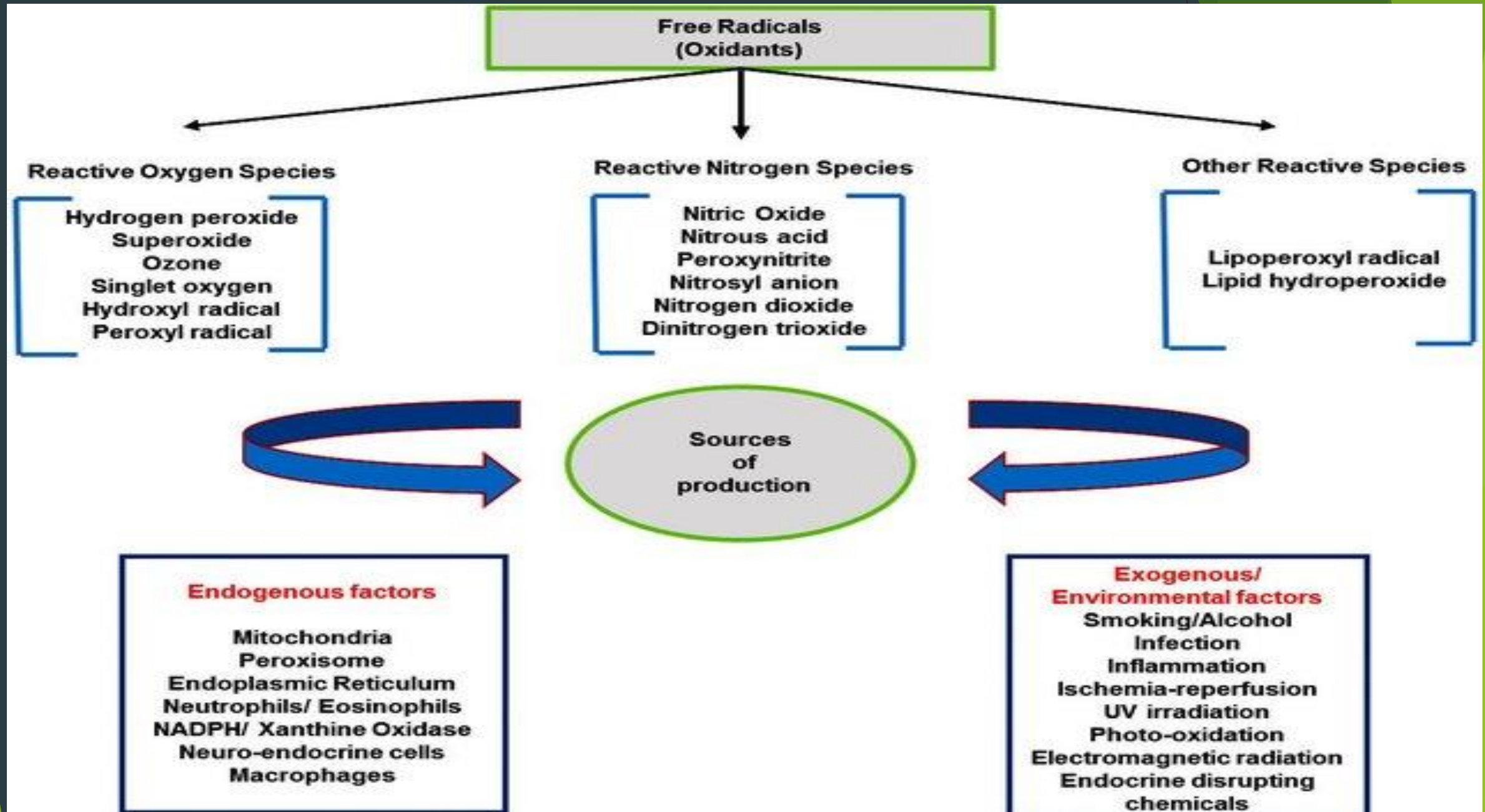
- Oksidan = senyawa penerima elektron, (*electron acceptor*), yaitu senyawa-senyawa yang dapat menarik elektron.
- Radikal Bebas :
  - Oksidan : OH-
  - Non oksidan : H2O2
- Radikan bebas sbg oksidan lbh berbahaya krn reaktifitas yang tinggi dan kecenderungannya membentuk radikal baru, yang pada gilirannya jk menjumpai molekul lain akan membentuk radikal baru lagi, sehingga terjadilah rantai reaksi (*chain reaction*) Reaksi rantai tersebut baru berhenti apabila radikal bebas tersebut dapat diredam (*quenched*).

- Contohnya ialah reaksi radikal bebas •OH (radikal hidroksil) terhadap glutation (GSH) :

  $GSH + {}^{\bullet}OH \rightarrow H_2O + GS^{\bullet}$ (radikal glutation)

  $GS^{\bullet} + GS^{\bullet} \rightarrow$ GSSG (glutation teroksidasi, dy perusak lbh besar)

Source of Free Radicals



Sumber endogen

1. Autoksidasi :
   - Merup produk dr proses metabolisme aerobik mis pd katekolamin, hemoglobin, mioglobin, sitokrom C yang tereduksi dan thiol.
2. Oksidasi enzimatik
   - *xanthine oxidase*, *prostaglandin synthase*, *lipoxygenase*, *aldehyde oxidase*, dan *amino acid oxidase*.
3. Respiratory burst
   - proses dimana sel fagositik menggunakan oksigen dlm jumlah >>> selama fagositosis.
   - Paparan thd bakteri yg diselimuti Ig, kompleks imun, komplemen 5a atau leukotrien ➔mengaktifkan enzim *NADPH-oxidase* ➔ membran sel memproduksi superoksida
4. Subselluler organella
   - kebocoran elektron yang terjadi dari rantai transport elektron, mis yg ada dlm mitokondria dan endoplasma retikulum, molekul oksigen menghasilkan superoksida

Free radicals are produced during:

Normal cellular activities	Pathological events	Disease states
• ETC reactions • Liver detoxification reaction • Immune reactions	• Ionizing radiation • Toxic chemicals • Tissue ischemia	• Inflammatory disease • Degenerative disease • carcinogenesis

Sumber eksogen

1. Obat-obatan :
   - Pro oksidan : antibiotika kelomp quinoid atau berikatan logam untuk aktifitasnya (nitrofurantoin), obat kanker seperti bleomycin, anthracyclines (adriamycin), dan methotrexate.
   - fenilbutason, as fenamat dan aminosalisilat dari sulfasalasin ➔menginaktifasi *protease*
   - asam askorbat dlm jumlah >>> ➔ mempercepat peroksidasi lemak
2. **Radiasi :**
   - Radioterapi ➔ Radiasi elektromagnetik (sinar X, sinar gamma) dan radiasi partikel (partikel elektron, photon, neutron, alfa, dan beta) ➔ radikal primer ➔ reaksi sekunder bersama oksigen yg terurai atau bersama cairan seluler ➔ kerusakan jaringan

3. Asap rokok :

- aldehida, epoxida, peroxida & radikal bebas lain ➔ durasi panjang ➔ kerusakan alveoli.
- nitrit oksida, radikal peroksil & radikal yg mengand karbon ada dalam fase gas.
- radikal dalam fase tar (relatif stabil) meliputi *semiquinone moieties* dihasilkan dari bermacam-macam *quinone* dan *hydroquinone*.
- disposisi besi dalam jaringan paru ➔ pembentukan radikal hidroksil yang mematikan dari hidrogen peroksida ➔ perdarahan kecil berulang.
- netrofil sal napas bwh ↑ ➔ konsentrasi radikal bebas ↑

4. Metal (aluminium, lead,arsenic dll)

5. Gas

6. Lain-Lain (alcohol, halogenated hydrocarbon)

- Produksi radikal bebas meningkat pd keadaan :
  - sinar u.v
  - polusi udara
  - asap rokok
  - insektisida
  - olah raga berat, stress dll
  - Kontaminan dalam makanan

Reaksi perusakan oleh radikal bebas

- tekanan oksidatif (*oxidative stress*) = keadaan dimana tingkat oksigen reaktif intermediate (ROI) yg toksik melebihi pertahanan anti-oksidan endogen.
- kelebihan radikal bebas $\rightarrow$ bereaksi dg lemak, protein, as. nukleat seluler kerusakan lokal & disfungsi organ tertentu.
- Lemak = biomolekul yg rentan thd $\rightarrow$ serangan radikal bebas.

