

Occupational Hematology



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معاینات سلامت شاغلین و اختلالات هماتولوژیک مرتبط با شغل

■ بدو استخدام:

- توجه به مواجهات شغلی با هموتوکسینها
- وضعیت پایه در بدو بیمه و استخدام (ملاحظات قانونی)
- احتمال تاثیر شغل در بدتر شدن یا شعله ور شدن بیماری خونی
- احتمال تداخل در تشخیص اختلالات خونی مرتبط با شغل

■ دوره ای :

- غربالگری اختلالات خونی
- اقدامات تکمیلی جهت تشخیص بیماری خونی
- بررسی ارتباط بیماری با شغل
- مداخله مناسب

اختلالات خونی ناشی از مواجهات شغلی

- بیماری های جدی خونی ناشی از مواجهات شغلی مانند
benzene-induced aplastic anaemia
- اختلالات خونی ناشی از تاثیر مستقیم مواجهات شغلی
مانند lead-induced anaemia
- اثرات ثانویه خونی ناشی از خطرات شغلی مانند پلی
سیتمی ثانویه به بیماریهای ریوی شغلی

HEMATOLOGIC EFFECTS OF OCCUPATIONAL HAZARDS

- **Disorders Associated With Shortened RBC Survival**

- Hemolysis produced by oxidant chemicals
- Hemolysis Associated With Exposure To Heavy Metals

- **Disorders Affecting Blood Cell Formation & Morphology**

- Hematologic Cancers
- Aplastic Anemia (Benzene, Ionizing Radiation)
- Myelodysplastic Syndromes
- Toxic Thrombocytopenia

- **Agents That Interfere With Oxygen Delivery**

- Methemoglobinemia
- Sulfhemoglobinemia
- Carboxyhemoglobinemia

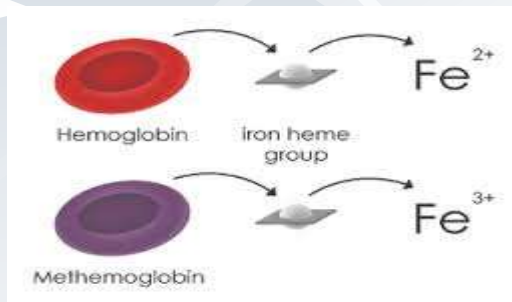
Methemoglobinemia and Hemolysis Produced By Oxidant Chemical

- Overexposure to chemicals (anilines, nitrobenzene) was common.
- Workers in these plants be known as "blue workers," because they suffered *tram* "blue lip" as a result of the chronic cyanosis from methemoglobinemia that developed in almost them.



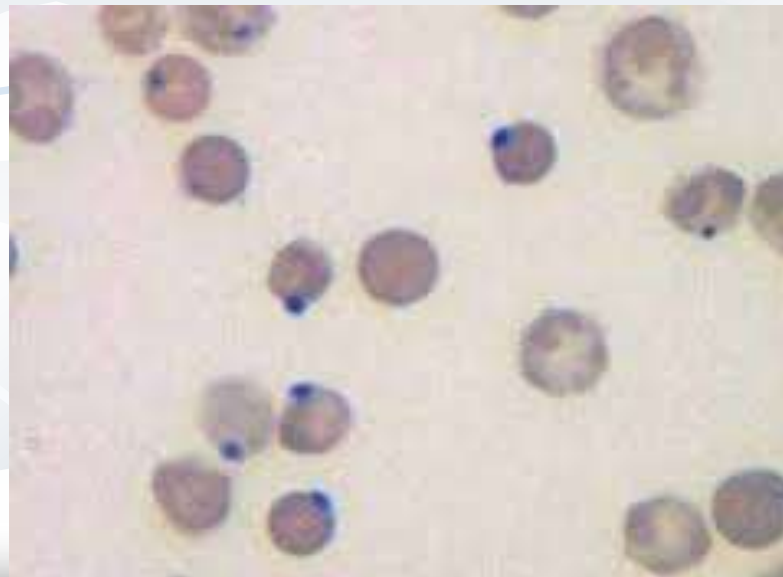
Methemoglobinemia and Hemolysis Produced By Oxidant Chemical

- Methemoglobin is formed by oxidation of ferrous Hb to ferric Hb (incapable of delivering oxygen to the tissues)



