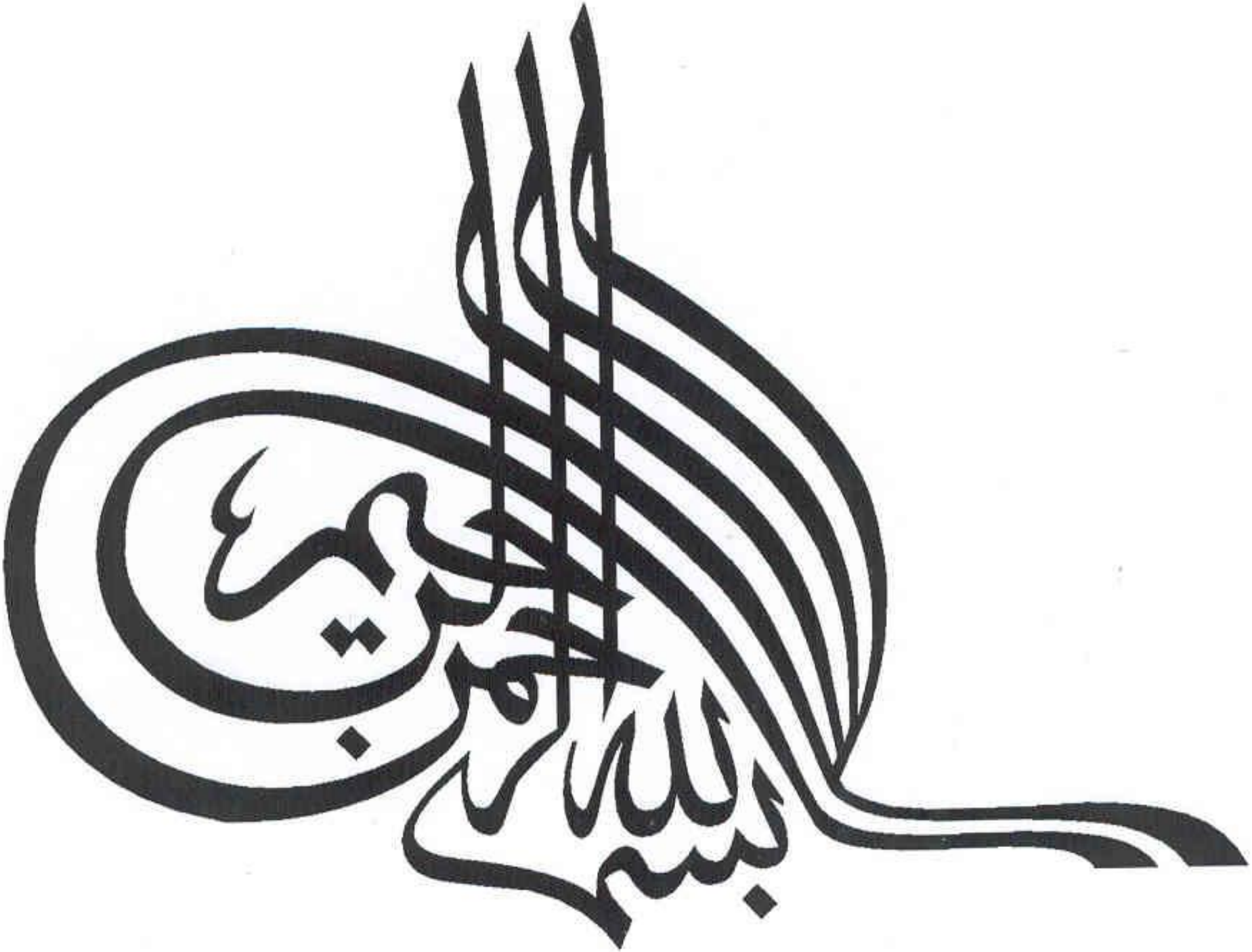
بسم الله الرحمن الرحيم

Occupational Hematologic Disease

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Hematologic disorders

- Haematological problem is the most important health effect, such as benzene-induced aplastic anaemia
- Effects on the blood are direct but of less significance than the effects on other organ systems, such as lead-induced anaemia
- Secondary effect of a workplace hazard (polycytemia)

Screening

- History
- Physical Examination
- Examination of Blood
- Bone Marrow Examination
- Other Examinations

