

In the Name of GOD



Drugs for Treatment of Anemia

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pharmD

Ph.D in pharmacology

IRON



Normal body iron content

3 to 4 grams



*Storage iron:
ferritin or hemosiderin*





10-20 mg daily intake
1-2 mg daily uptake

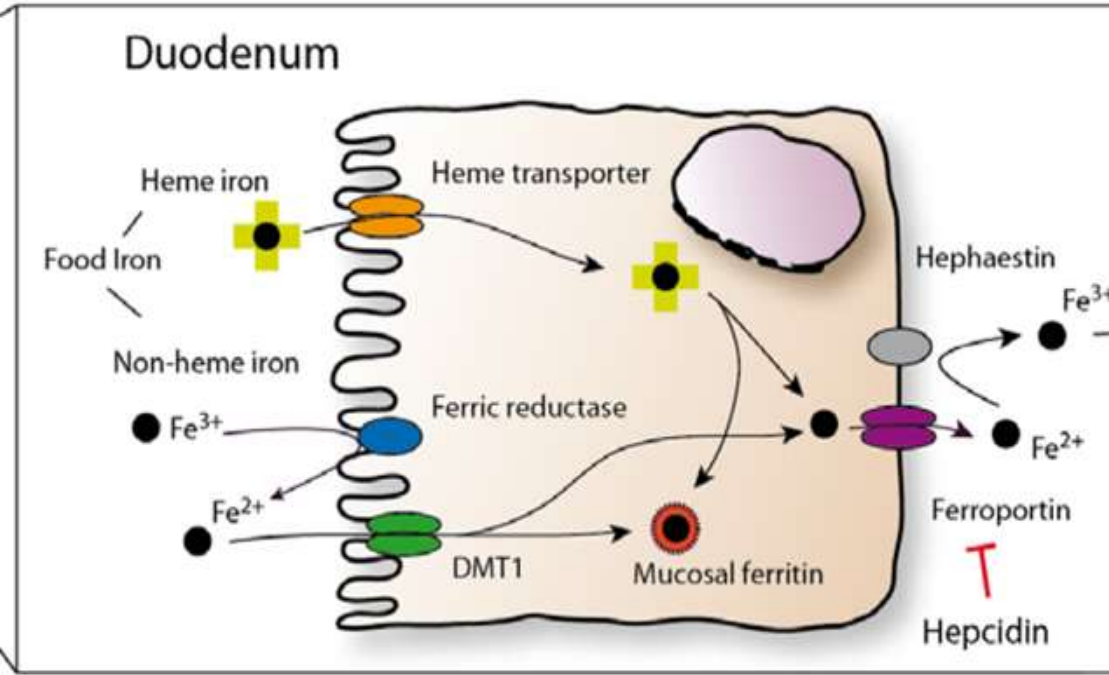
* Oral iron



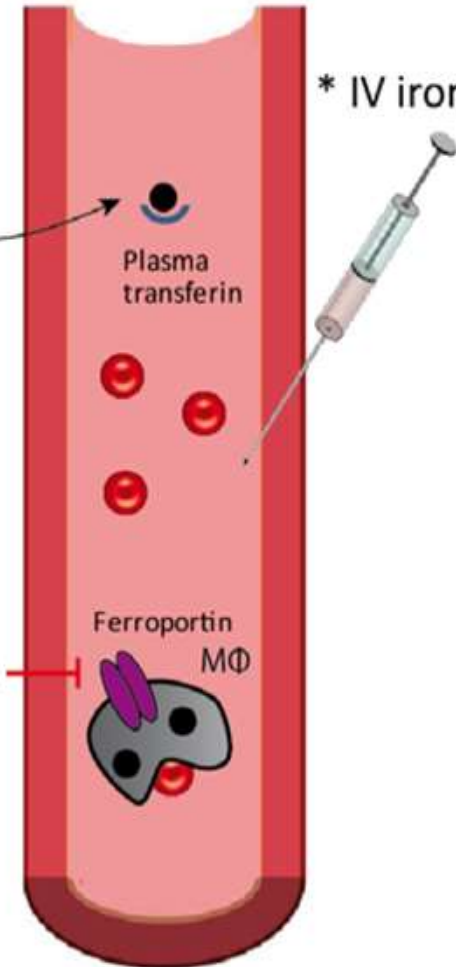
Intestinal
inflammation
(IL-1, IL-6)

* IBD treatment

1-2 mg daily excretion from
epithelial desquamation
- additional from bleeding



* IV iron



Hepcidin ↑

* Anti-hepcidin

Low serum iron

Impaired
erythropoiesis

Clinical symptoms

➤ **Heme iron** \approx 3X more absorbable than **non-heme iron**





IRON REPLACEMENT PRODUCTS

Oral

Most patients are treated with
oral iron

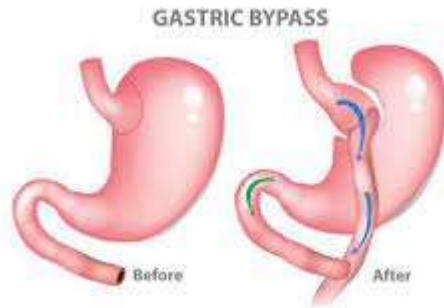


- ❖ Cost
- ❖ Contraindications
- ❖ inadequate response
loss
- ❖ administration for
- ❖ Total costs may be higher

personnel
higher

IV IRON

- unable to tolerate gastrointestinal side effects



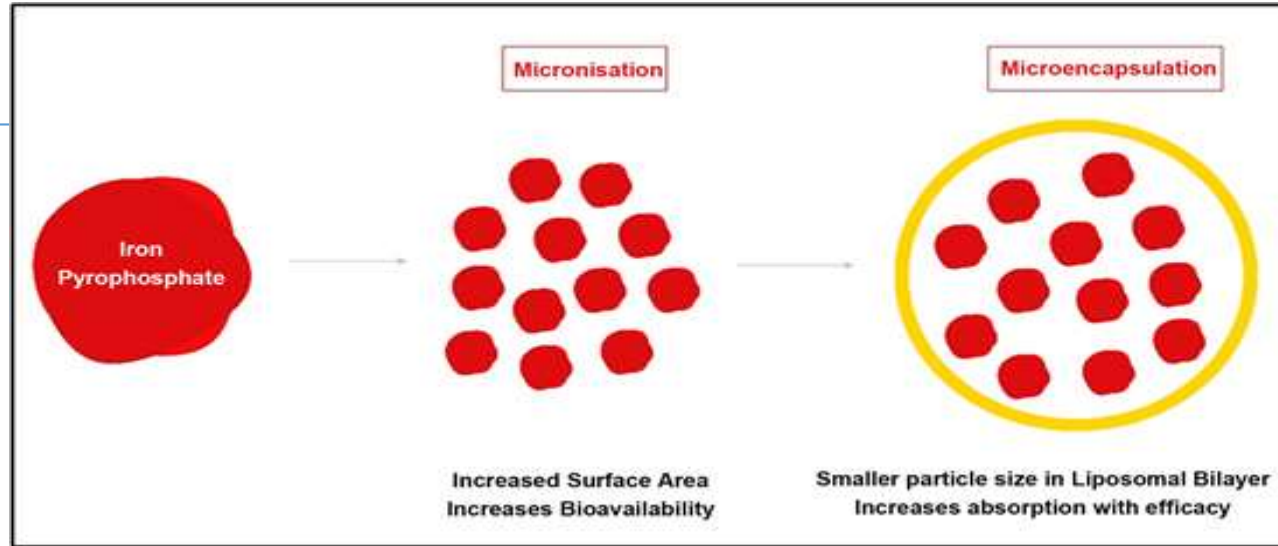
Choice of oral preparation

Iron salt	% Elemental Iron
Ferrous fumarate	33
Ferrous gluconate	12
Ferrous sulfate	20
Ferrous sulfate, dried	30
Ferrous bisglycinate	20