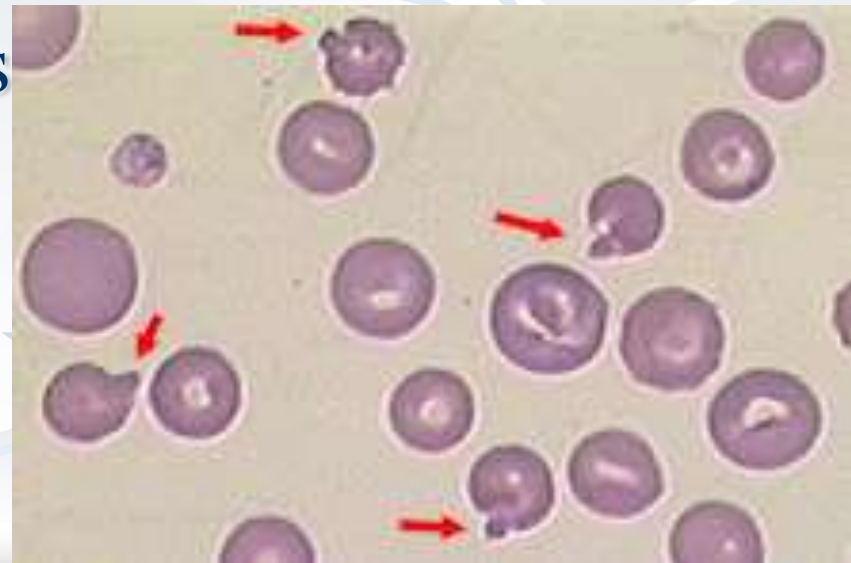
- Oxidation of Hb was toxic to RBC and could be followed by an acute hemolysis known as **Heinz body anemia**

- Heinz body are RBC inclusions that represent precipitated Hb and are classically seen in individuals with a deficiency G6PD after exposure to an oxidant stress
- individuals with G6PD-D to be much more susceptible to oxidant stress than others.



Pathophysiology of Oxidant Hemolysis

1. Oxidation HB
2. Denaturation HB
3. Precipitated HB within RBC
4. Alter the surface membrane of RBC
5. Increased rigidity and leakage
6. Extravascular hemolysis
7. Bite cell or blister cell



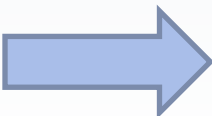
Aniline

- 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 through clothing
- Vapor form may enter to the body through the lung

Clinical presentation

- Symptoms vary depending on the **concentration of methemoglobin**
- Most cases are mild and as asymptomatic **blueness of the lips and nail beds**
- In more severe cases, the patient will appear deeply cyanotic
- Methemoglobin > 1.5 gr/dl = 10% of total hemoglobine  cyanosis

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

- cyanotic
- Freshly drawn blood appear dark maroon-brown and does not become red after exposure to air
- Normoxia or mild hypoxia at pulse oximetry
- Normal oxygen tension in ABG
- **Co-oximetry** (measures concentraton of metHb)
- Reticulocytosis in PBS (Polychromasia, possibly nucleated red cells)
- Bite or blistered red cell in PBC (supravital)
- Heinz body anemia
- Polycythemia in chronic methemoglobinemia



Prevention

- Minimize atmospheric and cutaneous exposure to oxidizing chemicals (most important)
- **Biologic monitoring** in the workplace by measuring **methemoglobin levels** and **reticulocyte counts**
- identification of susceptible individuals such as those with G6PD deficiency & avoid significant toxicity in high-risk job situations
- Screening for G6PD deficiency before a hemolytic episode or 1-2 month after the hemolysis

Treatment

- ❑ Removal of the offending agents
- ❑ Decontamination
- ❑ Mild intoxication(<%20) → observation
- ❑ Moderate to severe (>%30) → oxygen%100, methylene blue
- ❑ solution %1 at a dose of 1-2 mg/kg over 10 minutes
- ❑ The maximal effect should be seen within 1 hour
- ❑ If no response methylene blue may be repeated
- ❑ exchange transfusion

Chlorate Salts

- Use in pesticide and herbicide
- Uremic patient , public water supply as a disinfectant
- Denaturation of HB caused by chlorate is thought to be due to their **direct oxidizing** capacity and their **ability to inhibit the hexose monophosphate shunt**
- Treatment —→ Supportive