Reaksi perusakan oleh radikal bebas

a. Peroksidasi lemak

- Membran sel = sumber *poly unsaturated fatty acid* (PUFA), mudah dirusak o/ bhn pengoksidasi →disruption of hydrophobic nature of membranes fragmentation and loss of membrane-bound enzymatic activities.

$$LH + R^{\cdot} \rightarrow L^{\cdot} + RH$$

$$L^{\cdot} + O_2 \rightarrow LOO^{\cdot}$$

$$LOO^{\cdot} + L'H \rightarrow LOOH + L'^{\cdot}$$

$$LOOH \rightarrow LO^{\cdot}, LOO^{\cdot}, \text{aldehydes.}$$

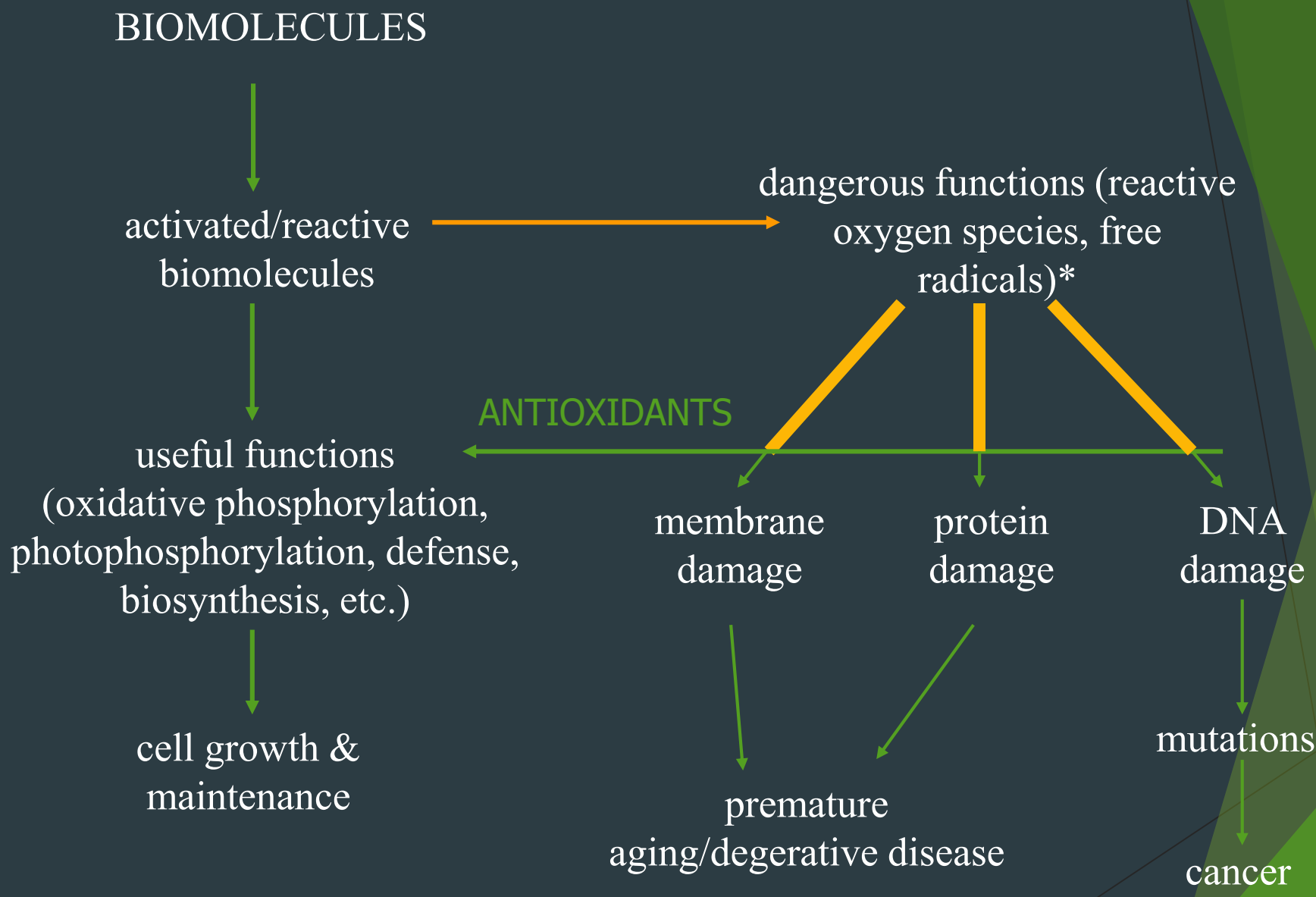
Reaksi perusakan oleh radikal bebas