- Polysaccharide-iron complex



Liposomal iron



- Better Bioavailability
- **Better Tolerability**
- No Interaction with Dietary Inhibitors





1ml=15mg
Fe sulphate



1ml = 125 mg=25 mg
11000 t



1ml = 125 mg=25 mg
8000 t



Fe 15 mg
Vit C 12.5
20000T



6200T
Fe 25 mg



Ferrous Sulfate 25 mg
Vitamin C 40 mg



76000T
10 mg
Microcapsulated fe
pirofosphate



Liposomal fe= 7 mg
48000T



64000T
Fe liposomal 7 mg



fe 7 mg
microencapsulate
Sustain released
65000



92000
Fe = 15 mg
microencapsulated



65000T
15mg
microencap
soulated



Fe liposomal 14mg
73000



81000T

Microencapsulation

Fe 8 mg

P 6.72

K 0.26

Na 0.05

B2 1.4

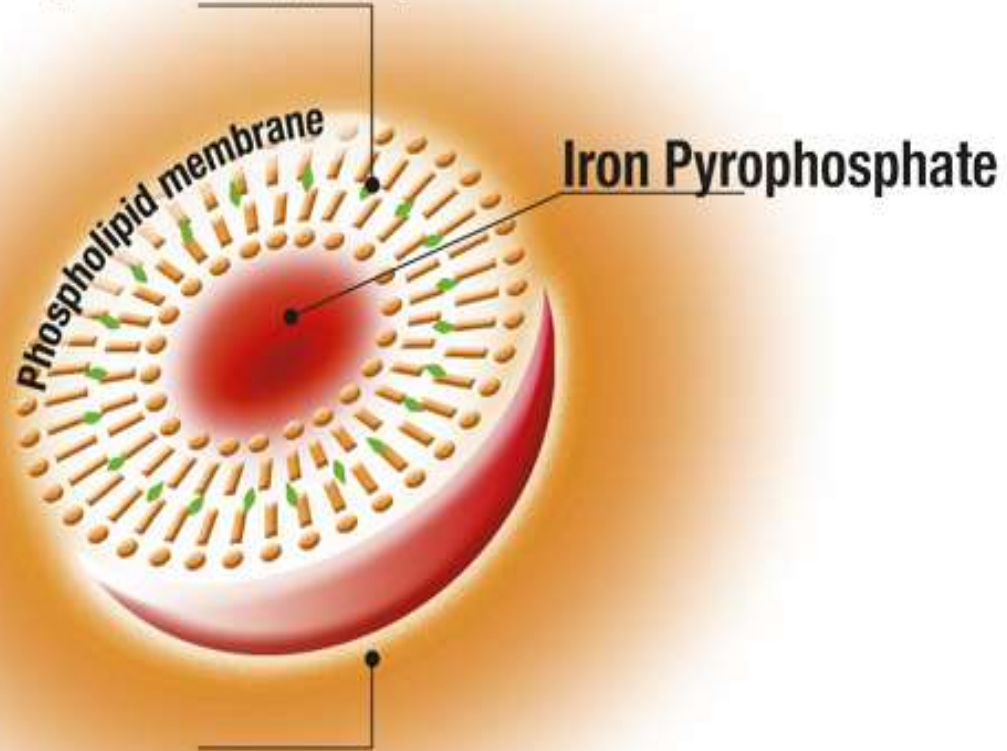
Vit A 555



Liposomal iron 15 mg

89000T

**TPC - Tricalcium Phosphate
(bonds support)**

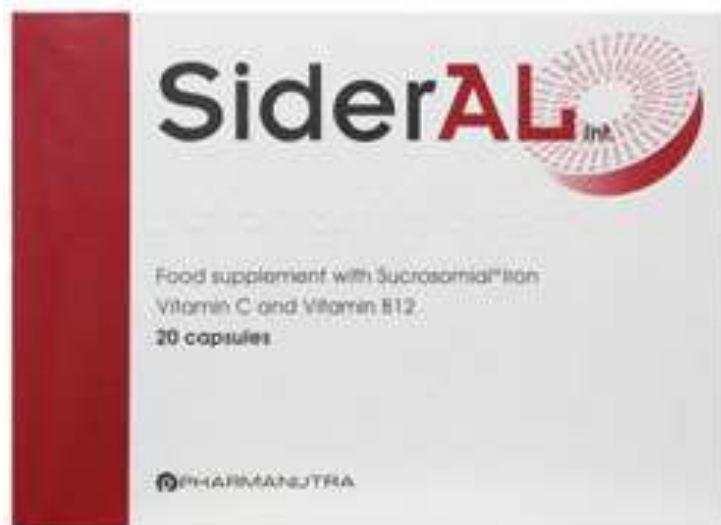


**Sucrester's Enveloped
(absorption enhancer)**



130000t

7 mg Liposomal iron



130000T
14 mg fe
60 mg vitamin c
0.375 vitamin b12



200000T
30 mg fe
70 mg vitamin c



WWW.MAADPHARMA.COM



WWW.MAADPHARMA.COM



40mg fe in 5 ml



16000T
Fe 50mg



www.parsanharooof.com



Each spansule sustained-release capsule contains 150 mg dried ferrous sulphate (45 mg elemental iron - Fe^{++}) and 0,5 mg folic acid.





Fe 100 mg
Ecoated



Fe 100 mg
Enteric
coated
54000T



Fe 80 mg
Acid folic 1 mg

75000



Fe = 100 mg
88000
EC



Vitamin c= 60 mg
 Folic acid 400
 B12 8
 Iron (as Ferrous Bis-glycinate) 28 mg

93000T



Iron Bisglycinate 36 mg



Iron Bisglycinate 30 mg
 Vitamin c120 mg
 68000T

197000T

fe liposomal 20 mg

Vit c 206 mg

B12 2

B6 3.75

Folic acid 500

Zn 18 mg

Cu 1000



Ferrous fumarate



Fe= 20mg
Acidfolic = 400 micro
32000



Daru Namak



B12 50
Vitamin c 220
Acid folic 400
Iron foumarat 27 mg

30000 T
20 mg Fe

15 mg
8000T

Ferrous gluconate

Fe gluconate
27 mg
پیوسته رهش



Ferric maltol



163,500 تومان

Dosing and administration (oral iron)



