

**An Assignment on**

**Drugs used in heamopoietic system**

**Course No:** PHARM-2111

**Course Title :** Pharmacology-1

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**Drugs used in heamopoietic system**

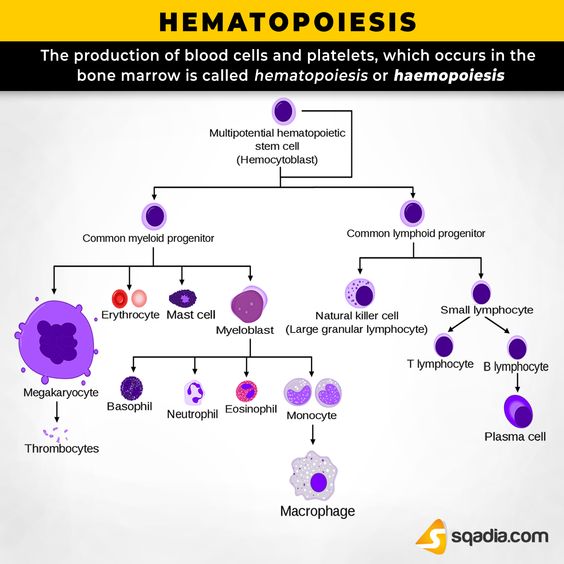
**Heamatopoiesis**: Production of red blood cells,white cells and platelets(blood cell formation).

* All cellular blood components are derived from [haematopoietic stem cells](https://en.wikipedia.org/wiki/Hematopoietic_stem_cell). In a healthy adult person, approximately 1011–1012 new blood cells are produced daily in order to maintain steady state levels in the peripheral circulation.

 Haematopoietic system :

The Haematopoietic system is the **system** of organs and tissues, including the bone marrow, spleen, thymus and lymph nodes, involved in the production of cellular blood components.

**Classification:-**



**ANTICOAGULANTS**

Anticoagulant are the drugs,which are used to prevent unwanted coagulation.

**Classification**

A.acting in vitro:-

* Na and salt of oxalate ,citrate
* EDTA
* Heparin,dextran sulfate etc

B.acting in vivo:-

* Dicoumarol
* Warfarin

C.Acting both in vitro and in vivo:-

* Heparin,dextran sulfate

D.According to M/A:-

1.Direcly acting:-

* Heparin,dextarn sulfate

2.Indirectil acting:-

* Coumarin derivatives

E.According to route of administration:-

Injectable-

* Heparin

Oral-

* Warfarin

**Heparin**

Heparin is a heterogeneous mixture of water soluble strong electronegative charge. It is so called because of its abundance in hepatic cell. It is also found in mast cells ,basophil,commercially prepared form beef lungs and hog intestinal mucosa.

**Route of administration:-**

Parenterally:i/v or s/c route.it is not given orally as it is destroyed by amylase enzyme.

## Uses

* This [medication](https://www.webmd.com/drugs/index-drugs.aspx) is used to prevent and treat [blood clots](https://www.webmd.com/dvt/blood-clot-symptoms).
* It may be used to prevent and treat [blood clots](https://www.webmd.com/dvt/blood-clots) in the [lungs](https://www.webmd.com/lung/picture-of-the-lungs) .
* It may be used to treat certain [blood](https://www.webmd.com/heart/anatomy-picture-of-blood) clotting disorders.
* It may also be used to prevent blood clots after surgery, during [dialysis](https://www.webmd.com/a-to-z-guides/kidney-dialysis), during blood transfusions, when collecting blood samples, or when a person is unable to move for a long time.
* [Heparin](https://www.webmd.com/drugs/2/drug-3918/heparin+(porcine)+injection/details) helps to keep blood flowing smoothly by making a certain natural substance in your body work better. It is known as an anticoagulant.

**Heparinization**

Continuous intravenous infusion via an infusion pump. Initial loading dose:5000-10000 units. Then continuous infusion:900 units/hour.

Intermittent IV infusion:75-100 units/kg every four hours.

**Protamine sulphate**

it is the antidote of heparin obtaind from fish sperm.