History

- Attention to nonspecific symptom of anemia
- A history of jaundice or pigmenturia
- Symptom of infection
- Symptom of thromcytopenia
- Drug history
- Work history
- History of exposure to any potential toxic substance

Physical Examination

- Examination of skin and mucous membranes
- Cyanosis
- Abnormal bleeding or petechiae
- Examination of the fundi and mucous membrane
- Examination of the lymph nodes and spleen
- Examination of the bone (bone tenderness)

Examination of Blood

- Measurement of Hb, Hct, MCV,MCH
- Examination of peripheral blood smear :
  - Number of cells
  - Morphology
  - Differential count
- Retic count

Bone Marrow Examination

- Observation of erythroid of myeloid cells at all stages of maturation
- Presence of cells foreign to the marrow
- Presence of abnormal hematopoetic cells
- Chromosomal study

Other Examinations

- Platelet count
- Bleeding time
- PT
- PTT
- Serum iron
- TIBC
- LDH
- Billirubin(Indirect)
- Uric acid

Hemato Toxins Effect

- Blood cell survival (Denaturation HB & Hemolysis)
- Metabolism(Porphyria)
- Formation(Aplasia)
- Morphology and Function (Preleukemia & leukemia)
- Coagulation (through development of thrombocytopenia)

Methemoglobinemia and Hemolysis Produced By Oxidant Chemical

- Methemoglobin is formed by oxidation of ferrous Hb to ferric Hb.
- Oxidation of Hb was toxic to RBC and could be followed by an acute hemolysis
- Individuals with G6PD-D to be much more susceptible to oxidant stress than others.

Aniline

- Historically, most work-related episode of methemoglobinemia and hemolytic anemia were a result of exposure to aromatic nitro and amino compound.
- Intermediate in the synthesis of aniline dyes, accelerator and antioxidant in rubber industry, Production of pesticides ,plastics, paints and varnishes.

Aniline

- Fat-soluble and readily penetrate the skin, even the through clothing
- Vapor form may entry to the body through the lung

Clinical Presentation

%Methemoglobinemia	Symptoms
10-30	Cyanosis,mild fatigue,tachycardia
30-50	Weakness,breathlessness Headache ,exercise intolerance
50-70	Altered consciousness
>70-80	Coma, death

Clinical Presentation

- Patient appear deeply cyanotic.
- Freshly drawn blood appear dark maroon-brown and does not become red after exposure to air.
- Normoxia or mild hypoxia at pulse oximetry.
- Reticulocytosis in PBS(Polychromasia,possibly nucleated red cells).
- Polycythemia in chronic methemoglobinemia.

Treatment

- Removal of the offending agents
- Decontamination
- Mild intoxication(<%20) observation
- Moderate to severe (>%30) oxygen%100,methylene blue solution %1
- Exchange transfusion

Prevention

- Minimize atmospheric and cutaneous exposure to oxidizing chemicals such as coal tar.
- Biologic monitoring in the workplace by measuring methemoglobin levels and reticulocyte counts.
- Screening for G6PD deficiency 1-2 months after the hemolysis has resolved.

HEMOLYSIS ASSOCIATED WITH EXPOSURE TO HEAVY METALS

- Arsine
- Lead
- Copper
- Cadmium

Arsine

- Arsine poisoning:

  Volatile,colorless,Nonirritating gas

  - Exposure sources:
    - Refining of metals
    - Processes of galvanizing , soldering-plating
    - Treatment of metals with acid
    - Semi conductor industry

Signs & Symptoms

- Acute arsine poisoning are caused by acute and massive IV hemolysis +/_delayed 2-24 h after exposure
- Nausea
- vomiting
- abdominal cramping
- headache
- malaise
- dyspnea
- Tea-colored urine

Physical Exam

- Peculaire garlickly odor of arsine,fever,tachycardia,tachypnea and hypotension
- Jaundice, generalized nonspecific abdominal tenderness
- Acute tubular necrosis(oliguria or even anuria is usually evident within a day)
- CNS dysfunction, including alterations of mental status.
- Acute myopathy is seen with muscle tenderness and elevations of creatine phosphokinase

Laboratory Findings

- Hemoglobinuria
- Decreased plasma haptoglobin & increased free HB levels
- Dramatic elevation of lactate dehydrogenase (LDH).
- Reticulocytosis/leukocytosis/ platelet count may be low
- Altered renal function AND increased serum Cr
- Arsenic levels in blood and urine are useful as indicators of exposure rather than as guidelines for therapy.