Monday	Tuesday	Wednesday	Thursday	Friday
Yes	No	Yes	No	Yes



ONCE DAILY



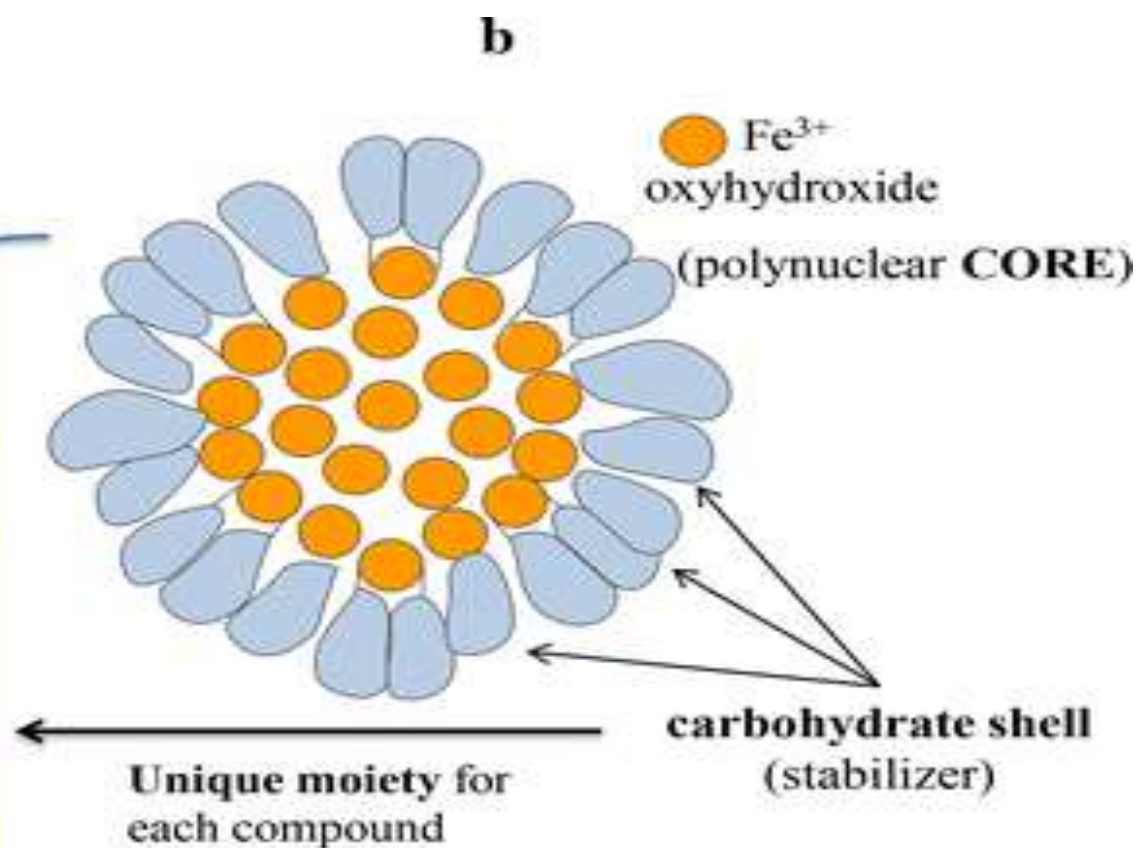
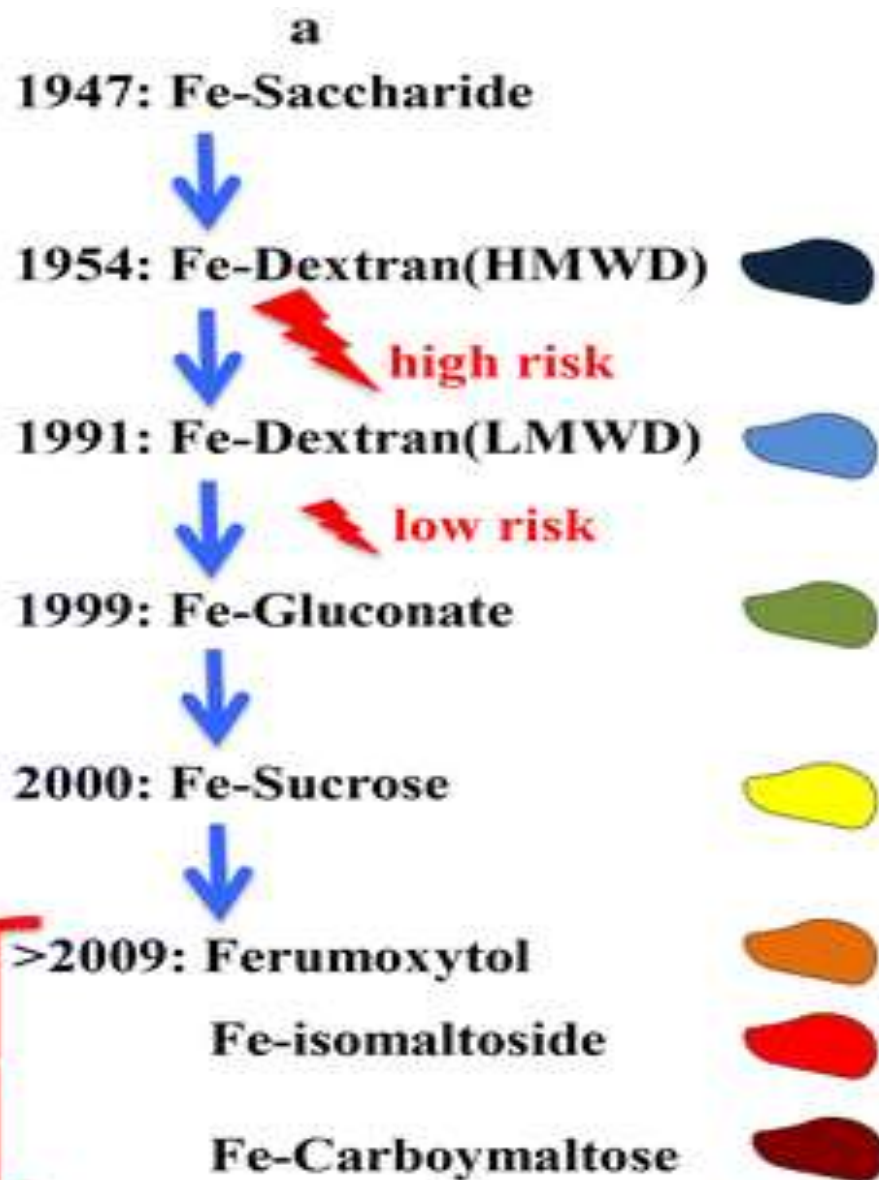




Side effects



History of i.v. iron



Key differences in:

- ✓ Immunogenicity
- ✓ Strength of stabilization

Choice of IV formulation

- ferric carboxymaltose



- ferric gluconate

- Ferumoxytol



- iron sucrose

- ferric derisomaltose (isomaltoside)



- low molecular weight iron dextran



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Dose calculation

- Hemoglobin iron deficit (mg) =
 $BW \times (14 - Hgb) \times (2.145) + \text{iron to replenish stores if desired (mg)}$

Volume of product required (mL) =
 $BW \times (14 - Hgb) \times (2.145) \div C$ (if no added iron for stores)