**M/A:**it is an electropositive charge,combines with heparin molecule as an iron pair to form a stable complex ,which lacks anticoagulant activity .

**Antidote dose**: for every 100 units of heparin remaining in the patient ,1 mg protamine sulphate should be administered intravenously.

**Oral anticoagulants**

**Oral anticoagulants**, also called vitamin K antagonists , are used to prevent the occurrence or increase of unwanted blood clots. They inhibit enzymes called vitamin K epoxide reductase and vitamin K reductase. These enzymes are required for chemical reduction of oxidized vitamin K.

Example of some oral anticoagulants are-

Coumarin derivatives-

1.Dicoumarol

2.warfarin.

3.phenindione

**Preparation and dosage of oral anticoagulants**:warfarin Na 5mg tablets. It is used once a day in the dose of 2.5-10 mg.the drug

**Monitoring of oral anti-coagulant therapy:** therapy with oral anticoagulants is monitored by the patients prothromin time. The results are reported as the international normalized ratio(INR). The INR is the prothrombin time ratio obtaind .Normal INR=1

**In vitro anticoagulants**

**Oxalates and citrates**: These act by removal of calcium ions.potassium oxalate 0.1 percent precipitate serum calcium and forms calcium oxalate.the anticoagulant solution contains 2.5%of Na –citrate in 0.9% saline. Citrate is usually employed as anticoagulant during blood transfusion.

**EDTA:**is a chelating agent.it has a great affining for calcium and its sodium salt is used as an anticoagulant.

**Anemia**

* Decreased capacity of RBCs to carry oxygen to tissues.

Depending on the causes of your anemia, you might have no symptoms. Signs and symptoms, if they do occur, might include:

* Fatigue
* Weakness
* Pale or yellowish skin
* Irregular heartbeats
* Shortness of breath
* Dizziness or lightheadedness
* Chest pain
* Cold hands and feet
* Headaches

## Causes:

Anemia occurs when your blood doesn't have enough red blood cells.

This can happen if:

* Your body doesn't make enough red blood cells
* Bleeding causes you to lose red blood cells more quickly than they can be replaced
* Your body destroys red blood cells

## Treatment

There is a [range of treatments](https://www.nhlbi.nih.gov/files/docs/public/blood/anemia-yg.pdf) for anemia. Each aims to increase the number of RBCs, which, in turn, increases the amount of oxygen in the blood.

Below, we outline treatments for several types of anemia:

* **Iron-deficiency anemia:** Iron supplements and dietary changes can help, and, when relevant, a doctor will identify and address the cause of excessive bleeding.
* **Vitamin deficiency anemia:** Treatments can include dietary supplements and [vitamin](https://www.medicalnewstoday.com/articles/195878) B-12 shots.
* **Thalassemia:** [Treatments](https://www.nhlbi.nih.gov/health-topics/thalassemias) include [folic acid](https://www.medicalnewstoday.com/articles/219853) supplements, iron chelation, and, for some people, blood transfusions and bone marrow transplants.
* **Anemia due to chronic disease:** The doctor will focus on resolving the underlying condition.
* **Aplastic anemia:** Treatment involves blood transfusions or bone marrow transplants.
* **Sickle cell anemia:**Treatment typically involves oxygen therapy, pain relief medication, and intravenous fluids, but it can also include antibiotics, folic acid supplements, blood transfusions, and a cancer drug called [hydroxyurea](https://www.cdc.gov/ncbddd/sicklecell/recommendations.html).
* **Hemolytic anemia:** The treatment plan may include immunosuppressant drugs, treatments for infections, and plasmapheresis, which filters the blood.

**Haematinic agents**

Haematinics are the **agents** used for formation of blood to treat various types of anemias.