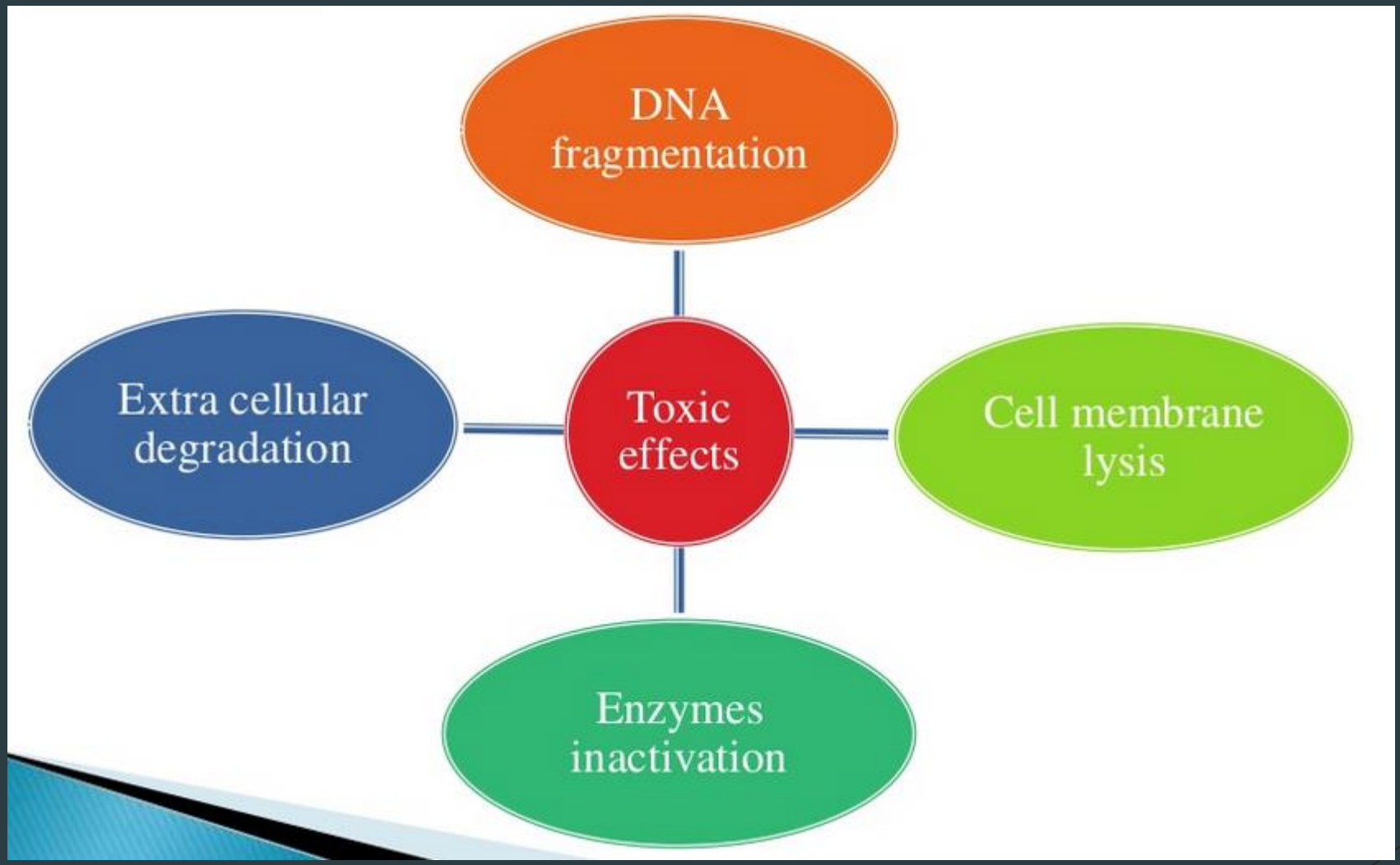
b. **Kerusakan protein**

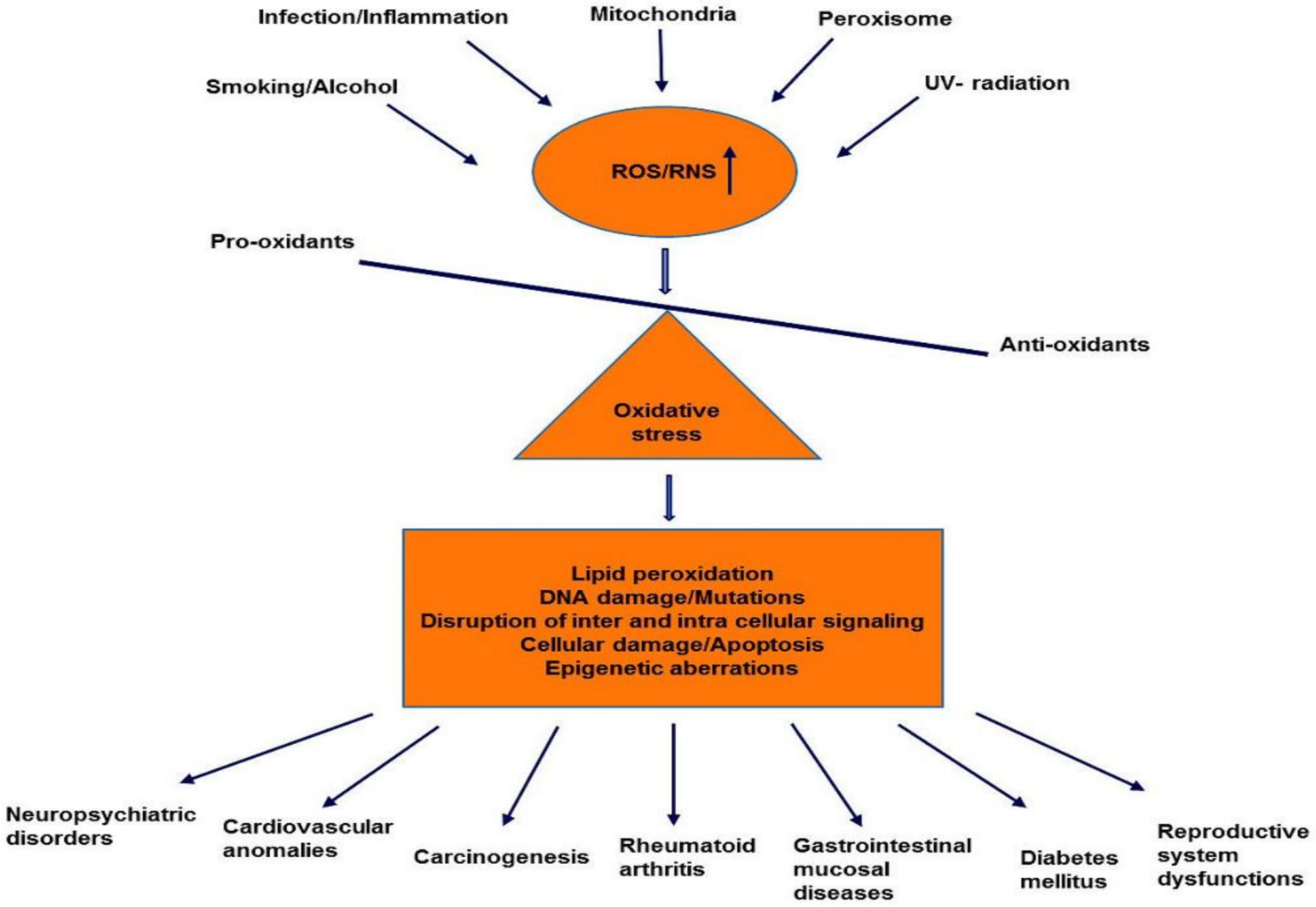
- Jarang, protein & asam nukleat lbh tahan thd radikal bebas dp PUFA , kecuali bila sangat ekstensif (Radikal terakumulasi atau ada kerusakan yg terfokus pada daerah tertentu dalam protein akibat ikatannya dengan ion logam transisi) → affect enzyme / receptor.

c. Kerusakan DNA

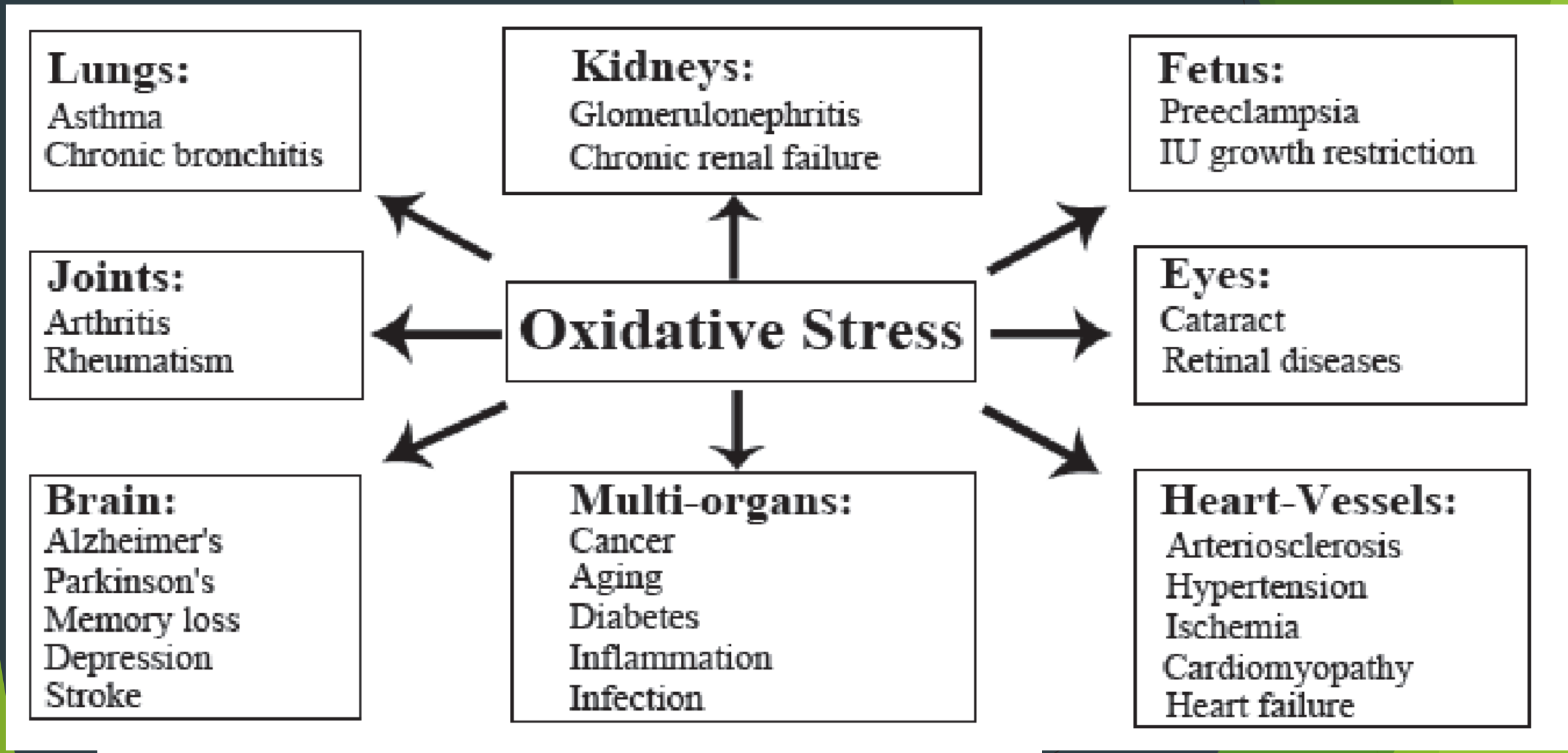
- Sda protein, jarang terjadi
- Lesi pd susunan molekul, jk tidak dpt diatasi & tjd sebelum replikasi ➔ leading to strand breaks → mutations