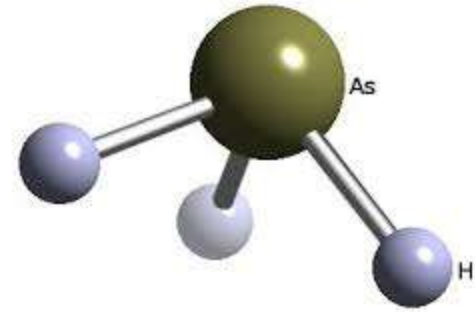
Chemicals associated with methemoglobinemia or oxidative hemolysis

Chemical	Use
Aniline	Rubber,dyestuffs,production of MBI
Nitroaniline	Dyes
Toluidine	Dyes,organic chemicals
P-Chloraniline	Dyes,pharmaceuticals,pesticides
O-Toluidine	Laboratory analytic reagent,production of trypan blue stain,chlorine test kits,test tapes
Naohthalene	Fumigants used in clothing industry
Paradichlorobenzene	Fumigants used in clothing industry
Nitrates	Soil fertilizers
Trinitrotoluene	Explosives

Hemolysis Associated With Exposure To Heavy Metals

- **Arsine**
- **Lead**
- **Mercury**
- **Copper**
- **Antimony**
- Mechanism of hemolysis is unknown
- it is thought to be related to the affinity of this directly cytolytic metals to thiol groups such as are found on the surfaces of RBC
- RBC membrane becomes permeable and takes on solute and water and burst (intravascular hemolysis)

Arsine



- Volatile, colorless, Nonirritating gas
- Produced by the action of acid on a metal contaminated with arsenic
 - Exposure sources:
 - Smelting & Refining of metals +/- stibine
 - Processes of galvanizing , soldering-plating
 - Treatment of metals with acid
 - Semi conductor industry
 - Preparation of crystals
- Respiratory tract is the most important portal of entry

Clinical Presentation

- Acute arsine poisoning are caused by acute and massive IV hemolysis +/- delayed 2-24 h after exposure
 - Nausea , vomiting , abdominal cramping , headache , malaise and dyspnea
 - Tea-colored urine (causing them to seek medical attention)
 - Phys/Exam garlickly odor + fever, tachycardia, tachypnea and hypotension
- Jaundice, generalized nonspecific abdominal tenderness
- Acute myopathy is seen with muscle tenderness and elevations of creatine phosphokinase

Laboratory Findings

- Hemoglobinuria (The earliest laboratory finding)
- Decreased plasma haptoglobin & increased free HB levels
- The plasma may be brownish-red from the presence of methemalbumine
- Poikilocytosis, basophilic stippling and polychromasia at PBS
- Dramatic elevation of lactate dehydrogenase (LDH).
- Reticulocytosis/leukocytosis/ platelet count may be low, direct Coombs' or tests for fibrinolytic factors (e.g., fibrin split products) are negative.
- Decreased HCT
- increased indirect bilirubin
- DIC (low fibrinogen level & prolonged PT)
- Altered renal function → increased serum Cr
- Arsenic levels in blood and urine are useful as indicators of exposure rather than as guidelines for therapy.

Treatment

- Vigorous hydration & adequate renal perfusion
- Exchange transfusion if plasma Hb levels >400-500mg/dl
- Hemodialysis if ARF developed
- All survivors of acute arsine poisoning must be evaluated for at least 1 years for renal function
- Reduction of exposure or removal from exposure in chronic arsine poisoning

Copper

- White washing & leather industry
- IV hemolysis , methemoglobinemia and RF
- Treatment is supportive

Lead

- Suppression erythropoiesis
- Decrease heme synthesis
- Hemolytic anemia (very high atmospheric exposure, as in power sanding and use of a blowtorch)
- Pathogenesis of lead induced hemolysis is related to inhibition of pyrimidin 5''-nucleotidase

Lead Poisoning

- Exposure sources
 - Lead miners
 - Workers that clean old painting rooms
 - Person that responsible for disposal of lead-containing batteries
 - Workers that product illicit alcohol
 - Use of lead plate
 - Embedded bullet in body