**Important haematinics are-**

* **Iron**
* **Folic acid**
* **Vitamin B12**

**Iron**

**Iron** is part of hemoglobin, a protein which carries oxygen from our lungs throughout our bodies.

### ****Iron****

##### **Storage**

Iron is the integral component of haeme. In our body:

1. 66-67% of iron is present in hemoglobin.
2. 3% occurs in myoglobin
3. 1% in enzymes -cytochrome, catalase, peroxidase
4. 25% is stored in form of ferritin and hemosiderin

**Symptoms:**

iron deficiency anemia signs and symptoms may include:

* Extreme fatigue
* Weakness
* Pale skin
* Chest pain, fast heartbeat or shortness of breath
* Headache, dizziness or lightheadedness
* Cold hands and feet
* Inflammation or soreness of your tongue
* Brittle nails
* Unusual cravings for non-nutritive substances, such as ice, dirt or starch
* Poor appetite, especially in infants and children with iron deficiency anemia

**Causes:**

causes of iron deficiency anemia include:

* **Blood loss.** Blood contains iron within red blood cells. So if you lose blood, you lose some iron. Slow, chronic blood loss within the body — such as from a peptic ulcer, a hiatal hernia, a colon polyp or colorectal cancer — can cause iron deficiency anemia. Gastrointestinal bleeding can result from regular use of some over-the-counter pain relievers, especially aspirin.
* **A lack of iron in your diet.** Your body regularly gets iron from the foods you eat. If you consume too little iron, over time your body can become iron deficient. Examples of iron-rich foods include meat, eggs, leafy green vegetables and iron-fortified foods. For proper growth and development, infants and children need iron from their diets, too.
* **An inability to absorb iron.** Iron from food is absorbed into your bloodstream in your small intestine. An intestinal disorder, such as celiac disease, which affects your intestine's ability to absorb nutrients from digested food, can lead to iron deficiency anemia.
* **Pregnancy.** Without iron supplementation, iron deficiency anemia occurs in many pregnant women because their iron stores need to serve their own increased blood volume as well as be a source of hemoglobin for the growing fetus.

**Clinical uses of iron**

A.**Prophylactic use**:

* Pregnancy –from the 4th month of pregnancy and should be continued during the lactation period
* Menstruation
* Infancy and childhood
* Premature babies
* Professional blood donors

B.**Therapeutic use**:

* Chronic blood loss
* Lncreased demand
* Inadequate dietary intake
* Inadequate absorption

**Unwanted effects of iron treatment**

##### **Clinical Toxicity**

Toxicity occurs due to overdosage.

###### ****Acute Iron Toxicity:****

Seen after ingestion of tablets of iron. Common in children.

**Lethal dose**10 or more tablets are lethal due to accidental ingestion. Adults can tolerate larger doses than children

**Fatal period**4-6 hours.

**Manifestations**

1. Immediate
2. Delayed

Death may occur within 4-6 hours.

**Symptoms**

1. Vomiting
2. Necrotizing gastroenteritis (abdominal pain, bloody diarrhea)
3. Followed by metabolic acidosis
4. Abdominal pain
5. Bloody diarrhea
6. shock
7. Dypsnoea- may improve or lead to:

* Comma
* Death

**Treatment**

1. Gastric lavage/aspiration of what is ingested, usually with sodium bicarbonate

Home made remedy of egg yolk and milk, which complexes iron and renders it non-absorbable.

1. Chelating agents –Deferroximine given I/V, binds iron and prevents its absorption and eliminates it from body.
2. Supportive therapy required for correction of metabolic acidosis, treatment of shock and usually Diazepam for convulsions.

Activated charcoal does not bind iron so is not effective.

###### ****Chronic Iron Toxicity:****

Slow and gradual accumulation of iron in body. Different organs are involved like heart, liver, and pancreas. Iron gets accumulated in these organs producing end organ failure and hemochromatosis. In thalassemia, when repeated blood transfusions are given, aplastic anemia might occur.

**Treatment**

1. Intermittent Phlebotomy -1 unit blood is removed each week or till iron overload is corrected.
2. Iron Chelation therapy – Deferasirox, given orally. There is no role of deferoximine and is actually hazardous.

Deferasirox may not chelate iron in the heart.

**Vitamin B12 and folic acid**

Both vitamin B12 and folic acid are necessary for DNA synthesis .