BIOMOLECULES
activated/reactive biomolecules
dangerous functions (reactive oxygen species, free radicals)*
ANTIOXIDANTS
useful functions (oxidative phosphorylation, photophosphorylation, defense, biosynthesis, etc.)
membrane damage
protein damage
DNA damage
cell growth & maintenance
premature aging/degerative disease
mutations
cancer


DNA fragmentation
Extra cellular degradation
Toxic effects
Cell membrane lysis
Enzymes inactivation


Infection/Inflammation
Mitochondria
Peroxisome
Smoking/Alcohol
UV- radiation
ROS/RNS
Pro-oxidants
Anti-oxidants
Oxidative stress
Lipid peroxidation
DNA damage/Mutations
Disruption of inter and intra cellular signaling
Cellular damage/Apoptosis
Epigenetic aberrations
Neuropsychiatric disorders
Cardiovascular anomalies
Carcinogenesis
Rheumatoid arthritis
Gastrointestinal mucosal diseases
Diabetes mellitus
Reproductive system dysfunctions

Oxidative Stress-induced disease in human



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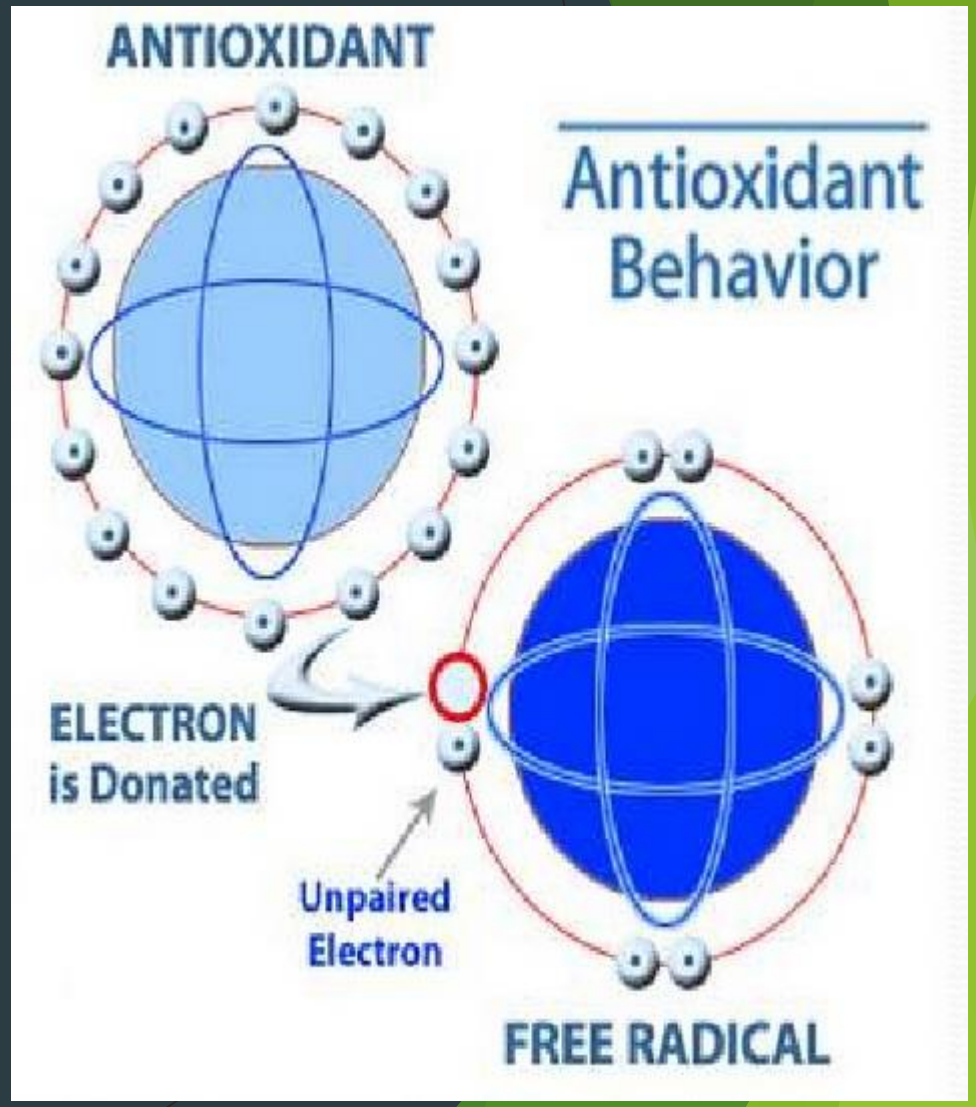
Pertahanan tubuh terhadap radikal bebas

- Pengaruh buruk radikal bebas dapat ditangkal oleh ANTIOKSIDAN
- Antioksidan tdd :
  - Antioksidan endogen, mis SOD, GSH
  - Antioksidan eksogen , mis Vit C, Vit E, beta karoten
- Perlu ada keseimbangan antara kandungan antioksidan dan radikal bebas di dalam tubuh
- Apabila jumlah radikal bebas terus bertambah sedangkan antioksidan endogen jumlahnya tetap, maka kelebihan radikal bebas tidak dapat dinetralkan. Akibatnya radikal bebas akan bereaksi dengan komponen- komponen sel dan menimbulkan kerusakan sel

ANTIOKSIDAN

- Oksidasi= reaksi kimia yg mentransfer electron/hydrogen dr substrat shg mjd ‘oxidizing agent’
- Reaksi oksidasi dpt menghasilkan *free radical*. Selanjutnya, krn bersifat reaktif, dpt terjadi rekasi berantai
- Substansi apa pun yang bila berada dalam konsentrasi rendah dibandingkan dengan substrat yang dapat teroksidasi - akan memperlambat atau menghambat oksidasi substrat tsb secara signifikan = antioksidan



Mode of action of antioxidants

1. Catalycally remove ROS (enzymes)

Superoxide dismutase (SOD)

- $2O_2^{-\bullet} + 2H^+ \xrightarrow{SOD} H_2O_2 + O_2$

Catalase

- Breaks down H_2O_2 (the source of $HO^\bullet$) to harmless H_2O and O_2

Glutathione/glutathione peroxidase

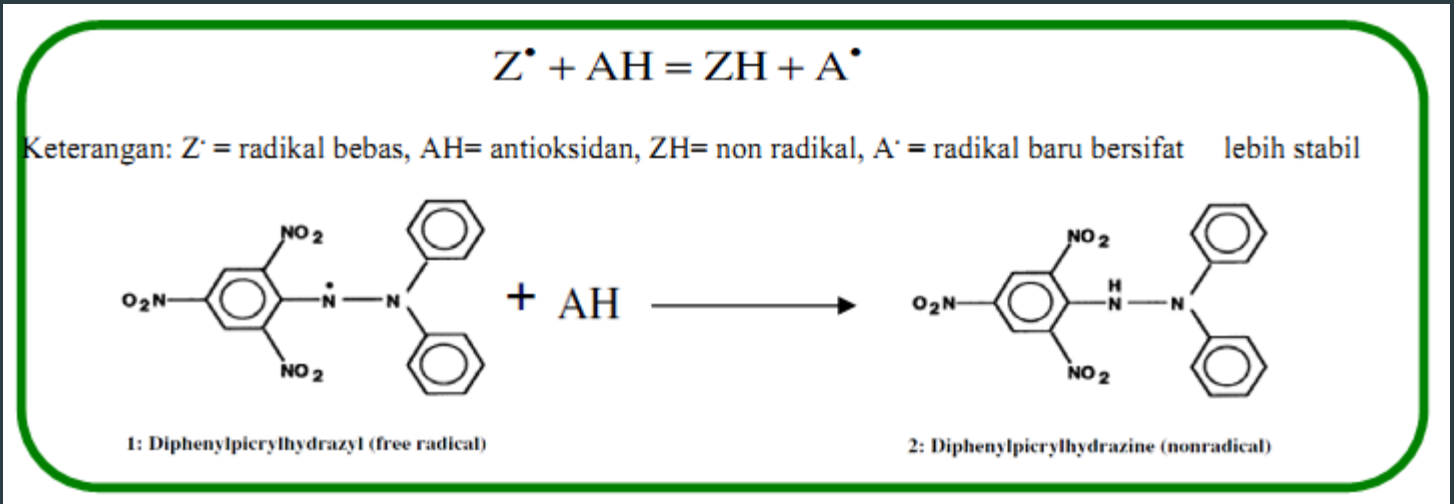
- $2GSH + H_2O_2 \xrightarrow{GSH\ peroxidase} GSSG + 2H_2O$