Signs & Symptoms

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

Laboratory Finding

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

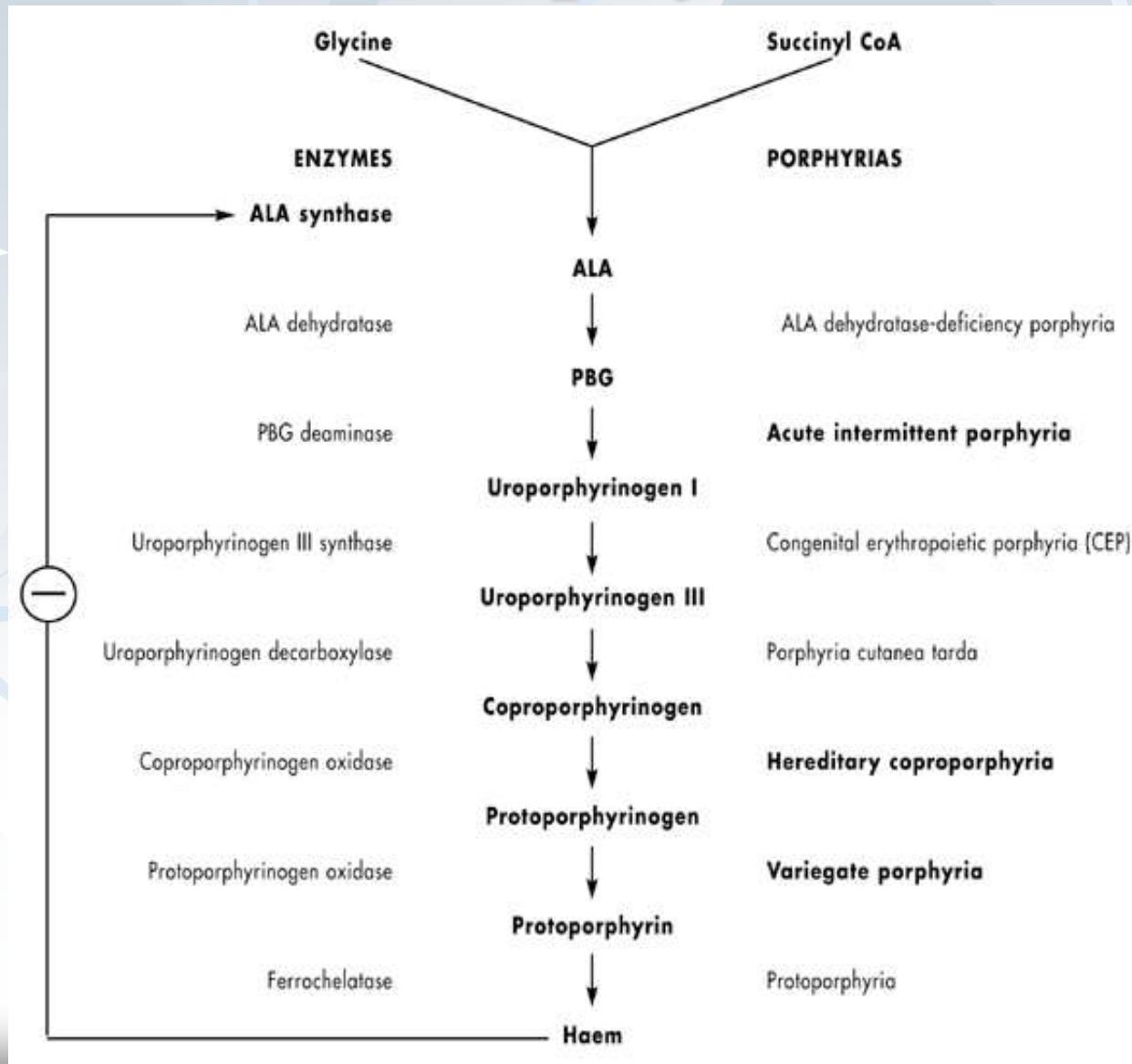
Lead

- Tests for other causes of hemolysis, such as Coombs' and G6PD tests, are negative.
- The diagnosis of acute lead poisoning is made by measurement of the whole blood lead level, which is generally very high in this setting, usually over 70 $\mu\text{g}/\text{dl}$.
- The ZPP or FEP levels also are usually very high (inhibition of heme synthetase)

Porphyrias

- A group of disorders characterized by abnormalities in the heme biosynthetic pathway that result in the abnormal accumulation of heme precursors.
- **genetic disorders** :of enzymatic activity
- **acquired porphyria** : exposure to various toxins
- liver and bone marrow and to a certain extent in nervous tissue