Use of premedication



Asthma Or More Than One Drug Allergy

125 mg of methylprednisolone and an H2 blocker

History Of Inflammatory Arthritis

methylprednisolone, 125 mg IV,
a short course of prednisone (1 mg/kg per day orally for four days)

specific IV iron preparations

COSMOFER

LMW iron dextran

50 mg/mL

- Single dose of 1000 mg (diluted in 250 mL normal saline) given over 1 hour

- Multiple doses of 100 mg

25 mg (0.5 mL) prior to the first dose

500mg



Ferric gluconate

12.5 mg/mL

- Multiple doses of 125 to 250 mg

Not required, but recommended if the patient has a history of multiple drug allergies

Ferrlecit
62.5 mg
125mg



Iron Sucrose

20 mg/mL

Multiple doses of 100 to 300 mg

Not required, but recommended if the patient has a history of multiple drug allergies

100mg



نام دارو	صاحب نام تجاری	کشور	صاحب امتیاز	وضعیت
۱. ونوفر	Vifor Pharma		برسین دارو	✓ فعال
۲. فرینفرا	Help		پاسین داروی فارس	✓ فعال
۳. آبرون	عرفان طب پارس		عرفان طب پارس	✓ فعال
۴. فرمد	Medice		بهدارو	✓ فعال
۵. همتوفر	کار خانات دارو پخش		کار خانات دارو پخش	✓ فعال
۶. همتوفر	کار خانات دارو پخش		کار خانات دارو پخش	✓ فعال
۷. آبرون سوکروز	ایران هورمون		ایران هورمون	✓ فعال
۸. آبرون سوکروز	ایران هورمون		ایران هورمون	✓ فعال
۹. آیروکم	صنعتی کیمیدارو		صنعتی کیمیدارو	✓ فعال
۱۰. اکسوفر	داروسازی اکسیر		داروسازی اکسیر	✓ فعال

65000

87000

Ferumoxytol

30 mg/mL

Single dose of 1020 mg

2 doses of 510 mg, given 3 to 8 days apart

510mg



Ferric carboxymaltose

50 mg/mL

•Weight ≥ 50 kg: 1 or 2 doses of 750 mg, given 7 or more days apart

Weight < 50 kg: 1 or 2 doses of 15 mg/kg, given 7 or more days apart

hypophosphatemia



Ferric derisomaltose/iron isomaltoside

100 mg/mL

Weight ≥ 50 kg: Single dose of 1000 mg

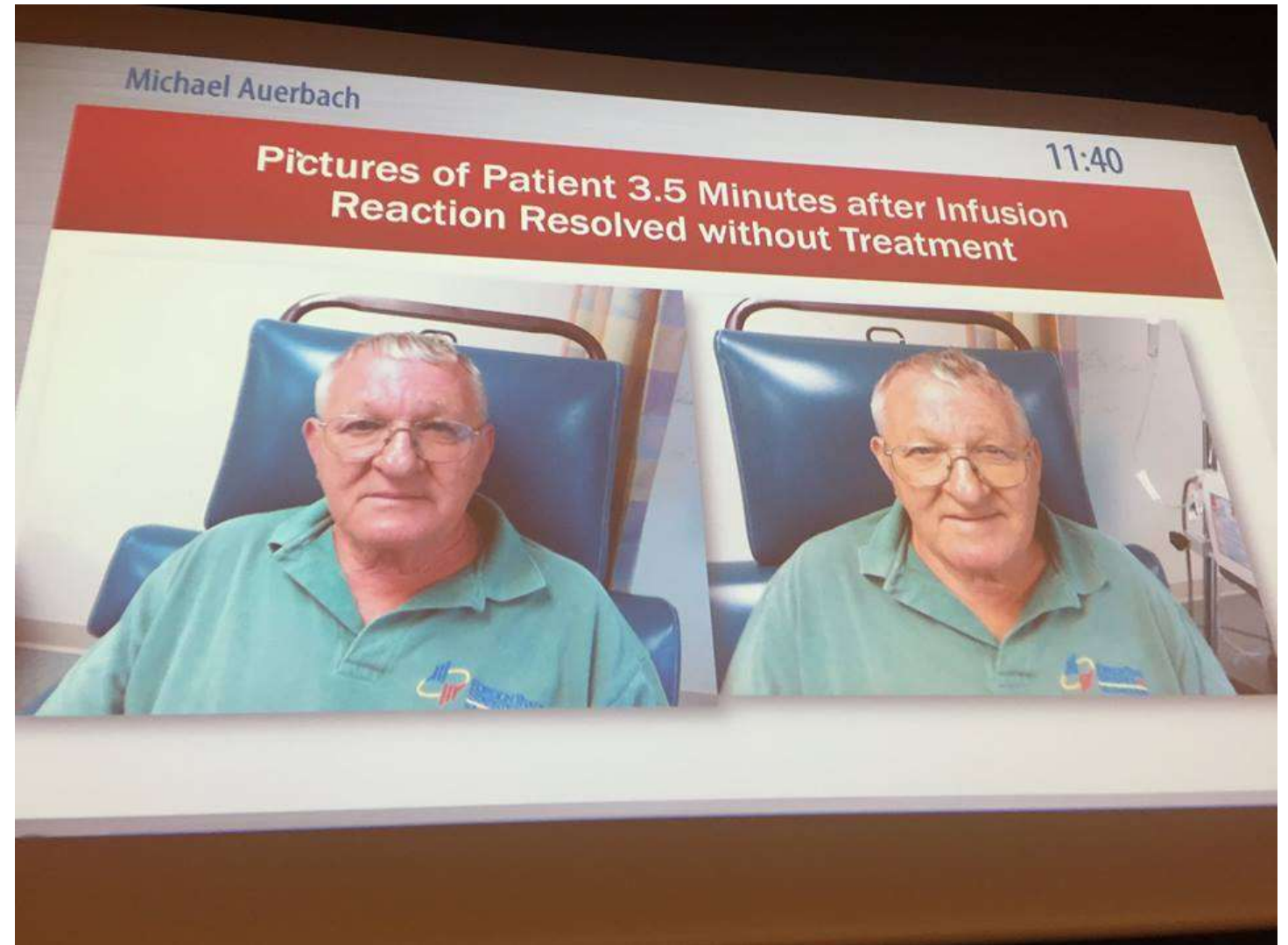
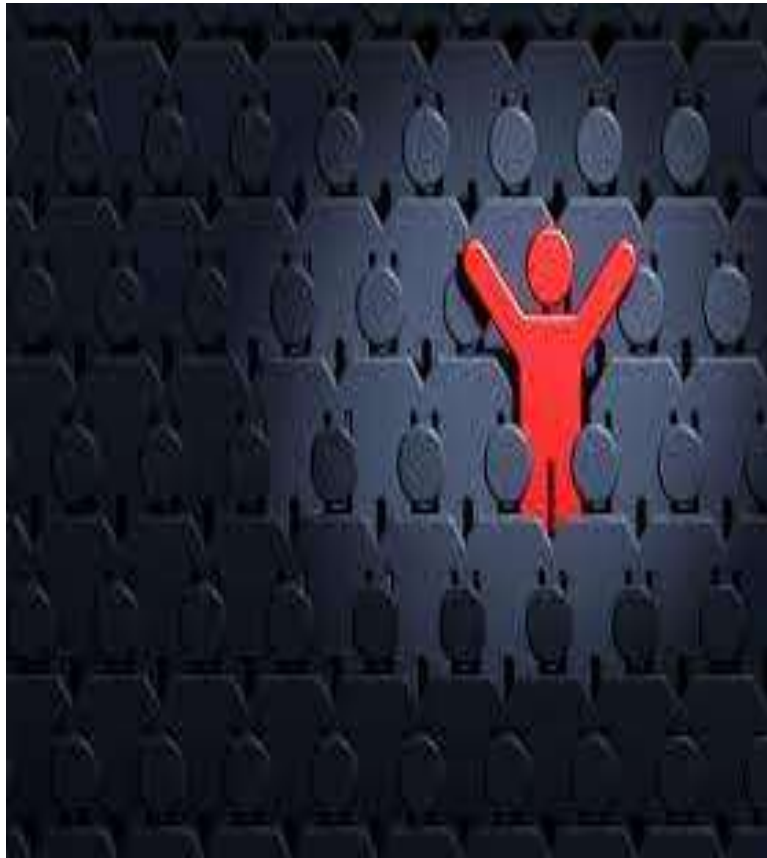
•Weight ≥ 50 kg: Up to 3 doses of 500 mg given over 7 days