2. Minimize the avaibility of pro oxidant (transferin, metal chelation)

Iron and copper binding proteins (prevent metal ions from being in their free form)

- Transferrin and ferritin bind Fe
- Ceuruloplasmin and albumin bind Cu
- Prevents reaction of H_2O_2 with these transition metals to form $HO^\bullet$

3. Protect biomolecules against ROS (heat shock protein)
4. Low-molecular-mass agents that scavenge ROS (gluthatione, uric acid, bilirubin ,vitamin)



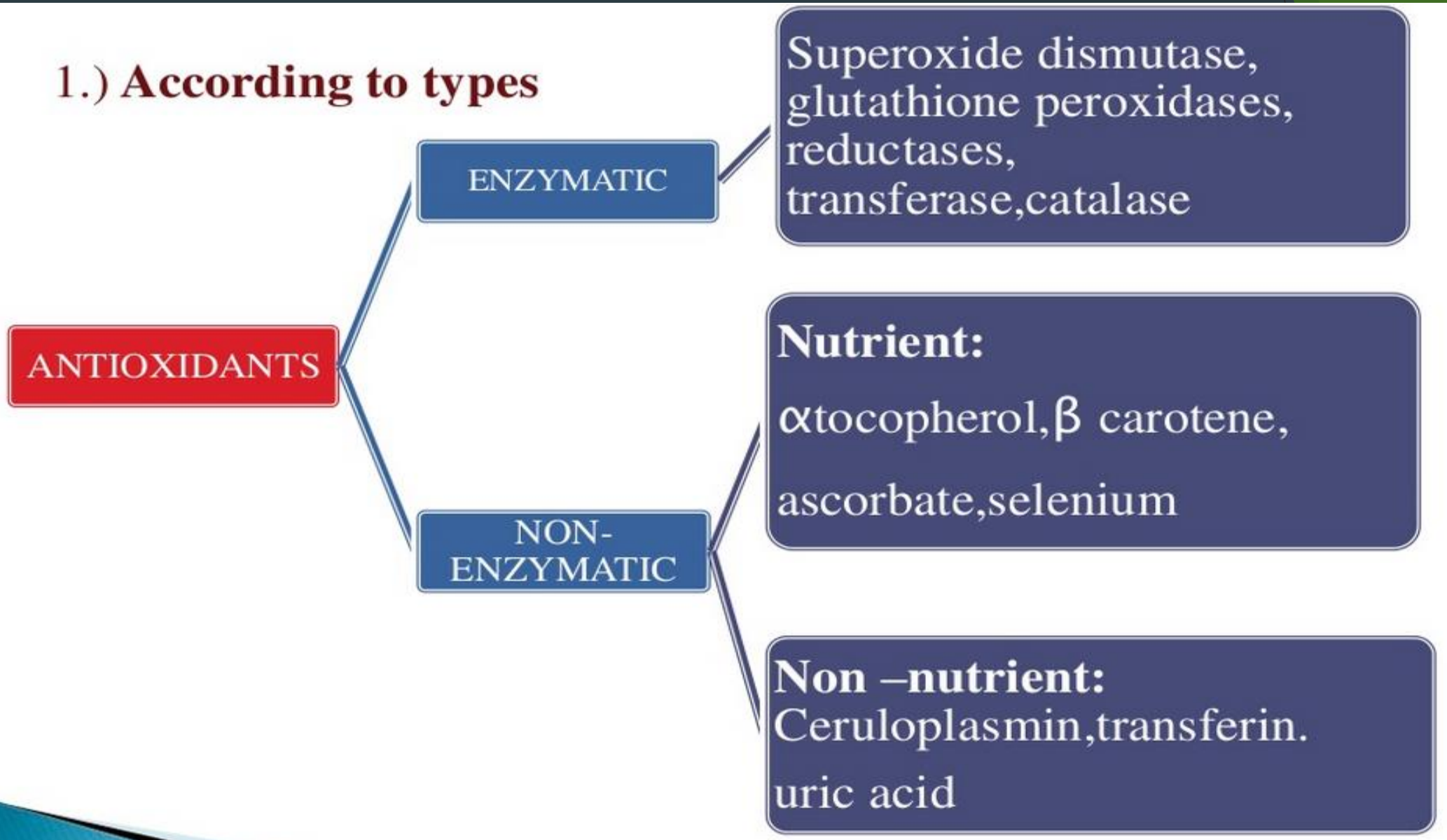
Ideal Antioxidants

- No harmful physiological effects
- Not contribute an objectionable flavor, odor, or color to the fat
- Effective in low concentration
- Fat-soluble
- Carry-through effect → No destruction during processing
- Readily-available
- Economical
- Not absorbable by the body

ANTIOKSIDAN DPT DIKATEGORIKAN BERDASAR BEBERAPA HAL

- TIPE
- MEKANISME KERJA
- LOKASI
- KELARUTAN
- STRUKTUR YANG DILINDUNGI
- ASAL

1.) **According to types**



BERDASAR MEKANISME KERJA

Preventif

- Antioxidant enzyme
  - Catalase, glutathione peroxidase, glutathione reductase, superoxide dismutase
- Metals binding protein
  - Ceruloplasmin, ferritin, latoferrin, metallotheinein, transferrin, hemoglobin, myoglobin

Scavenger

- Ascorbate, carotenoid, alfa-tokoferol, uric acid, bilirubin, flavonoid, ubiquinone, thiol

Superoxide dismutase (SOD)

Eliminating ROI by reducing (adding an electron to) superoxide to form H_2O_2.

Catalase and the selenium-dependent glutathione peroxidase are responsible for reducing H_2O_2 to H_2O.

The catalase enzyme

Catalase and glutathione peroxidase seek out hydrogen peroxide and convert it to water and diatomic oxygen.

Glutathione peroxidase enzyme

Glutathione peroxidase reduces H2O2 to H2O by oxidizing glutathione (GSH)

Antioxidants

Enzymes	Antioxidant	Role	Remarks
	Superoxide dismutase (SOD) Mitochondrial Cytoplasmic Extracellular	Dismutates $O_2^{\cdot -}$ to H_2O_2	Contains Manganese (Mn.SOD) Contains Copper & Zinc (CuZnSOD) Contains Copper (CuSOD)
	Catalase	Dismutates H_2O_2 to H_2O	
	Glutathione peroxidase (GSH.Px)	Removes H_2O_2 and lipid peroxides	Selenoproteins (contains Se^{2+}) Primarily in the cytosol also mitochondria Uses GSH

Vitamins	**Alpha tocopherol**	Breaks lipid peroxidation Lipid peroxide and $O_2^{\cdot -}$ and ·OH scavenger	Fat soluble vitamin
	Beta carotene	Scavenges ·OH, $O_2^{\cdot -}$ and peroxy radicals Prevents oxidation of vitamin A Binds to transition metals	Fat soluble vitamin
	Ascorbic acid	Directly scavenges $O_2^{\cdot -}$, ·OH, and H_2O_2 Neutralizes oxidants from stimulated neutrophils Contributes to regeneration of vitamin E	Water soluble vitamin