Porphyria



Chemical Causes Acquired Porphyria

- Hexachlorobenzene.....fungicide
- Vinyl chloride.....plastic
- Lead.....paint compound
- Aluminum.....phosphorus binder

Acquired Porphyria

■ Neurotoxicity

- Abdominal colic
- Constipation
- Autonomic dysfunction
- Sensory motor neuropathy
- Psychiatric problem

■ Cutaneous photosensitivity

- Repetitive vesiculation
- Scarring
- Deformity
- Hypertrichosis of sun exposed area
- discoloration of teeth
- hemolysis of erythrocytes

- Cutaneous photosensitivity



Hexachlorobenzene

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

Lead

- **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

TREATMENT OF TOXIC PORPHYRIAS

- No effective means of eliminating toxin
- exposure to porphyrinogenic compounds must be avoided
- Phlebotomy
- high-dose carbohydrate infusions (400 g of dextrose per day)
- hematin infusions (3 mg/kg IV every 12 hours for 10-12 doses).

Disorders Associated With Decreased Oxygen Saturation

- Carbon monoxide poisoning
 - odorless, colorless, nonirritating gas produced by the incomplete combustion
- The workers at greatest risk are :
 - Automobile mechanics
 - foundry workers
 - miners
 - Fire fighters
 - Chemical workers exposed to methylene chloride

- Hemoglobin has an affinity for carbon monoxide that is **210 times** greater than that for oxygen.
- Carbon monoxide also increases the **stability** of the hemoglobin-oxygen combination
- Carbon monoxide binds to the cytochrome oxidase chain. These properties of carbon monoxide result in chemical asphyxiation

Clinical Finding

- **Symptoms:** general malaise, headache, nausea, dyspnea, vomiting, coma, seizures, Arrhythmias and death without cyanosis (the cherry-red color of carboxyhemoglobin)

Signs of carbon monoxide poisoning



Headaches



Nausea



Dizziness



Breathlessness



Collapse



Loss of
consciousness

Laboratory findings:

- polycythemia (chronic low levels)
- Hypoxia (at higher levels)
- **Carboxyhemoglobin** levels should be measured
- a level less than 6% may cause impairment in vision and time discrimination
- At 40-60% alterations in mental status and death may be seen

- Carboxyhemoglobin levels should be measured; a level less than 6% may cause impairment in vision and time discrimination
- At 40-60% alterations in mental status and death may be seen

Treatment

- At low levels **without symptoms**, removal from the source of exposure is sufficient.
- At higher levels or **with symptoms**, the treatment of choice is **hyperbaric oxygen**

CARBON MONOXIDE POISONING

- Half life of CO-HB

- In breathing air is 4-5 hours
- By giving 100% O₂ is 80 min
- By giving hyperbaric O₂ is 25 min

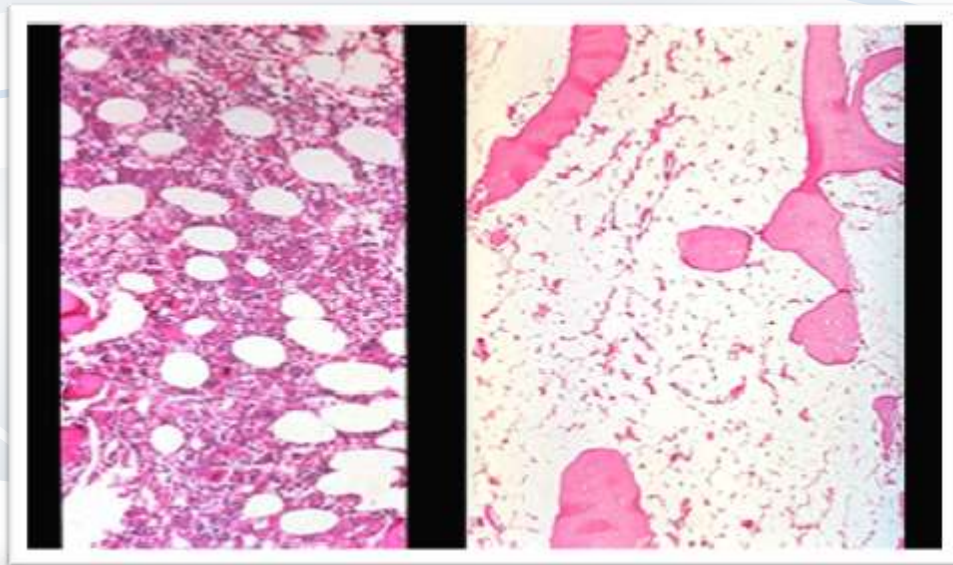
□ **Prevention : adequate ventilation, with venting of combustion devices to the outside air**

