

Hematopoiesis,

- **200 billion new blood cells per day**
- **The hematopoietic machinery requires a constant supply iron, vitamin B₁₂, and folic acid.**
- **hematopoietic growth factors, proteins that regulate the proliferation and differentiation of hematopoietic cells.**
- **Inadequate supplies of either the essential nutrients or the growth factors result in deficiency of functional blood cells.**
Anemia,
a deficiency in oxygen-carrying erythrocytes, is the most common and several forms are easily treated



Iron Deficiency Anemia

- Iron forms the nucleus of the iron-porphyrin heme ring, which together with globin chains forms hemoglobin.
- In the absence of adequate iron, small erythrocytes with insufficient hemoglobin are formed, giving rise to microcytic hypochromic anemia.
- Iron deficiency is the most common cause of chronic anemia.
- The cardiovascular adaptations to chronic anemia—tachycardia, increased cardiac output, vasodilation—can worsen the condition

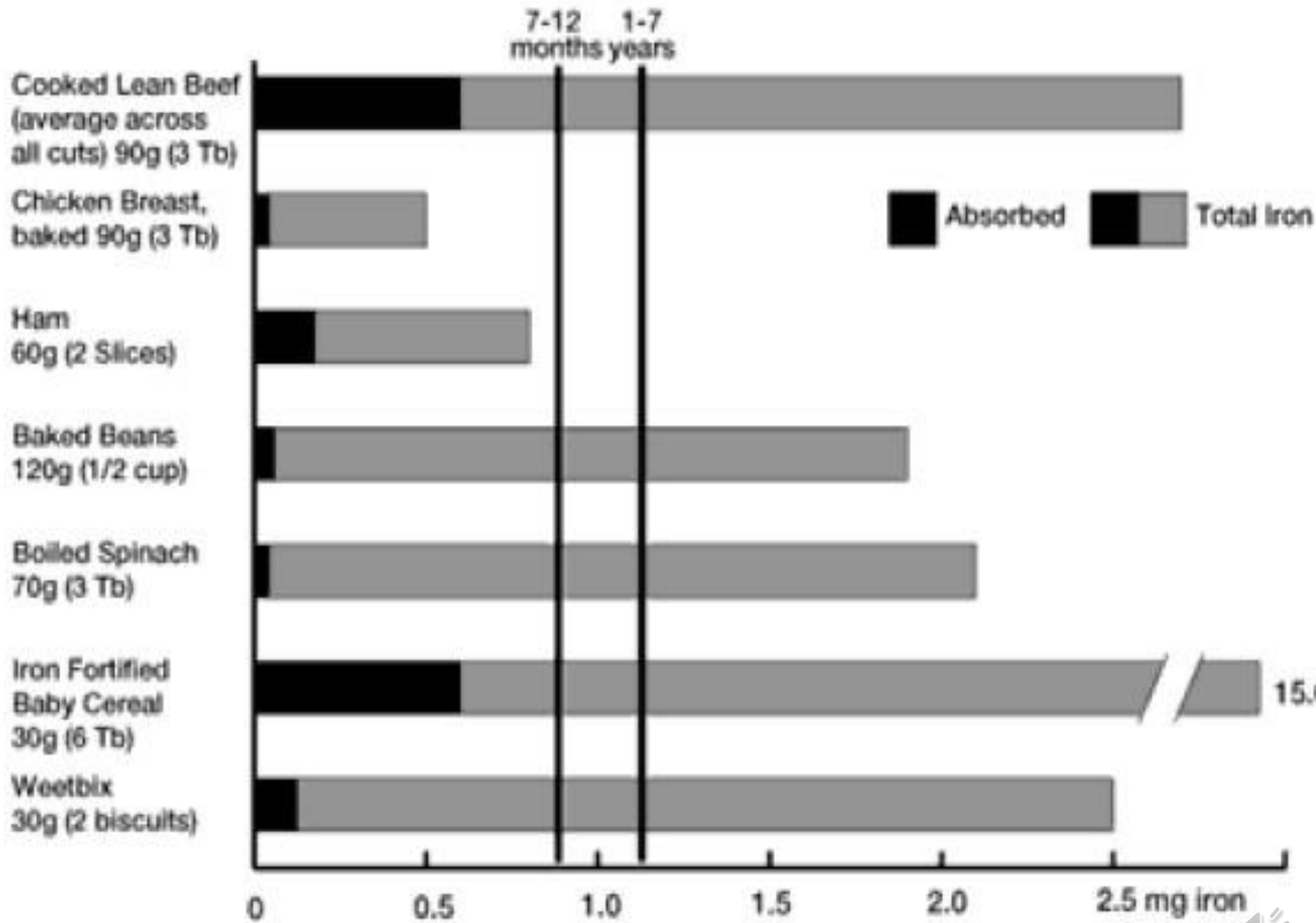


Iron Deficiency Anemia

- **Body has ~ 3.5 g total iron; 2.5 g is in hgb.**
- **Humans are poor at absorption- usually only 5-10% of intake is absorbed (this is increased to 20-30% in deficiency)**
- **Requirement:**
 - Adult males 13 ug/kg.**
 - Female 21 ug/kg,**
 - pregnant women and infants 80 ug/kg.**
- **dietary iron in form of heme (meat) can be absorbed intact**
- **Non-heme iron from vegetables, grains, therapeutic iron must be broken down to elemental iron for absorption**



ABSORBED IRON REQUIREMENT



Indications for the Use of Iron

- Treatment or prevention of iron deficiency anemia.
- Iron deficiency is commonly seen in populations with increased iron requirements.
 - ✓ infants, especially premature infants; children during rapid growth periods;
 - ✓ pregnant and lactating women;
 - ✓ chronic kidney disease who lose erythrocytes at a relatively high rate during hemodialysis