LOKASI

INTRACELLULAR	• SOD 1 and 2, catalase, glutathione peroxidase, DNA repair enzymes
EXTRACELLULAR	• SOD 3, reduced glutathione, ascorbate,carotenoids, uric acid
MEMBRANE ASSOCIATED	• α-Tocopherol

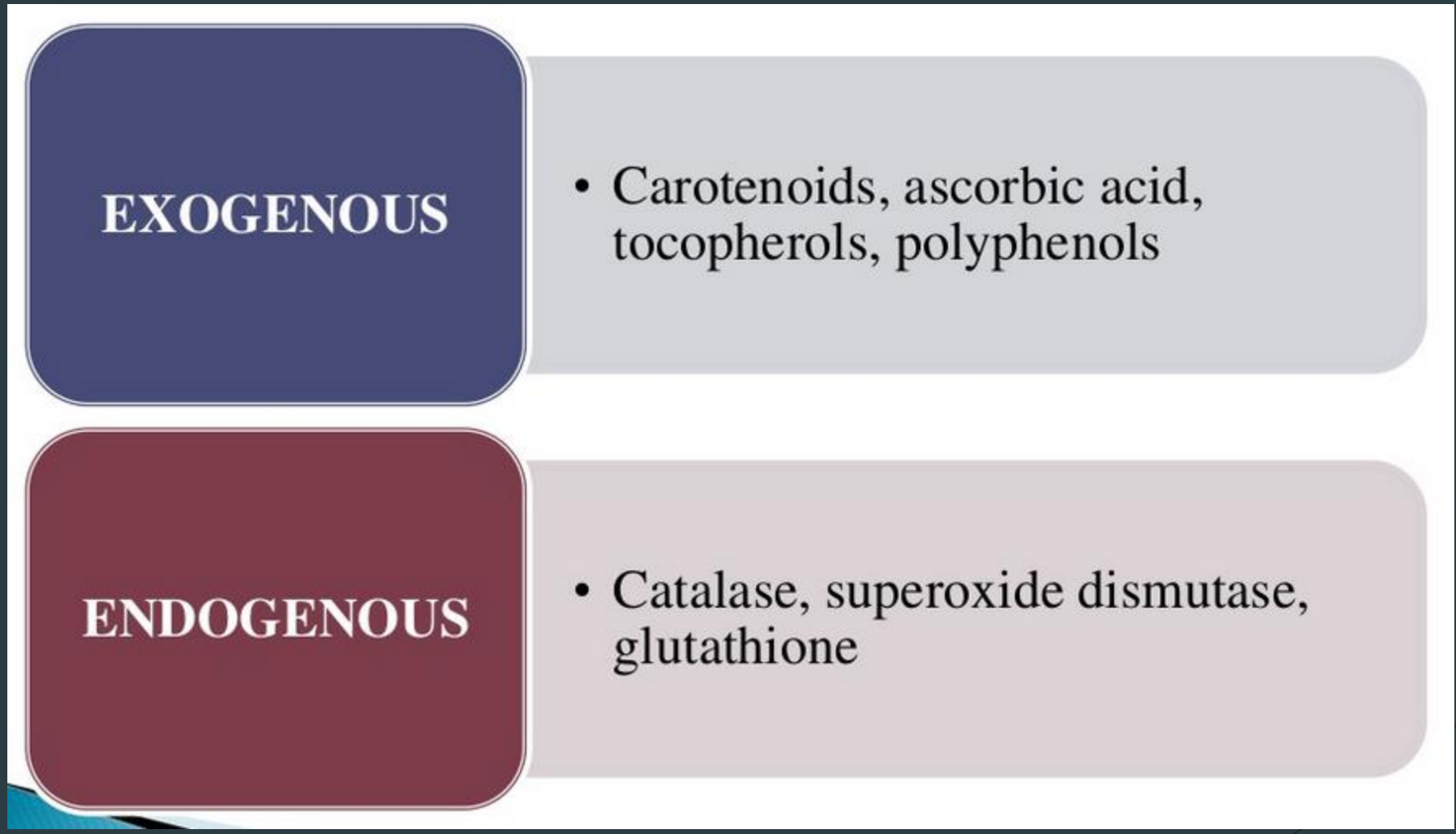
KELARUTAN

WATER SOLUBLE	• Ascorbate, Uric acid, Flavenoids, thiols, Cysteine,Transferins
LIPID SOLUBLE	• α-Tocopherol, Carotenoids,bilirubin

STRUKTUR YANG DILINDUNGI

DNA	• SOD1 and 2, glutathione peroxidase, DNA repair enzymes, reduced glutathione, cysteine
PROTEIN	• Sequestration of transition metals by preventive antioxidants
LIPID	• α-Tocopherol, ascorbate, carotenoids, glutathione

ASAL


EXOGENOUS
• Carotenoids, ascorbic acid, tocopherols, polyphenols
ENDOGENOUS
• Catalase, superoxide dismutase, glutathione

JENIS

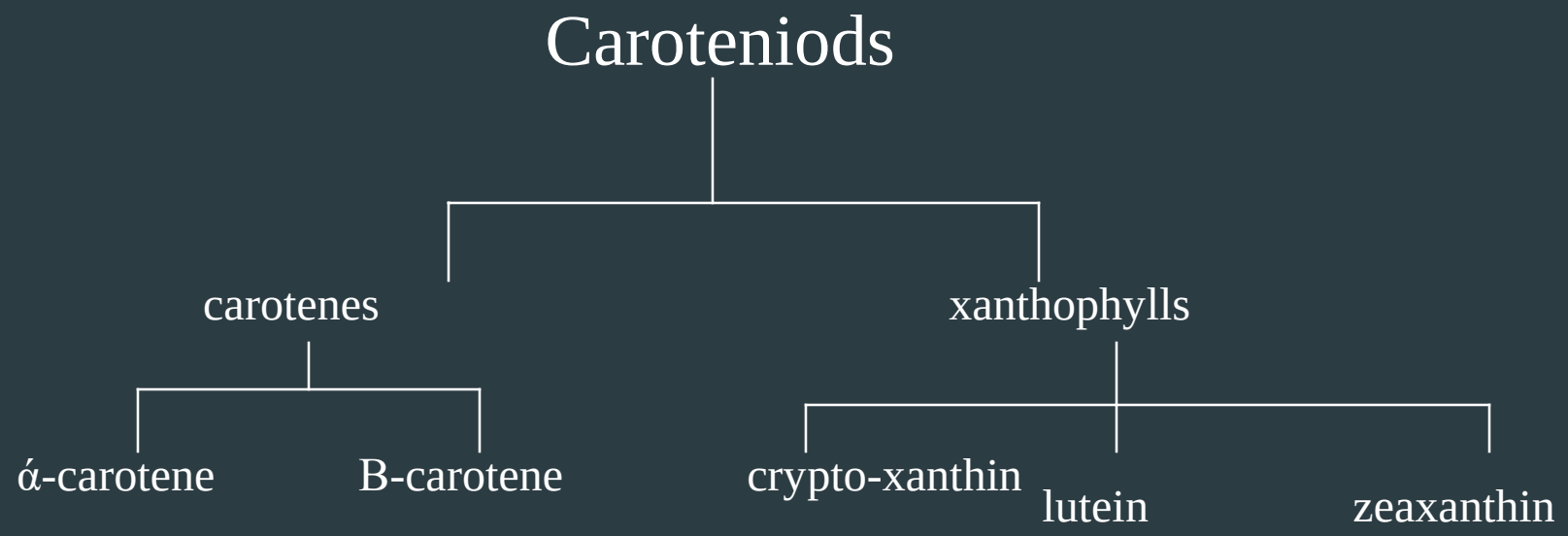
Natural	Synthetics
Tocopherols (delta >gamma>beta>alpha)	Butylated hydroxy anisole (BHA)
Nordihydroguaretic acid (NDGA)	Butylated hydroxy toluene (BHT)
Sesamol	Propyl gallate (PG)
Gossypol	Tertairy butyl hydroquinone (TBHQ)

Antioxidant therapy in cancer

The following is a list of common antioxidants used in cancer programs.