Disorders Affecting Blood Cell Formation & Morphology

- Aplastic anemia ; Benzene, Ionizing Radiation
- Myelodysplastic Syndromes
- Multiple Myeloma
- Toxic Thrombocytopenia
- Hematologic cancer

Aplastic Anemia

- acquired abnormality of the pluripotent hematopoietic stem cells → pancytopenia
- 50% are idiopathic
- most of the remainder are secondary aplastic anemias



Aplastic Anemia

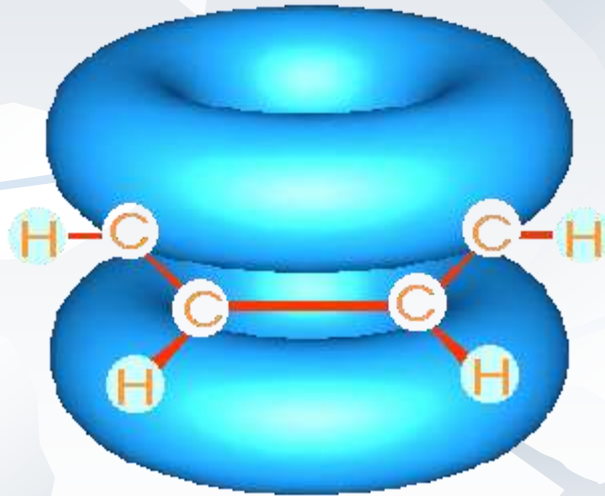
- Idiopathic & secondary →
 - Drugs(largest category)
 - Chemicals
 - Radiation
 - Infection
 - Immunologic
- Drugs(chloramphenicol , acetazolamide, phenylbutazone, phenytoin , sulfonamide,....)
- Benzene , Ionizing Radiation & cytotoxic drugs such as antimetabolites and alkylating agents

Chemical Causes Aplastic Anemia

- Benzene..... pesticides, rubber, fabric, solvents for glues, ink, paint
- TNT.....production of explosive
- Lindane.....pesticide
- Arsenic.....manufacture of glass, paint, weed killer, pesticide

Benzene

- Workers at greatest risk of exposure: Rubber manufacturing , shoemaking , petroleum and chemical production, dye industry, dry cleaning , printing & steel working



Benzene

- **Toxicity related to:**
- amount and duration of exposure
- individual variation in susceptibility
- The current US exposure limit is 1 ppm.

Diagnosis :

- examination of the bone marrow after an abnormal complete blood count is reported
- BM Hypocellularity with fatty replacement

Benzene

Prognosis:

- Up to 40% patient may recover completely after removal of exposure
- If hypocellularity persists for more than several months, recovery is not likely to occur. Exposure is associated with ANLL & CML

Treatment:

- supportive(transfusion , GCSF,GMCSF, erythropoietine), Androgens
- **Allogenic BM trasplantation**

Other causes of aplastic anaemia

- **Trinitrotoluene**, which is absorbed readily through the skin, has been associated with aplastic anaemia in munition plants
- **Pesticide lindane** (gamma-benzene hexachloride)
- **Ethylene glycol ethers**
- **Arsenic**
- **Ionizing Radiation**: monitoring with badges has virtually eliminated aplastic anemia except in cases of accidental overexposure

Myelodysplastic syndrome

- acquired genetic disorder of the blood-forming cells similar to cancer
- Ineffective hematopoiesis
- Clinically resulting in anemia , neutropenia & thrombocytopenia
- presence of bizarre hematopoietic morphology
- tendency to transform into acute leukemia.

Myelodysplastic syndrome

■ Occupational risk factors:

- Benzen
- Ionizing radiation
- Pesticide
- Solvent

■ Specific works:

- Farming
- Textile
- Health care workers

Myelodysplastic syndrome

- Median survival: 12 months
- All patients died → leukemia or cytopenia complications
- More common in men
- 85% patients are older than 40 years old

Myelodysplastic syndrome

Lab test:

Cytopenia & bizarre hematopoietic morphology (PBS)

Bone marrow aspiration:

- dysplasia in all three cell line
(granulocyte/erythroid/megakaryocyte)
- hypercellular.
- There is an abnormal increase in the percentage of blast cells.

