HEAVY METAL TOXICITY: IMPLICATION FOR CANCER AND ORTHOPAEDIC EFFECT
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TOXICOKinetics

- **HEAVY METAL**: e.g Pb, Ar, Hg, Cd, Cr etc. are generally regarded as environmental chem.

- **SOURCE AND MODE OF ENTRY**:

  - Air, agric products, marine products, industrial works,
HEAVY METALS AND BIOLOGICAL REACTIVE LIGANDS

HEAVY METALS = exert their toxic effects by combining with one or more reactive grps essential for normal physiological fnx.

E.G = -OH, -COO,

Sulfur grp: -SH, -S-S-

Nitrogen grp: NH₂ and NH (Klaasen 1996)
CANCER FORMATION

• Definition:
• A disease condtn. of uncontrolled cell proliferation and spread
• NEOPLASM = (new cell growth) interchanged with cancer
• BENIGN = neoplasm with localized growth
• MALIGNANT = neoplasm with characteristics of invasiveness and metastasis
Xteristics of cancer cell

• UNCONTROLLED PROLIERATION

• LOSS OF FUNCTION

• INVERSIVENESS

• METASTASIS
CASINOGENS

• DEFINITION: Agents or subst. that cause cancer
• E.g = Heavy metals
  • = Asbestors
  • = Benzen
  • = Radon
• = Virus
• = etc (Chu and Santorelli 2012)
CASINOGEN (mechanism of action)

• **Inactivation** of tumor suppressor gene in a cell

• **Activation** of proto- oncogens
ORTHOPAEDIC ANGLE (ARTHRITEIS)

• Seen generally as the dx of the joint and the surrounding tissues

• Symptoms include pain, joint stiffness and swelling mostly in the morning, aching

• Arthritis also affects other parts of the body like liver, heart, lungs etc.
HEAVY METALS

• HOW CAN THEY CAUSE ARTHRITIS?
• = They cause generation of free radicals, autoimmune reaction of B and T lymphocytes that affects the synovium.

• = They cause increase in cytokine generation and entry into affected joints and increase in inflammation
TYPES OF ARTHRITIS

• OSTEO ARTHRITIS

• RHEUMATOID ARTHRITIS

• GOUT ARTHRITIS
HEAVY METALS AS HUMAN CASINOGEN

• Mechanism of Action:
  • Distortion of DNA conformation during replication and transcription
  • Mutational activation of protooncogens and/or inactivation of tumor suppressor genes
  • Clonal expansion of pre-malignant cells
BIOIMPORTANCE OF SOME METALS AS TRACE ELEMENTS

• Needed in very minute amount e.g. Zn, Mg, molybdenum, Cr etc. found in some enzymes

• Fe and Ca needed in fairly large amount
LEAD

• Sources
• Uses
• Exposure/Contamination
• Organs affected
• CNS, Kidney, Liver, Immune system etc.
LEAD CASINOGENICITY/ TOXICITY

- Direct DNA damage
- DNA synthesis inhibition
- Clastogenicity
- Generation of free radicals (Arthritis)
- Pb can substitute for Zn in several enzymes in DNA replication leading to altered gene expression
MERCURY

• Exist as sulphide
• HUMAN EXPOSURE
• Mining, industries, paint, electrical wks

• Hg classified by IARC as CLASS 3 CASINOGEN
NICKEL

• HUMAN EXPOSURE

• TOXICITY/CANCER:
  • Inhibition of intercellular communications
  • Immortalization of fibroblasts and epith. Cells
  • Induction of DNA deletions and aberrations
  • Oxidative damage which also causes Arthritis
  
  (Miki et al 1987, Biedermann and Landolph, 1987,
BENEFICIAL EFFECT OF NICKEL

• Trace Element by WHO
• Enzymes containing nickel in plants and animals (WHO, 1996)
ARSENIC

• SOURCE
• HUMAN EXPOSURE
• From commercial appl. In semiconductors, wood preservatives, non ferrous alloy, glass, insecticide
• UNDERGROUND WATER CONTAMINATION
ARSENIC TOXICITY

• CACINOGENICITY

• By alteration in cell differentiation and proliferation: thro. Increased cellular tyrosine phosphorylation

• (Leonard and Gerber 1994; Hayes, 1997; Hayes, 1997).
CADMIUM

• SOURCE:
• T ½.....10-30 yrs
• TOXICITY:
• Accumulates in kidney = tubular dysfunx
• Displaces Zn in biological raxn in synthesis of DNA and RNA (Brzóska and Moniuszko, 2001)
• Induces single stranded DNA break
• Inhibits DNA repair
• Activates pro-oncogens. (McMurray and Tainer, 2003; Waalkes ,2000; Abshire et al,1996)
COBALT

• Trace element contained in Vit B (cyanocobalamin)
• Essential in DNA synthesis
• CASINOGENICTY:
• Causes production of fibrosarcoma, rhabdomyosarcoma etc.
• IARC status........ Can be casinogenic
COBALT EXPOSURE

- In metal smelting
- In alloys..... Steel, magnet
- Orthopaedic implants......(cobalt-chromium-molybdenum-nickel alloy)
IRON (Fe)

• **SOURCE:** = earth
• **EXPOSURE:**= Agric product, meat, sea foods, smelting and arc welding

• **TOXICITY:**
• Rare in human
• **In animal model:** high dose= sarcoma attributed to Fe CHO complex
ARTHRITIS AND Fe

• Increases RA through prod. of OH- radicals.

• By ferrous ion promoting hyaluronic acid break down in the joints
BORON ...A CONTRAST

• DEMOGRAPHY STUDY = BY NEUNHAM (1986)

• SOILS/REGIONS = WITH BORON DEFF. SUFFER RA more

• REGIONS = WITH HIGH BORON HAS LESS ARTHRITIS
MECHANISM OF ACTION

• BORON = acts as cell membrane catalyst allows ions to enter cells and on this basis ATP。(loughman 1983)

• Cartilage / collagen cells regenerate
• RA Overcomed
• Anti- infective == low conc. Inhibits bacteria
• THANK YOU FOR COMING