- Beta carotene
- Vitamin C
- Vitamin E
- Selenium
- Lipoic acid
- Poly MVA

Carotene Groups



CAROTENOIDS (ß-CAROTENE)

- Carotenoids : 90% α- dan ß-caroten
- Carotenoids → antioxidants (scavenger free radicals; peroxyl radicals, singlet oxygen, hydrogen peroxide, hydroxyl)
- Work together with vitamin C & vitamin E

Peroxyl Radical Scavenging

- Carotenoids have also been shown to be capable of inhibiting free radical reactions.
- ß-carotene → reduces trichloromethylperoxyl radicals.

CAROTENOIDS (ß-CAROTENE)…

Deactivation of Singlet Oxygen

- ß-carotene has been known to be an efficient quencher of O_2^-

- $O_2 + C \rightarrow {}^3O_2 + {}^3C^*$

  ${}^3C^* \rightarrow C$ + thermal energy

CAROTENOIDS (ß-CAROTENE)…

Inhibit cell transformation

- Correlated with both enhanced cell-cell communication and transcription of connexin43 (mRNA).
- Increased amounts of connexin43 mRNA can inhibit transformation in some cell systems.
- Canthaxanthin and ß-carotene.

Beta-carotene in Cancer

- Beta-carotene is a form of vitamin A.
- Vitamin A is a strong immune booster. It stimulates the activity of immune cells against tumor cells. Has been shown to inhibit the promotion of caner, while beta carotene (precursor to vitamin A) inhibits the initiation of cancer.
- Beta-carotene can decrease the amount of damage free radicals do to a cells DNA. Such DNA damage is thought to be one mechanism that causes cancer, and indeed, some early studies suggested that beta-carotene might reduce the risk of cancer.

VITAMIN C

- =Ascorbic acid
- Water soluble antioxidants
- Efficiently scavenges O_2^-, OH, peroxyl radicals.
- Be involved in the regeneration of vitamin E.
- Protect biomembrans and LDL from peroxidative damage

By efficiently trapping peroxyl radicals in aqueous phase of plasma or cytosol

VITAMIN C ...

Dua sifat Vit C sbg antioksidan

- Memiliki potensial reduksi yg rendah, dimn askorbat & radikal askorbil mampu bereaksi dgn radikal biologis & mereduksi oksidan-oksidan
- Stabilitas & reaktivitas yg rendah dr radikal askorbil

VITAMIN C ...

- Plasma vitamin C concentration : decrease triglyceride level and increase HDL level → prevent CHD
- As Coantioxidants → regeneration of vitamin E (α-tocopherol) from radical form.

Vitamin C can prevent cancer :

1. Inhibition DNA oxidation
2. Increase imun system to infection and virus
3. Protect from mutagenic *nitrosamin* (nitrat or nitrit reaction)

   $HNO_2 + H^+ \leftrightarrow H_2O_2^+$

VITAMIN C ...

Vitamin C level in foods (mg/100 g)

Foods	mg	Foods	mg
Daun singkong	275	Gandaria	110
Daun katuk	200	Jambu biji	95
Daun melinjo	150	Pepaya	78
Daun papaya	140	Mangga masak	41
Sawi	102	Durian	53
Kol	50	Kedondong masak	50
Bayam	60	Jeruk manis	49
Kemangi	50	Jeruk nipis	27
Tomat masak	40	Nanas	24
Kangkung	30	Rambutan	58

AKG 2004

- Man : 90 mg/day
- Woman : 75 mg/day

vitamin C

- Biochemical function: cofactor for at least eight enzymes
- At the tissue level, a major function → collagen synthesis (vit C deficiency can lead scurvy)
- The antioxidant properties→ protect NO, protect against age-related cataract
- Absorbed in the lumen intestine via an energy dependent process (saturable)
  - The daily intake > 100mg → excreted, in adult RDA: 60 mg/daily
  - The renal threshold for ascorbic acid : 1.5mg/dl. Urinary axcretion of oxalate and urate → 1000mg
- Toxicity
  - Megadosage treatment → formation of kydney stone and rebound scurvy
  - Pro oxidant / acts as reductant to the iron (be aggravated in disease and traumatic injury)?

Pro-oxidant activities

Antioxidants that are reducing agents can also act as pro-oxidants.

For example, vitamin C has antioxidant activity when it reduces oxidizing substances such as hydrogen peroxide, however, it will also reduce metal ions that generate free radicals through the Fenton reaction.

$$2\ Fe^{3+} + \text{Ascorbate} \rightarrow 2\ Fe^{2+} + \text{Dehydroascorbate}$$

$$2\ Fe^{2+} + 2\ H_2O_2 \rightarrow 2\ Fe^{3+} + 2\ OH\cdot + 2\ OH^-$$

Vitamin C

- vitamin C acts as an antioxidant and free radical scavenger that reacts directly with super oxide, hydroxyl radicals, and singlet oxygen produced during normal cellular metabolism.
- Oxygen is necessary for life. Oxygen also comes in several radical forms that have been implicatedin both initiation and post initiation stages of the carcinogenic process as well as in invasion and metastatic processes. Aside from its antioxidant properties, there is no single universal accepted and proven explanation for vitamin Cs cancer fighting properties.

VITAMIN E

- Potent inhibitors of lipid peroxdation.
- Effective antioxidant α-tocopherol
- Tocopherol

Donates the hydrogen atom from the hydroxyl group (OH) on the ring structure to free radicals

Free radicals become <u>unreactive</u>

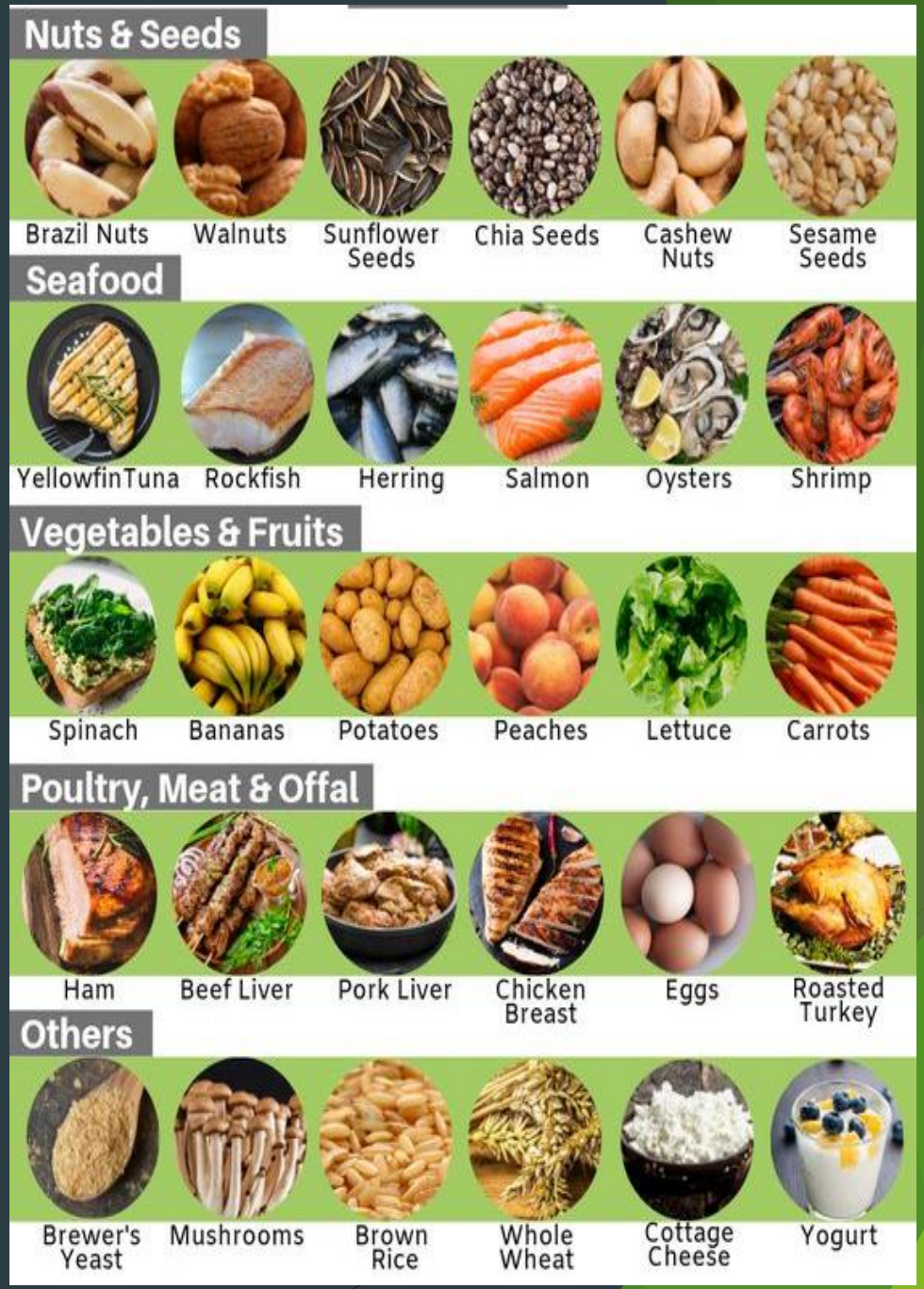
- Prevent heart and artery diseases.
- Inhibit LDL cholesterol oxidation.
- Anti carcinogenic : Increase imun system and inhibit cancer, etc.