Myelodysplastic syndrome

- TREATMENT:
- Allogeneic bone marrow transplantation is the only known cure
- Transfusions and treatment of infections may be aided by the use of hematopoietic growth factors
- 5-azacytidine (5-AZA) and decitabine, are showing some promise.

Multiple myeloma

- ❑ Chronic leukemia of plasma cell
- ❑ Peak incidence: 55-65
- ❑ Men = women

Multiple myeloma

Clinical finding:

- ❑ Anemia
- ❑ Painful lytic and osteopenic bone disease
- ❑ Monoclonal immunoglobuline production (serum / urine / both)
- ❑ Hypogammaglobulinemia
- ❑ Short survival

Multiple myeloma

Occupational risk factors:

- Petroleum products
- Organic solvents
- Heavy metals
- Pesticide
- asbestos
- Benzene
- Ionizing radiation

Multiple myeloma

Treatment:

- ❑ Thalidomide
- ❑ Chemotherapy
- ❑ Corticosteroid (↓ bone pain & prolonging life)
- ❑ Bone marrow transplantation soon after DX
improve survival

Toxic Agents Caused Thrombocytopenia

Agents

Toluene diisocyanate

DDT

Turpentine

Vinyl chloride

Use

Polymerizing agent

Insecticide

Organic solvent

Plastics

Mechanism

Immune

Megacaryocyte hypoplasia

Immune

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

Cobalt-induced polycythemia

- Consumption of cobalt-contaminated beer
- Hard metal manufacture and grinding
- Diamond cutting
- Increased hemoglobin is not part of the clinical picture of cobalt-induced asthma or parenchymal lung disease.

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

The background of the slide features a repeating pattern of stylized, light blue leaves. The leaves are rendered in a flat, graphic style with visible veins, creating a textured, organic feel. They are scattered across the entire frame, with some overlapping others.

fitness for work

Introduction:

- 1-Hematologic disorders found in accidental or with consultant
- 2- clinical aspects

Iron deficiency

Prevalence

Causes : *GI bleeding, drugs.*

Clinical findings : *weakness , fatigue, constitutional symptoms.*

Work related :

decreased work capacity

required more resting time

increased GI metal absorption

increased risk of metal toxicity in high risk jobs.

Polycythemia

types : polycythemia vera
secondary
pseudo

Clinical finding :
transient ischemic attack
visual disturbance
peripheral vascular disorders

Polycythemia

Work related :

- 1- in primary type phlebotomy 1 time per month
- 2- depend on background disease in secondary type

high mean cell volume

causes : 1- folic acid deficiency

2- vit. B12 deficiency

3- Myxedema

4-hepatic disorder

5- alcohol consumption

Low platelet count

Work related:

vaccination

veterinary and healthcare workers

malaria prophylaxis in passengers

avoid from heavy manual work

Acute myeloid leukemia

Clinical finding : *anemia , infection , other organ damage*

Work related : HCW , laundry , sewerage workers

Hodgkin and non Hodgkin lymphoma

Work related : *avoid from high risk infectious sites*

Treatment : *chemotherapy , radiotherapy*

Prognosis : *good in Hodgkin*

Hemoglobinopathies

Thalassemia major

Thalassemia trait

Sickle cell anemia

G6PD deficiency : 1-*farmers*

2-*workers exposed to oxidative agents; naphthalene; trinitrotoluene*

Sickle cell disease:

heterozygot without symptoms

homozygot hemolysis and vascular occlusion in :
hypoxia, dehydration, acidosis, hot
environment

Hemophilia A and B

Sex linked

Types : *severe , moderate , mild*

Work related : *driving license no problem*

armed forces and airplane

crew not accepted

in severe cases hard manual tasks

is not recommended

Treatment : *self administration of factor*

The background of the slide features a stylized, light blue and white pattern of overlapping leaves or branches, creating a textured, organic feel. The text is centered and written in a bold, italicized, purple font.

A physician should be provided a proper work site and situation for working and self administration of patients.

The background of the slide features a large, stylized leaf pattern in shades of light blue and white. The leaves are arranged in a way that they overlap, creating a sense of depth and texture. The overall color palette is cool and professional.

THANKS FOR ATTENTION