Weight < 50 kg: Single dose of 20 mg/kg

Iron isomaltoside
Monofer



Allergic and infusion reactions



rate-related infusion
reactions

true allergic
reactions



Treatment of allergic and infusion reactions



Transient fever, arthralgias, myalgias, or flushing

hypotension, tachypnea, tachycardia, wheezing, stridor, or periorbital edema



a dose of intravenous methylprednisolone, wait 30 minutes,

Response To Iron Supplementation

uncomplicated iron deficiency with oral iron



Wellbeing

7-10
DAYS

3
WEEKS

6-8
WEEKS

Monitoring and hemoglobin



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two weeks



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four to eight weeks

Treatment of iron deficiency

- **Oral:** 100 to 200 mg daily in 2 to 3 divided doses
- **3 to 6 mg/kg/day** in 3 divided doses
- Extended release tablets are intended for once daily use



ORAL IRON THERAPY

- ☐ oral ferrous sulfate
- ☐ 3 mg/kg elemental iron
- ☐ once daily



- abdominal pain, constipation, and diarrhea

SIDE EFFECT



- Hgb ≥ 9 g/dL four weeks after treatment initiation 1 g/dL
- Hgb < 9 g/dL 7 to 10 days after treatment initiation 1 g/dL



Follow up!

- CBC, Hgb, MCV, RDW, serum ferritin
- serum ferritin value of >20 ng/mL

One Month

Example

$3 \times 20 = 60 \text{ mg}$



$60 / 25 = 2.4 \text{ ml}$



$60 / 15 = 4 \text{ ml}$



$60 / 7 = 8.5 \text{ ml}$



$60 / 15 = 4 \text{ ml}$



INTRAVENOUS IRON THERAPY

- ✓ Persistent anemia with oral iron intolerance
- ✓ Malabsorption
- ✓ Nonadherence to oral iron therapy
- ✓ Ongoing or poorly controlled blood loss
- ✓ Underlying gastrointestinal disease



Iron sucrose

most common form

anaphylaxis very low

No test dose or routine premedications

Iron- deficient anemia associated with CKD

Hemodialysis-dependent: 0.5 mg/kg IV q2weeks for 12 weeks; not to exceed 100 mg/dose

Non-dialysis dependent or peritoneal-dependent (on erythropoietin): 0.5 mg/kg IV q4weeks for 12 weeks; not to exceed 100 mg/dose