Treatment

- Vigorous hydration
- Exchange transfusion if plasma Hb levels>400-500mg/dl
- If oliguric renal failure ensues, exchange transfusion is considered the treatment of choice because the hemolytic reaction itself may persist for up to 4 days after a single acute exposure.

Treatment

- There is no role in acute management for chelating agents such as British Anti-Lewisite because it cannot bind arsine or stibine to any appreciable degree.
- Hemodialysis if ARF developed
- All patients must be monitored closely until all evidence of hemolysis has resolved and renal function has stabilized.
- All survivors of acute arsine poisoning must be evaluated for at least 1 years
- Reduction of exposure or removal from exposure in chronic arsine poisoning

Lead

- Suppression erythropoiesis and heme synthesis
- Hemolytic anemia
- Pathogenesis of lead induced hemolysis is related to inhibition of pyrimidin 5”-nucleotidase
- Rarely is hemolysis the major presenting sign of acute lead poisoning

Signs & Symptoms

- Abdominal pain
- Constipation
- Vomiting
- Anorexia
- Peripheral neuropathy
- Lead encephalopathy (convalsion, headache,confusion)
- Anemia
- Lead line
- Stippling of retina

Laboratory Finding

- Anemia
- Mild increase of retic count
- Elevated of urinary levels of ALA & coporoporpherine III
- Elevated of urinary or blood levels of lead

Copper

- Manufacture of wire, sheet metal, pipe, and other metal products,
- In agriculture as a fungicide, and as a preservative for wood, leather, and fabrics
- Mildly elevated serum copper levels
- IV hemolysis ,methemoglobinemia and RF
- Treatment is supportive

Cadmium

- Battery and solar cell manufacture,
- Electroplating,
- Silver soldering,
- work around cadmium-containing pigments and coatings.

- Most notably on its nephrotoxic effects
- Acute anemia related, in part, to a hemolytic process
- Occupational cadmium exposure has not yet been definitively implicated as a cause of hemolytic anemia in workers.

Chemical Causes Acquired Porphyria

- Hexachlorobenzene……..fungicide
- Vinyle chloride……..plastic
- Lead……paint compound
- Aluminum……..phosphorus binder
- Chlorophenol….. Cleanser and disinfectant
- Polyhalogenated Aromatic Hydrocarbons
- Dioxin/PCBs /DDT

Acquired Porphyria

- **Neurotoxicity**
  - Abdominal colic
  - Constipation
  - Autonomic dysfunction
  - Sensory motor neuropathy
  - Psychiatric problem
- **Cutaneous photosensivity**
  - Repetitive vesiculation
  - Scarring
  - Deformity
  - Hypertricosis of sun exposed area

Hexacholorobenzene

- **In adults**
  - Hyperpigmentation
  - Hypertricosis
  - Bulla
  - Weakness
  - Hepatomegaly
- **In infants**
  - Weakness
  - Convulsion
  - Cutaneous annular erythema

Lead

- Blood lead level greater than 60 µg/dL
- The classic acute intermittent porphyria triad:
  - Abdominal pain, constipation, and vomiting all representing the neurotoxic effects of excess 8-aminolevulinic acid and porphobilinogen.
  - This triad is seen with equal frequency in lead intoxication.
  - Other shared characteristics include: neuromuscular pains, paresis or paralysis, paresthesias, diarrhea, and seizures.

- The major differences between the two diseases are :
  - 1- An increase in neuropsychiatric signs in acute intermittent porphyria compared with lead intoxication
  - 2- Anemia, which is present in lead intoxication but virtually absent in porphyria

Aplastic Anemia

- Idiopathic
- Secondary

(Drugs,Chemicals,Radiation,Infection,Immunologic)

- Drugs:

chloramphenicol,acetazolamide,phenylbutazone, phenytoin,sulfonamide, cytotoxic drugs such as antimetabolites and alkylating agents ….