and also form them at a high rate as a result of treatment with the erythrocyte growth factor erythropoietin.



Indications for the Use of Iron

- **Inadequate iron absorption can also cause iron deficiency.**
 - **This is seen frequently after gastrectomy**
 - **severe small bowel disease that results in generalized malabsorption.**



Oral Iron

- Preparations:
 - **ferrous fumarate 33% elemental iron,**
 - **ferrous gluconate 12% iron,**
 - **ferrous sulfate 20%.**



Oral Iron

Adverse Effects: 20-25% have GI problems: nausea, epigastric pain, constipation, abd. cramps.

- **Food decreases absorption by 30 - 50%.**
- **– Drug interactions: tetracycline and antacids decrease iron absorption.**



Oral Iron

- **Treatment with oral iron should be continued for 3–6 months in order to replenishes iron stores.**
- **Patients taking oral iron develop black stools;**



Parenteral Iron

- should be reserved for
 - (1) patients with documented iron deficiency
 - (2) patients who are unable to tolerate or absorb oral iron
 - (3) patients with extensive chronic anemia who cannot be maintained with oral iron alone. This includes
 - patients with advanced chronic renal disease requiring hemodialysis and treatment with erythropoietin,
 - various post gastrectomy conditions and previous small bowel resection, inflammatory bowel disease involving the proximal small bowel, and malabsorption syndromes.



Parenteral Iron

- It can be given by deep intramuscular injection or by intravenous infusion, although the intravenous route is used most commonly.

Intravenous administration eliminates the local pain and tissue staining that often occur with the intramuscular route and allows delivery of the entire dose of iron necessary to correct the iron deficiency at one time.

- Adverse effects of intravenous iron dextran therapy include
 1. headache, light-headedness,
 2. fever, arthralgias, back pain,
 3. flushing, urticaria, bronchospasm, and, rarely, anaphylaxis and death.