Deficiency particularly affect erythropoiesis, causing macrocytic megaloblastic anaemia. In almost 95% of the case with megaloblastic bone marrow vitamin b12 and folic acid deficiency in present.

**Vitamin B12**

**Vitamin B12**, also known as cobalamin, is an important water-soluble **vitamin** . It plays an essential role in the production of your red blood cells and DNA, as well as the proper functioning of your nervous system. **Vitamin B12** is naturally found in animal foods, including meats, fish, poultry, eggs and dairy

## Food Sources of Vitamin B12

You can get vitamin B12 in animal foods, which have it naturally, or from items that have been fortified with it.

Animal sources include dairy products, eggs, fish, meat, and poultry. If you're looking for a food fortified with B12, check the product's Nutrition Facts label.

## Vitamin B12 Deficiency

Most people in the U.S. get enough of this nutrient. If you're not sure, you can ask your doctor if you should get a blood test to check your vitamin B12 level.

With age, it can become harder to absorb this vitamin. It can also happen if you have had weight loss surgery or another operation that removed part of your stomach, or if you drink heavily.

You may also be more likely to develop vitamin B12 deficiency if you have:

* Atrophic [gastritis](https://www.webmd.com/digestive-disorders/digestive-diseases-gastritis), in which your [stomach](https://www.webmd.com/digestive-disorders/picture-of-the-stomach) lining has thinned
* Pernicious anemia, which makes it hard for your body to absorb vitamin B12
* Conditions that affect your small intestine, such as [Crohn's disease](https://www.webmd.com/ibd-crohns-disease/crohns-disease/default.htm), [celiac disease](https://www.webmd.com/digestive-disorders/celiac-disease/default.htm), bacterial growth, or a parasite
* [Immune system disorders](https://www.webmd.com/a-to-z-guides/autoimmune-diseases), such as [Graves' disease](https://www.webmd.com/women/understanding-graves-disease-basics) or [lupus](https://www.webmd.com/lupus/default.htm)
* Been taking certain medications that interfere with the absorption of B12. This includes some heartburn medicines including proton pump inhibitors (PPIs) such as [esomeprazole](https://www.uptodate.com/contents/esomeprazole-drug-information?search=proton+pump+inhibitors&topicRef=5&source=see_link) ([Nexium](https://www.webmd.com/drugs/2/drug-20536/nexium-oral/details)), [lansoprazole](https://www.uptodate.com/contents/lansoprazole-drug-information?search=proton+pump+inhibitors&topicRef=5&source=see_link) ([Prevacid](https://www.webmd.com/drugs/2/drug-150285/prevacid-solutab-oral/details)), [omeprazole](https://www.uptodate.com/contents/omeprazole-drug-information?search=proton+pump+inhibitors&topicRef=5&source=see_link) ([Prilosec OTC](https://www.webmd.com/drugs/2/drug-77588/prilosec-otc-oral/details)), [pantoprazole](https://www.uptodate.com/contents/pantoprazole-drug-information?search=proton+pump+inhibitors&topicRef=5&source=see_link) ([Protonix](https://www.webmd.com/drugs/2/drug-18142/protonix-oral/details)), and [rabeprazole](https://www.uptodate.com/contents/rabeprazole-drug-information?search=proton+pump+inhibitors&topicRef=5&source=see_link) ([Aciphex](https://www.webmd.com/drugs/2/drug-17511/aciphex-oral/details)), H2 Blockers such as cimetidine ([Tagamet](https://www.webmd.com/drugs/2/drug-7035/tagamet-oral/details)) and famotidine ([Pepcid AC](https://www.webmd.com/drugs/2/drug-1821-2033/pepcid-oral/famotidine-oral/details)); and certain diabetes medicines such as [metformin](https://www.webmd.com/drugs/2/drug-11285-7061/metformin-oral/metformin-oral/details) ([Glucophage](https://www.webmd.com/drugs/2/drug-11294/glucophage-oral/details)).