Benzene, ionizing radiation, and cytotoxic drugs such as antimetabolites and alkylating agents are dose-dependent basis

Chemical Causes Aplastic Anemia

- **Benzene**….. pesticides, rubber, fabric, solvents for glues, ink, paint
- **Ionizing Radiation**
- **TNT**…….production of explosive
- **Lindane**…….pesticide
- **Arsenic**……manufacture of glass, paint, weed killer, pesticide
- **Ethylene glycol monornethyl** ……Production of paints, lacquers, dyes, Inks, cleaning agents

Inhibition of cell production

- Benzene poisoning
  - Exposure sources
    - Manufacture of explosive
    - Dye industry
    - Dry cleaning
    - Shoe making industry
    - Production of cosmetic soap, perfume, drugs
    - Rubber manufacturing, petroleum and chemical production
    - printing
    - Steel working

Sign and Symptom

- **Acute poisoning**
  - Headache, dizziness,vertigo
- **Chronic poisoning**
  - shortness of breath, paller,petecheia, purpura, infection, painful mouth
  - angina
- **Physiacal examination**
  - Pale
  - Petechiae,bruises
  - Fever

Benzene

- Bone marrow:

  Hypo cellularity with fatty replacement

  cytogenetic abnormalities are associated with benzene exposure, But specific chromosome changes are not.

- Prognosis:

  Up to 40% patient may recover completely after removal of exposure

  If hypo cellularity persists for more than several months, recovery is not likely to occur.

- Exposure is also associated with the development of acute non-lymphocytic leukemia and chronic myelogenous leukemia

- Treatment :supportive(transfusion,GFE,GCSF,GMCSF),

  Androgens, Allogenic BM trasplantation

Ionizing Radiation

- Risk of aplastic anemia is increased until 3-5 years after exposure, after which there is a marked decline in incidence
- Chromosomal aberrations may signify excessive exposure but is not predictive of aplastic anemia or leukemia
- Recovery may be seen after a prolonged period of aplastic anemia lasting 3-6 weeks.
- If recovery does not occur, permanent injury to the stem cell population will result in dysplasia or in leukemia.

Induction of leukemia

- **Radiation**
- **Benzene**
- **Formaldehyde**(myeloid leukemias)
- **Butadiene**(leukemia)
- **Ethylene oxide**(lymphoid tumors)
- **Styrene**
- **Petroleum refining work**

Multiple myeloma

- 15% of all hematologic cancers
- MM involves predominantly bone (skull), bone marrow and kidney
- Malignant proliferation of B-lymphocyte-derived cells that synthesize and secrete immunoglobulins
- Incidence of MM increases sharply with increasing age
- The peak incidence of multiple myeloma is between ages 55 and 65, and fewer than 2% of cases occur before the age of 40.
- Multiple myeloma is equally common in men and women

- Exposure to petroleum products, organic solvents, heavy metals, pesticides, and asbestos , high-dose radiation exposures implicated
- Workers thought to be at risk include :
  - Agricultural workers
  - Chemicals workers
  - Miners
  - Smelters
  - Stokers
  - Furniture workers

Non-Hodgkin's Lymphoma

- Pesticide (lindane or pentachlorophenol)
- Pentachlorophenol as a preservative
- Butadiene
- Benzene

Genotoxic and oxidative stress mechanisms, systemic immunosuppressive effects

Agents Caused Toxic Thrombocytopenia

Agents	Use	Mechanism
Toluene diisocyanate	Polymerizing agent	Immune
DDT	Insecticide	Megacarycyte hypoplasia
Turpentine	Organic solvent	Immune
Vinyl chloride	Plastics	Liver insufficiency with hypersplenism

Platelet Aggregation & Hypercoagulation

- Some environmental substance caused platelet aggregation and hypercoagulation
  - Methyl mercury
  - Cadmium
  - Triethyl lead
- Some pesticide inhibit platelet aggregation
  - Chlorophenyl
  - Arochlor

Polycythemia

- Metal *cobalt*
- Chronic exposure to asphyxiants, especially carbon monoxide.
- Secondary polycythemia also may be seen with lung diseases due to environmental factors

Neutrophils

- Transient neutrophilia is common in a host of acute occupational and environmental illnesses, such as:
  - Metal fume fever
  - Alveolitis caused by irritant gases

- Neutropenia may be seen in the setting of injury to the bone marrow due to:
  - Ionizing radiation
  - Arsenic
  - Benzene
  - Other agents affecting stem cells or the marrow microenvironment

Occupational Exposure to Anticancer Drugs

- Oncology nurses and pharmacist are at risk for exposure to potentially mutagenic agents.
- The agent most commonly implicated in mutagenic potential are Alkylating drugs.

Prevention

- Worker education
- Gloves and protective Clothing
- Laminar hood for preparing drugs
- Proper waste disposal
- Periodic atmospheric checks & Biologic monitoring


Thank You