Acute iron toxicity

- exclusively in young children who accidentally ingest iron tablets.
- as few as 10 tablets can be lethal in young children.
- Children who are poisoned with oral iron experience necrotizing gastroenteritis, with vomiting, abdominal pain, and bloody diarrhea followed by shock, lethargy, and dyspnea.
- **Whole bowel irrigation** should be performed to flush out unabsorbed pills.
- **Deferoxamine**, a potent iron-chelating compound, can be given **systemically** to bind iron that has already been absorbed and to promote its excretion in urine and feces.



Chronic iron toxicity (iron overload) hemochromatosis

- **excess iron is deposited in the heart, liver, pancreas, and other organs. It can lead to organ failure and death.**
- **It most commonly occurs in patients with inherited hemochromatosis, a disorder characterized by excessive iron absorption.**
- **and in patients who receive many red cell transfusions over a long period of time (eg, patients with thalassemia major).**
- **Chronic iron overload in the absence of anemia is most efficiently treated by intermittent phlebotomy. (One unit of blood can be removed every week)**



Megaloblastic Anemias

Megaloblastic Anemias:

Marrow disorder caused by defective DNA synthesis.

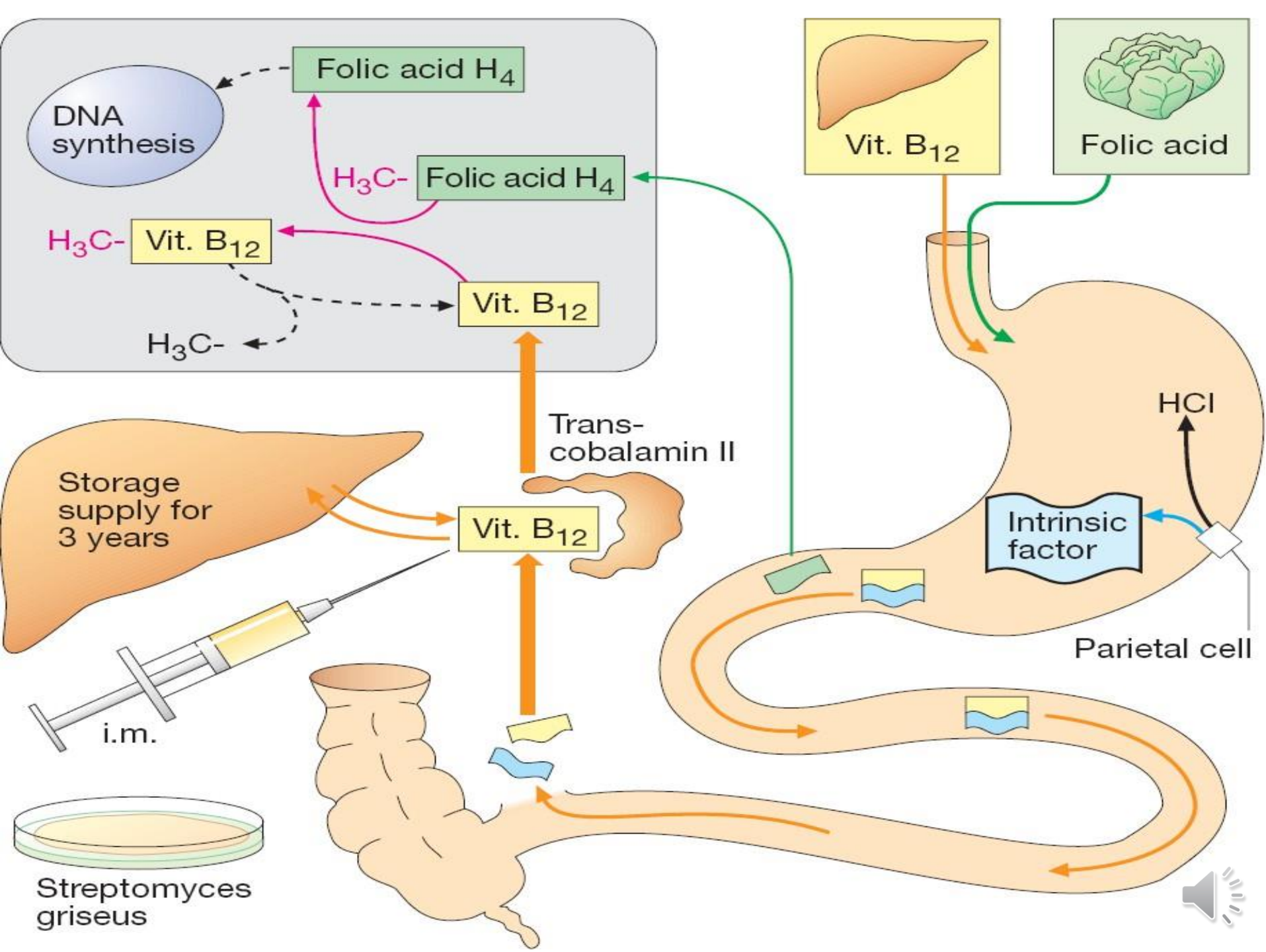
**Vit. B₁₂ Deficiency
Folic Acid Deficiency**

