Agents Used in Anemia

Drug		Route of Administration	Uses	Side Effects	Notes
Oral Iron Preparations	Ferrous Sulfate, Ferrous gluconate, Ferrous fumarate	Oral use	Treatment and prevention of iron deficiency anemia	-Nausea -Epigastric discomfort -Cramps -Constipation **(Ferrous Sulfate)** -Diarrhea and black stools **(Ferrous Gluconate)**	-All are effective and inexpensive -Have sugar covering (sugar coated tablets)
Parenteral Iron Therapy	Iron dextran	Given by deep IM injection or IV infusion	Reserved for patients with documented iron deficiency who are unable to tolerate or absorb oral iron and for patients with extensive chronic blood loss who cannot be effectively maintained with oral iron alone	-IM injection causes local pain and tissue staining -IV infusion causes hypersensitivity reactions: headache, fever, arthralgia, N, V, back pain, flushing, bronchospasm and rarely anaphylaxis and death	-Rarely used -Carry the risk of iron overload
	Iron-sucrose complex	Given only IV		-less likely to cause hypersensitivity	
	Iron –sorbitol citrate “Jectofer”				
	Iron sodium gluconate				
Deferoxamine “Desferal”		IV & IM	-Treatment of acute iron toxicity (binds already **absorbed** iron and promotes its excretion in urine and feces) -In chronic toxicity; **phlebotomy** is more efficient		-Can bind 2 iron molecules -This treatment doesn’t work for unabsorbed iron (we use whole bowel irrigation to flush unabsorbed pills out)
Deferasirox “Exjade”		Oral use (more convenient than deferoxamine)	Treatment of chronic iron toxicity		
Folic Acid		Oral use (well absorbed), parenteral is rarely used	-To treat folic acid deficiency -Routinely given in early pregnancy or before pregnancy (prophylactically)		-1 mg daily until cause is corrected -Given indefinitely in malabsorption or dietary inadequacy

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Vitamin B12 Therapy	Parenteral		Life-long treatment of vitamin B12 deficiency		-Daily or every other day for 1-2 weeks to replenish the stores. -Maintenance: injections every 1-4 weeks
	Oral		Only for patients who refuse or can not tolerate injections		
	Intranasal		For patients in remission		

	Absorption	Transport	Storage	Elimination	Deficiency	Diseases
Iron	-Heme iron in meat is more readily absorbed that non-heme iron -Daily absorption: 5-10% of the daily intake, usually from duodenum and proximal jejunum -(DMT1) → transports (Fe^{+2}) into enterocytes -Ferroportin1 (IREG1) → from basolateral membrane of enterocytes into the blood -Excess iron is stored in the mucosa as ferritin	-In plasma, iron binds transferrin → binds to transferrin receptors on erythrocytes → endocytosis	-Ferritin is the storage form of iron (stored in intestinal mucosa and macrophages in the liver, spleen, and bone) -Ferritin in serum is in equilibrium with storage ferritin	-No mechanism for excretion -Small amounts are lost by exfoliation of intestinal mucosal cells, bile, urine and sweat	-Caused by increased requirements, inadequate absorption and blood loss - Deficiency causes hypochromic microcytic anemia	**Acute iron toxicity:** -Caused by excess from accidental ingestion by children and as parenteral ingestion -Causes necrotizing gastroenteritis: vomiting, pain, bloody diarrhea, shock, lethargy and dyspnea. Patients may improve but may proceed to metabolic acidosis, coma and death. **Chronic iron toxicity:** -Caused by excessive iron absorption, patients with frequent transfusions e.g. in patients with hemolytic anemias -Excess iron deposits to different organs causing organ failure

	Chemistry	Absorption	Transport	Storage	Actions	Deficiency
Vitamin B12	-Porphyrin-like ring with a central cobalt atom -Forms: Methylcobalamine, Deoxyadenosyl cobalamine, Cyanocobalamine, Hydroxocobalamine . -Available in meat, liver, eggs, and dairy products. Nutritional deficiency only occurs in strict vegetarians.	-Requires the intrinsic factor (Castle's Factor) -Absorption and excretion can be tested by **Schilling's Tests**	-Transported by Transcobalamine II	-Storage pool: 300-5000mcg, it would take 5 years to exhaust all stored pool and for megaloblastic anemia to develop after stopping absorption as daily requirement is 2mcg.	1. Transfer of a methyl group from N5-methyltetrahydrofolate to homocysteine, forming methionine. *N5-methyltetrahydrofolate is the major dietary and storage folate. 2. Conversion of N5-methyltetrahydrofolate to tetrahydrofolate. →**Megaloblastic anemia of VB12 can be partially corrected by large amounts of folic acid** 3. Isomerization of methylmalonylCoA to succinyl-CoA by the enzyme methylmalonyl-CoA mutase.	-Causes megaloblastic anemia -Deficiency leads to accumulation of N5-methyltetrahydrofolate cofactors and depletion of tetrahydrofolate . -Vitamin B12 depletion leads to the accumulation of methylmalonyl-CoA , thought to cause the neurological manifestations of Vitamin B12 deficiency
Folic Acid	-Folic acid=Pteridine+ PABA+ Glutamic acid. -Folic acid is reduced to Di and Tetra hydrofolate and then to folate cofactors, which are interconvertible and can donate one-carbon units at various levels of oxidation.	-Readily and completely absorbed from the terminal jejunum. -Glutamyl residues are hydrolyzed before absorption by α-1-glutamyltransferase (Congugase), within the brush border of the mucosa.	-N5-methyltetrahydrofolate is transported into the blood stream actively and passively -Inside cells, it is converted into THF by demethylation reaction in the presence of Vitamin B12.	-Only 5-20 mcg are stored in the liver. -Excreted in urine and stool and also destroyed by catabolism.	-Production of dTMP from dUMP, which is needed in DNA synthesis. -Generation of methionine from homocysteine. -Synthesis of essential purines * Deficiency can result in: 1. Megaloblastic anemia (can develop within 1-6 months after stopping intake) 2. Congenital malformations 3. Occlusive Vascular Disease (due to elevated homocysteine)	*Megaloblastic anemia of folic acid deficiency can be caused by: **-Inadequate** dietary intake. **-Alcoholism.** -Liver disease causing **impaired hepatic storage.** **-Pr**egnancy and hemolytic anemia which **increase the demand.** **-Malabsorption** syndrome. -Renal dialysis. **-Drugs**: Methotrexate, Trimethoprim and Phenytoin.

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