Vitamin E in cancer

- Vitamin E is an important fat-soluble antioxidant,
- vitamin E s preventive role in cancer has been well proven.
  - Highly malignant melanoma cell in vitro has been shown to be converted into differentiated (normal) cell after 3 days of exposure to Vitamin E succinate.
  - Ovarian and cervical cancer - vitamin E slow downs the mitotic activity of cancer cell but normal cell dont get affected.
  - Glioma tumor cells (present in the brain) are also more effective attacked by vitamin E succinate, probably because of its better penetration of blood bran barrier.
  - Vitamin E succinate enhances radiation in cancer cell and protects the normal cell.

Selenium

- Selenium▫ It is a powerful mineral antioxidant with a central role in the protection of tissues from the damaging effects of oxygen free radicals.
- The use of selenium compounds as a cancer treatment predates most conventional treatments currently in use.▫ 200 mcg of selenium a day has been shown to reduce cancer death by 50% and prostate cancer by 62% after 4 years.
- Cancer patients are often found to be deficient in selenium. Selenium works synergistically with vitamin E.



Lipoic acid

- It is called the universal antioxidant for its ability to dissolve well in water and in fat environment,
- Lipoic acid increase the effectiveness or potency in other antioxidants.
- It can cross the blood brain barrier while others cannot .
- One of the most beneficial effects of alpha Lipoic acid is its ability to regenerate other essential antioxidants such as vitamins C and E, coenzyme, and glutathione

Poly MVA

- This is an alpha Lipoic acid complex with palladium.
- It is a non-toxic polynucleotide reductase named POLYDOX (USA trials), Poly-MVA (Canada and Mexico) or LAPd by some researchers.
  - ▫ The element platinum is very lethal to cancer cells, but also very toxic to humans.
  - ▫ Its close relative: palladium, however, is nontoxic in its present form.
  - ▫ The MVA stands for minerals, vitamins, and amino acids. LAPd stands for Lipoic acid/Palladium complex.

Antioksidan Sintetik

- Yaitu antioksidan yang diperoleh dari hasil sintesis reaksi kimia dan telah diproduksi untuk tujuan komersial.
- Contoh:
- Butil Hidroksi Anisol (BHA)
- Butil Hidroksi Toluen (BHT)
- propil galat,
- Tert-Butil Hidoksi Quinon (TBHQ)

Antioksidan Alami

(a) senyawa antioksidan yang sudah ada dari satu atau dua komponen makanan

(b) senyawa antioksidan yang terbentuk dari reaksi-reaksi selama proses pengolahan

(c) senyawa antioksidan yang diisolasi dari sumber alami dan ditambahkan ke makanan sebagai bahan tambahan pangan.

- Isolasi antioksidan alami telah dilakukan dari tumbuhan yang dapat dimakan, tetapi tidak selalu dari bagian yang dapat dimakan.
- Antioksidan alami tersebar di beberapa bagian tanaman, seperti pada kayu, kulit kayu, akar, daun, buah, bunga, biji, dan serbuk sari

Antioksidan Alami

- Nutraceuticals are naturally derived, bioactive compounds that have health promoting, disease preventing or medicinal properties.
- Nutraceuticals can be delivered in the form of food (functional foods) or as a dietary supplement or in both forms.
- Antioksidan alami umumnya mempunyai gugus hidroksi dalam struktur molekulnya (Sunarni, 2005)
- Faktor yang menentukan aktivitas suatu senyawa sbg antioksidan a.l : jumlah gugus hidroksil bebas, ikatan rangkap, dan tingkat kesimetrian struktur,

GUGUS FENOL

Senyawa antioksidan alami tumbuhan umumnya adalah senyawa fenolik atau polifenolik yang dapat berupa golongan

- flavonoid,
- turunan asam sinamat,
- kumarin,
- tokoferol,
- dan asam-asam organic polifungsional.

POLIFENOL

- Senyawa yg termasuk polifenol adalah semua senyawa yang memiliki struktur dasar berupa fenol.
- Fenol =struktur yangterbentuk dari benzena tersubtitusi dengan gugus– OH. Gugus – OH yang terkandung merupakan aktivator yang kuat dalam reaksi subtitusi aromatik elektrofilik
- Polifenol (polyphenol) = senyawa kimia yang bersifat antioksidan kuat.

- Sementara turunan asam sinamat meliputi asam kafeat, asam ferulat, asam klorogenat, dan lain-lain.
- Senyawa antioksidan alami polifenolik ini adalah multifungsional dan dapat beraksi sebagai

  (a) pereduksi

  (b) penangkap radikal bebas

  (c) pengkelat logam

  (d) peredam terbentuknya singlet oksigen.

Salah satu Polifenol : flavonoid

Golongan flavonoid yang memiliki aktivitas antioksidan meliputi:

- Flavon
- Flavonol
- Isoflavon
- Kateksin
- Flavonol
- Kalkon

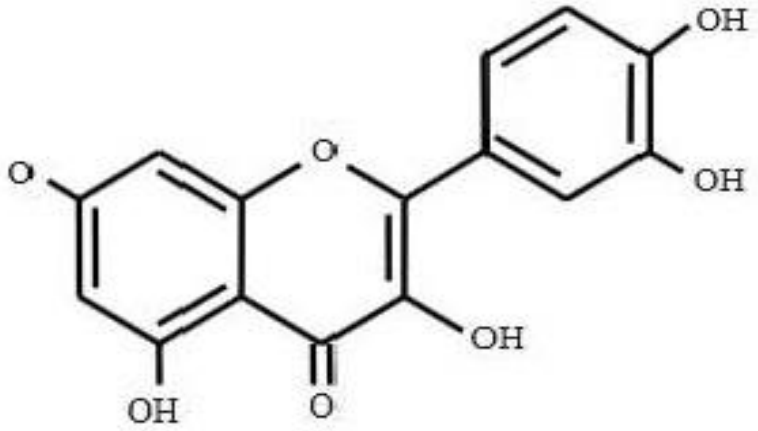
Flavonoids

Flavonols	Flavones	Flavonols	Flavanones	Anthocyanidins	Isoflavonoids
Quercetin	Apigenin	**Catechins**	Eriodictyol	Cyanidin	**Genistein**
Kaempferol	Chrysin	Epicatechin	Hesperitin	**Pelargonidin**	**Daidzein**
Myricetin	**Luteolin**	Epigallocatechin	Naringenin	Delphinidin	Glycitein
Galangin	**Baicalin**	Epicatechin gallate		Peonidin	Formononetin
Fisetin	**Baicalein**			Malvidin	

Synergistic effects of phytonutrients is current being investigated

FLAVONOID

- Flavonoid berperan sebagai antioksidan dengan cara mendonasikan atom hidrogennya atau melalui kemampuannya mengkelat logam, berada dalam bentuk glukosida (mengandung rantai samping glukosa) atau dalam bentuk bebas yang disebut aglikon



Gambar 1. Kerangka $C_6 - C_3 - C_6$ Flavonoid

TERIMA KASIH ATAS PERHATIANNYA

Semoga bermanfaat