- **Anemia may result from (1) deficiency (strict vegetarians)
(2) or impaired absorption (Pernicious anemia) from decreased intrinsic factor (protein secreted by stomach),
(3) gastrectomy,
(4) malnutrition, RA, thyroid conditions.**

Vitamin B₁₂ is used to treat or prevent deficiency.

**Distinguished from other anemias by its Neurological Syndrome
Delirium, numbness, tingling of hand and feet, loss of fine learned
movements, difficulty in walking, bladder and bowel dysfunction.**





- Vitamin B₁₂ is used to treat or prevent deficiency.
- Injections only benefit if deficiency
- Neurologic symptoms (paresthesias occur first, then balance) in severe deficiency may be irreversible after several months
- May need lifelong injections if malabsorption; can not absorb B12/intrinsic factor complex

- NOTE:**
1. Folic acid alleviates anemic syndrome but the neurological disorder progresses.
 2. Antagonism of Vit B₁₂ by nitrous oxide (inactivates Vit B₁₂ dependent enzymes) => megaloblastic response, neuropathies



Vitamin B₁₂

- Vitamin B₁₂ for parenteral injection is available as cyanocobalamin or hydroxocobalamin. Hydroxocobalamin is preferred because it is more highly protein-bound and therefore remains longer in the circulation.
- Initial therapy should consist of 100–1000 mcg of vitamin B₁₂ intramuscularly daily or every other day for 1–2 weeks to replenish body stores.
- Maintenance therapy consists of 100–1000 mcg intramuscularly once a month for life.
- If neurologic abnormalities are present, maintenance therapy injections should be given every 1–2 weeks for 6 months before switching to monthly injections.
- Oral vitamin B₁₂-intrinsic factor mixtures and liver extracts should not be used to treat vitamin B₁₂ deficiency; however, oral doses of 1000 mcg of vitamin B₁₂ daily are usually sufficient to treat patients with pernicious anemia who refuse or cannot tolerate the injections.



Megaloblastic Anemia- continued

- Folic Acid (folate, Vitamin B9) found in fresh green veggies, yeast, animal proteins but easily destroyed.
- Anemia may be indistinguishable from B12 deficiency but occurs rapidly.
- Must evaluate fully before treatment- folate therapy will correct hematological abnormalities but not neurological problems
- deficiency; B12 deficiency may be masked by folate supplementation



- because body stores of folates are relatively low and daily requirements high, folic acid deficiency and megaloblastic anemia can develop within 1–6 months after the intake of folic acid stops, depending on the patient's nutritional status and the rate of folate utilization.
- Patients with alcohol dependence and patients with liver disease can develop folic acid deficiency because of poor diet and diminished hepatic storage of folates.
- Patients who require renal dialysis develop folic acid deficiency because folates are removed from the plasma during the dialysis procedure.



FOLIC ACID

- Drug interactions:

In large doses may counteract the effects of anticonvulsants potentially leading to seizures.

- Adverse reactions:

Erythema, itching, and rash.