You can also get [vitamin B12 deficiency](https://www.webmd.com/vitamins-and-supplements/vitamin-b12-rm-quiz-html) if you follow a [vegan](https://www.webmd.com/food-recipes/guide/vegetarian-and-vegan-diet) diet meaning you don't eat any animal products, including meat, milk, cheese, and eggs) or you are a vegetarian who doesn't eat enough eggs or dairy products to meet your vitamin B12 needs. In both of those cases, you can add fortified foods to your diet or take supplements to meet this need.

## Symptoms of Vitamin B12 Deficiency

If you have vitamin B12 deficiency, you could become anemic. A mild deficiency may cause no symptoms. But if untreated, it may lead to symptoms such as:

* [Weakness](https://www.webmd.com/a-to-z-guides/tc/weakness-and-fatigue-topic-overview), tiredness, or lightheadedness
* Heart palpitations and shortness of breath
* Pale [skin](https://www.webmd.com/skin-problems-and-treatments/picture-of-the-skin)
* A smooth tongue
* Constipation, diarrhea, loss of appetite, or gas
* Nerve problems like numbness or tingling, muscle weakness, and problems walking
* Vision loss
* Mental problems like depression, memory loss, or behavioral changes

## Treatment

If you have pernicious anemia or have trouble absorbing vitamin B12, you'll need shots of this vitamin at first. You may need to keep getting these shots, take high doses of a supplement by mouth, or get it nasally after that.

**Folic acid**

Folic acid is composed of 3 subunits:-

* **Pteridine**
* **Para aminobenzoic acid**
* **Glutamic acid residues**–attached to pteryl portion forming monoglutamate, triglutamate, polyglutamate
* Liver and green vegetables are sources of folate . In healthy non-pregnant adults,the daily requirement is about 200g,but this is increased during pregnancy.

Folate deficiency means you have a lower-than-normal amount of [folic acid](https://medlineplus.gov/ency/article/002408.htm), a type of vitamin B, in your blood.

## Causes

Folic acid (vitamin B9) works with vitamin B12 and vitamin C to help the body break down, use, and make new proteins. The vitamin helps form red and white blood cells. It also helps produce DNA, the building block of the human body, which carries genetic information.

Folic acid is a water-soluble type of vitamin B. This means it is not stored in the fat tissues of the body. Leftover amounts of the vitamin leave the body through the urine.

Because folate is not stored in the body in large amounts, your blood levels will get low after only a few weeks of eating a diet low in folate. Folate is found primarily in legumes, leafy greens, eggs, beets, bananas, citrus fruits, and liver.

Contributors to folate deficiency include:

* Diseases in which folic acid is not well absorbed in the digestive system (such as [Celiac disease](https://medlineplus.gov/ency/article/000233.htm) or [Crohn disease](https://medlineplus.gov/ency/article/000249.htm))
* Drinking too much alcohol
* Eating overcooked fruits and vegetables. Folate can be easily destroyed by heat.
* [Hemolytic anemia](https://medlineplus.gov/ency/article/000571.htm)
* Certain medicines (such as phenytoin, sulfasalazine, or trimethoprim-sulfamethoxazole)
* Eating an unhealthy diet that does not include enough fruits and vegetables
* Kidney dialysis

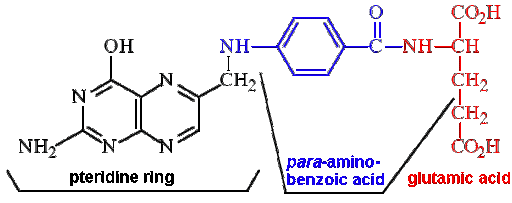


Fig: folic acid

##### **Treatment of Folic Acid Deficiency**

Parenteral administration is rarely needed.

**Oral therapy Dose**

1mg/day – continued until underlying cause is corrected or removed.

##### **Adverse effects**

Very rare. Only a few allergic manifestations have been reported.

##### **Uses**

1. Treatment of megaloblastic anemia
2. Prophylaxis of megaloblastic anemia
3. Also given in methotrexate toxicity. Toxicity is in form of encephalopathy. Folic acid is not given, rather reduced form of folic acid **5-formyl tetrahydrofolate,**also known as Leucovorin/citrovorum, but has to be given within an hour of toxicity. This should not be delayed.