Ferric gluconate

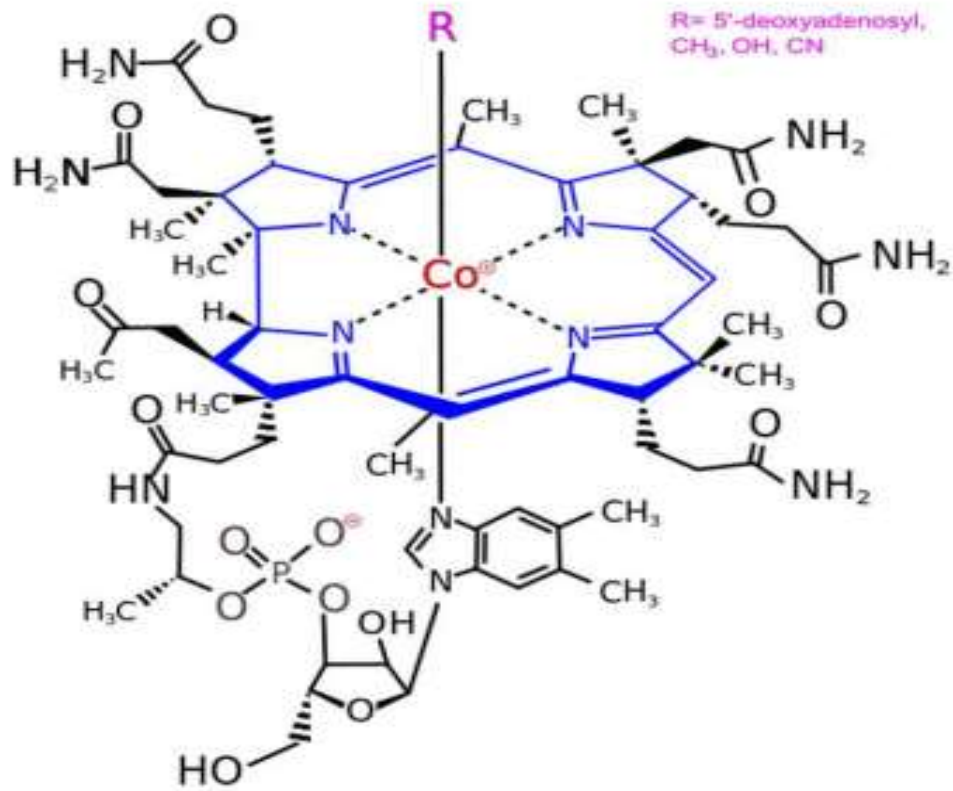
Iron dextran

Ferric carboxymaltose



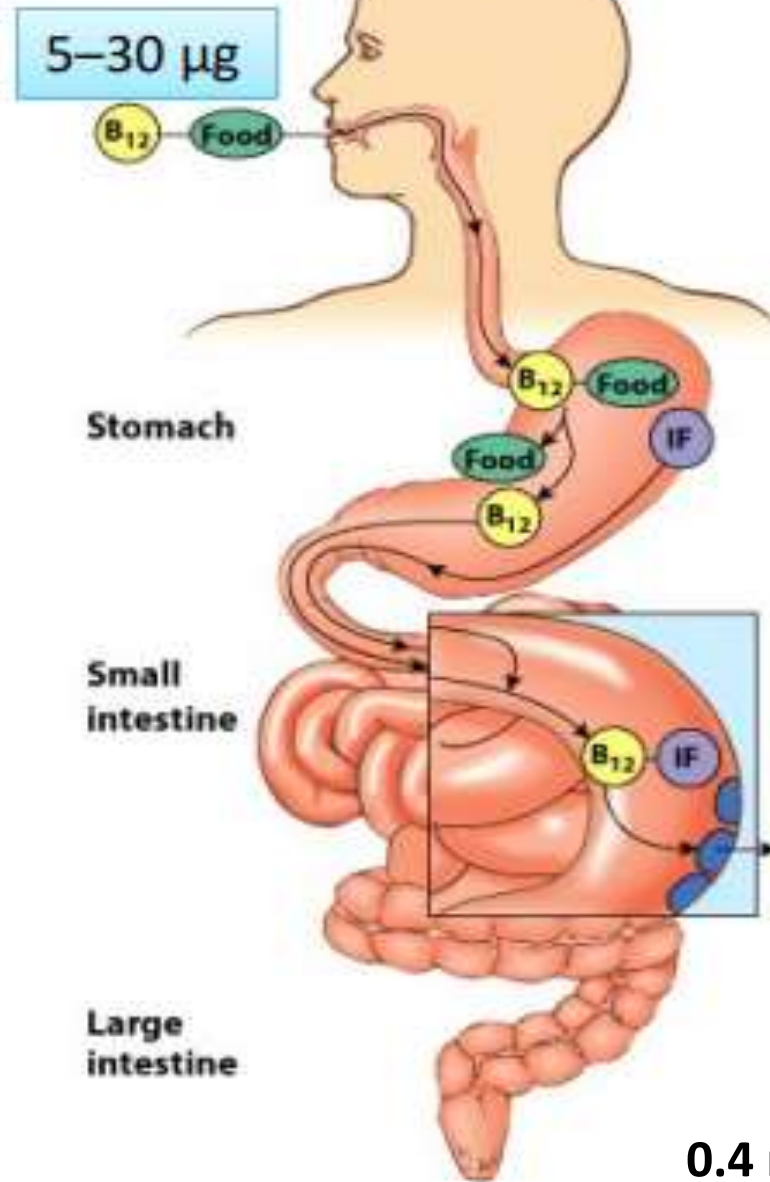
- 15 mg/kg IV in 2 doses separated by at least 7 days
- Pediatric studies and case series published to date have infused the drug over 30 minutes to 2 hours
- Hypophosphatemia is a common complication in adults





Vitamin B ₁₂ Congeners	
Permissive Name	R Group
Cyanocobalamin (Vitamin B ₁₂)	-CN
Hydroxocobalamin	-OH
Methylcobalamin	-CH ₃
5'-Deoxyadenosylcobalamin	-5'-Deoxyadenosyl

- **Microorganisms** that grow in soil or the intestinal lumen of animals that synthesize the vitamin
- The only source- from food of animal origin



5–30 μg



Food

B_{1.2}

Food

IF

Food

B₁₂

B₁₂



1–5 μg

Daily requirements of B 12: 2 mcg

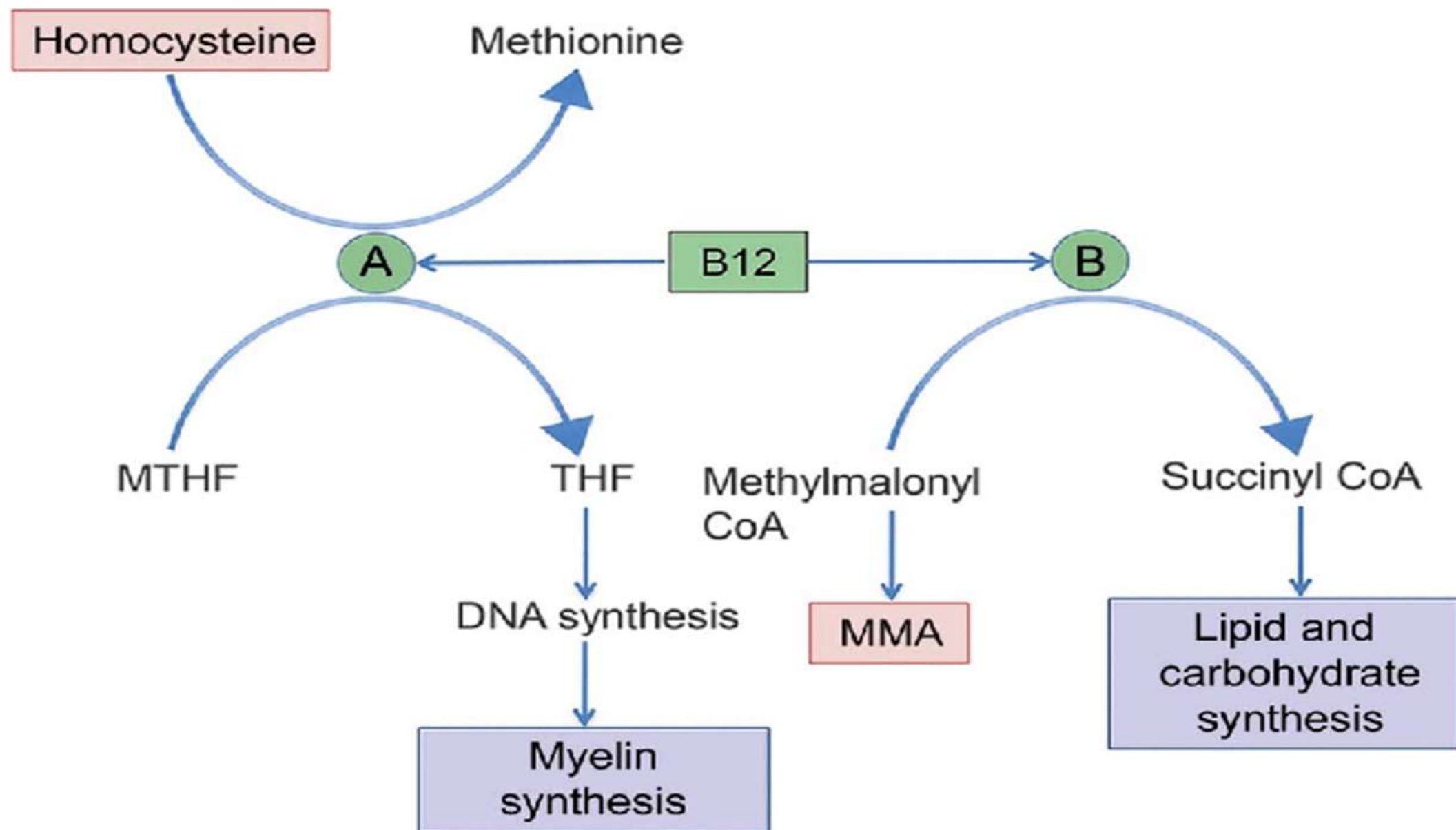
5 years

3000–5000 μg

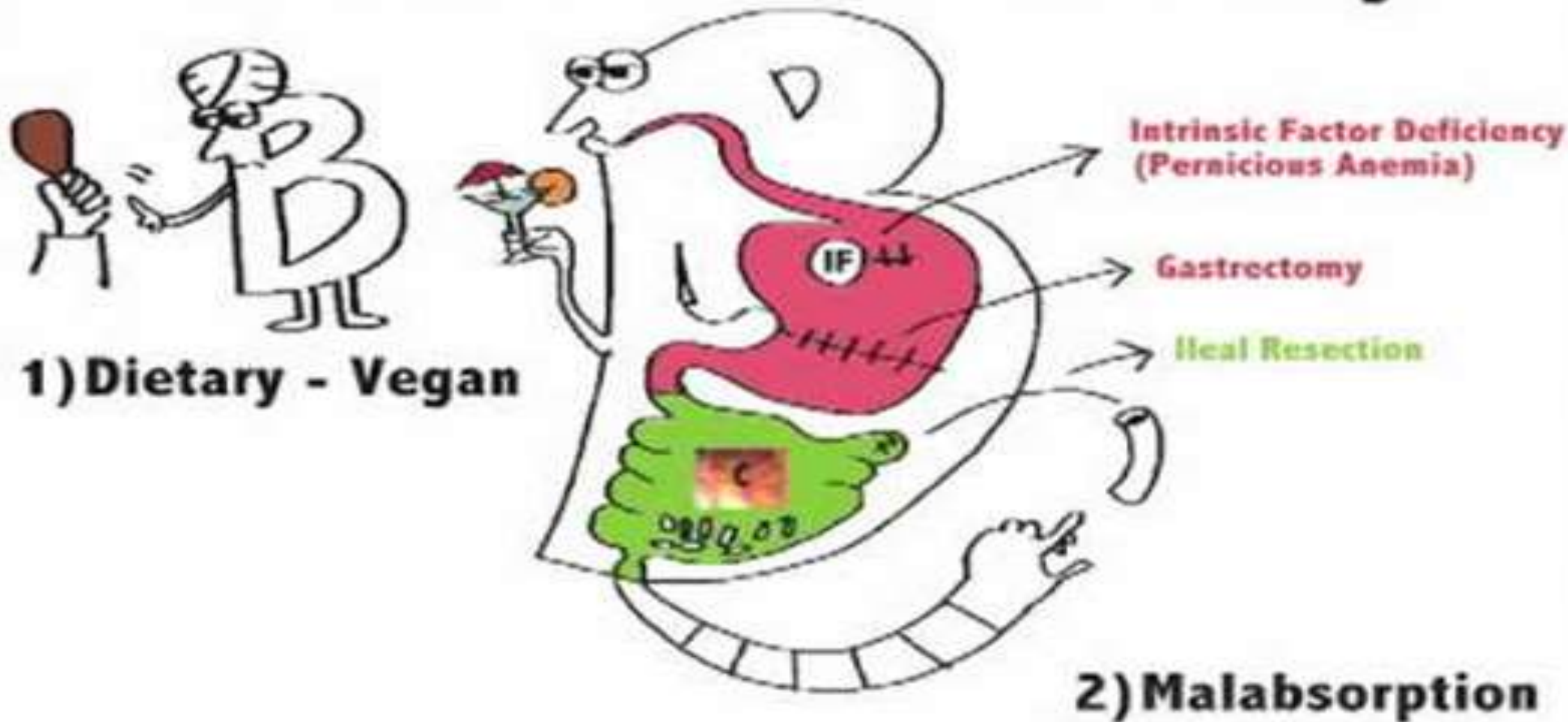
Transcobalamin

B12

0.4 mcg per day in young infants
2.4 mcg per day in adults



Causes of B12 Deficiency

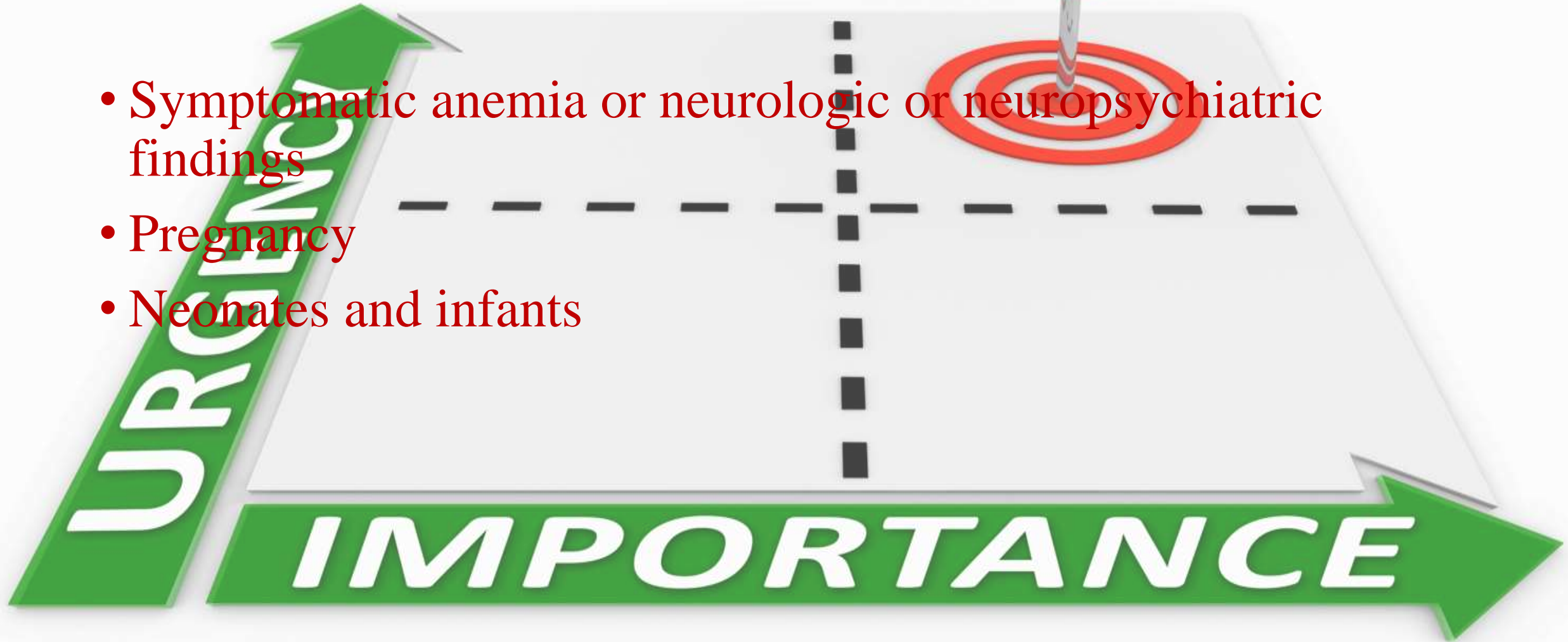


Medications/drugs (vitamin B12)

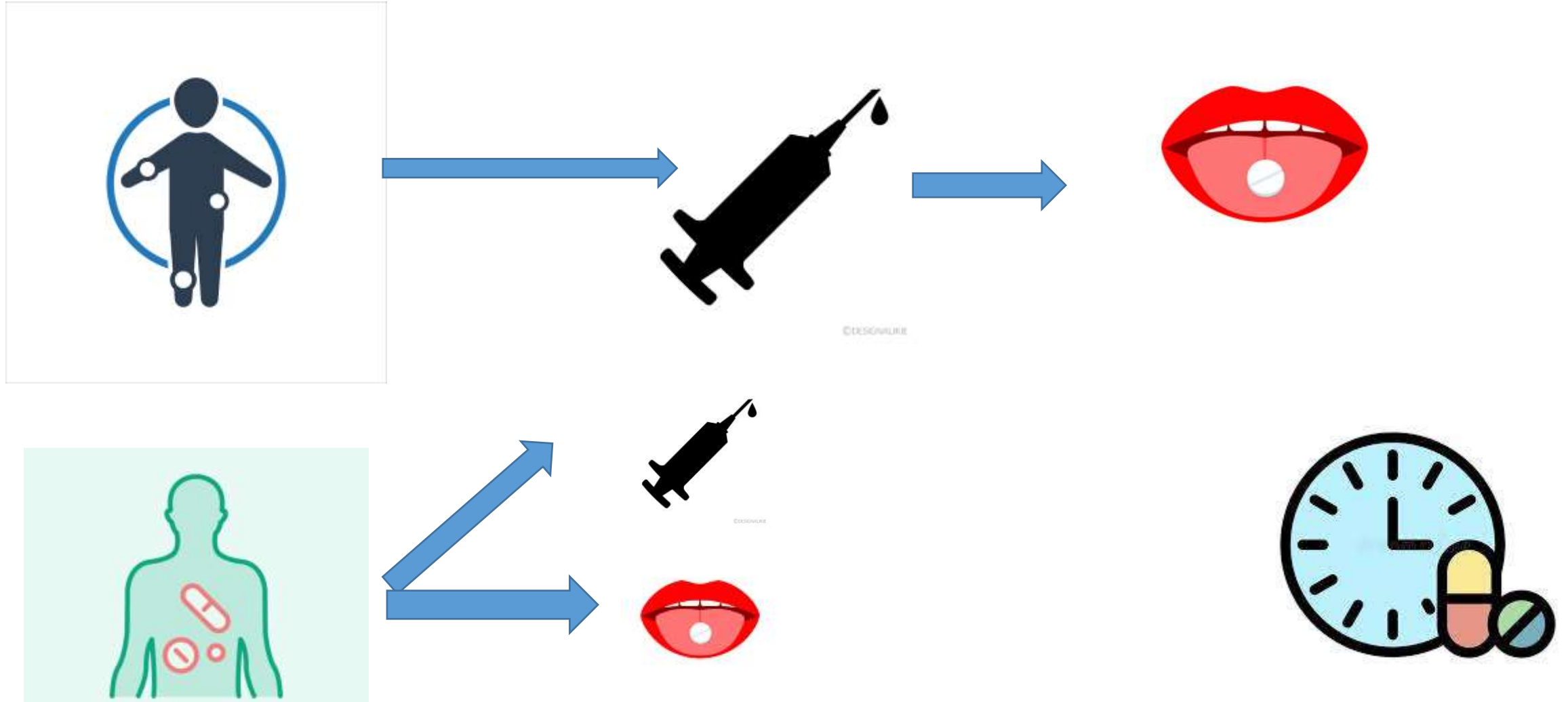
- **Proton pump inhibitors/H2 receptor blockers/antacids**
- **Metformin (after 5 to 10 years)**
- **Nitrous oxide**

Urgency of correction

- Symptomatic anemia or neurologic or neuropsychiatric findings
- Pregnancy
- Neonates and infants



Route of administration



Available therapeutic preparations

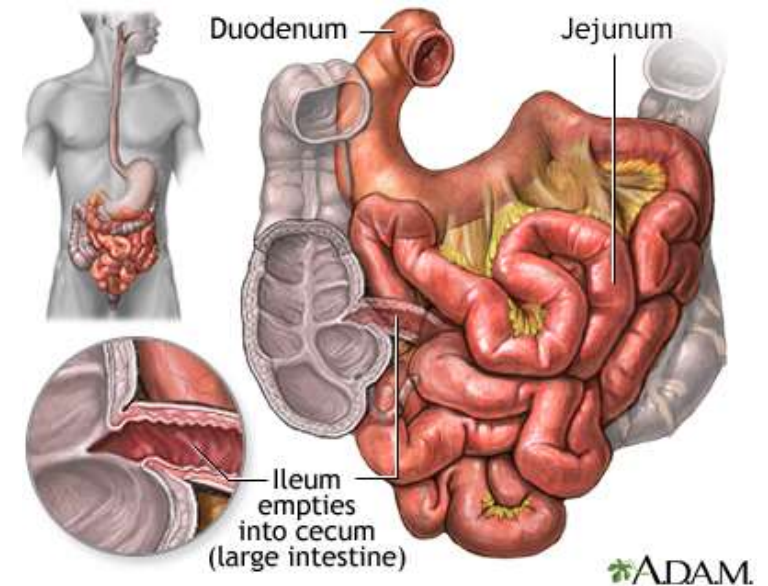
- Cyanocobalamin
- Hydroxocobalamin



Adverse effects/overdose



Prevention of vitamin B12 deficiency



Treatment of vitamin B12 deficiency

- **Parenteral**

50 to 100 mcg parenterally once per week

1000 mcg parenterally once per week

once per month (cyanocobalamin)

once every other month (hydroxocobalamin)

- **Oral**

1000 mcg orally once per day

1000 to 2000 mcg daily

- **Pernicious anemia**

initial dose of 1000 mcg (1 mg) once per week for four weeks, followed by 1000 mcg once per month.

- **Altered gastrointestinal anatomy**

- **Dietary deficiency**

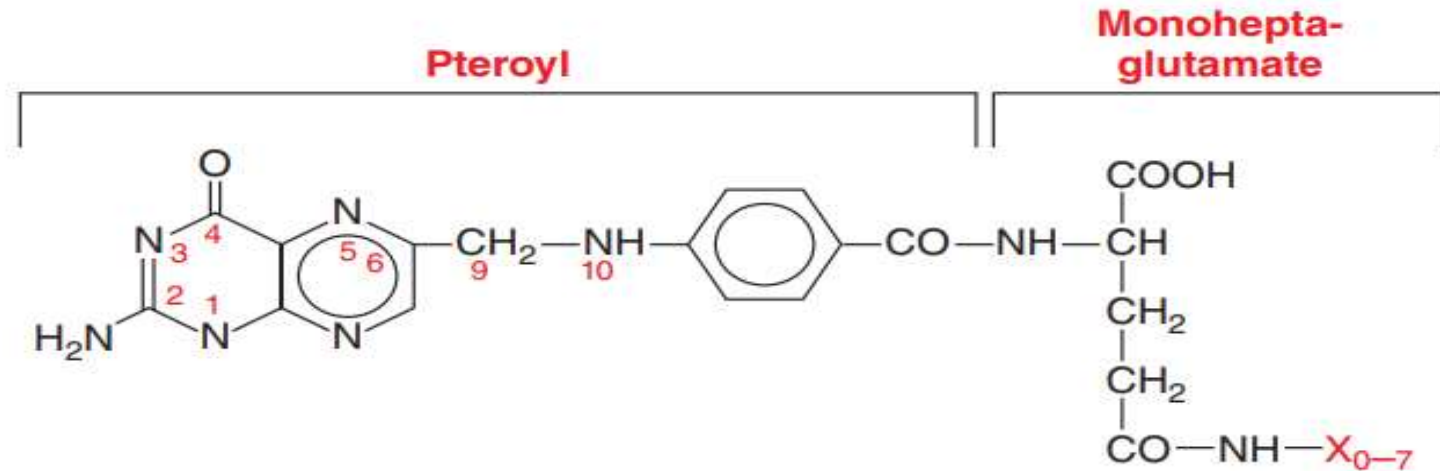
- **Concerning symptoms**

1000 mcg every other day initially two weeks

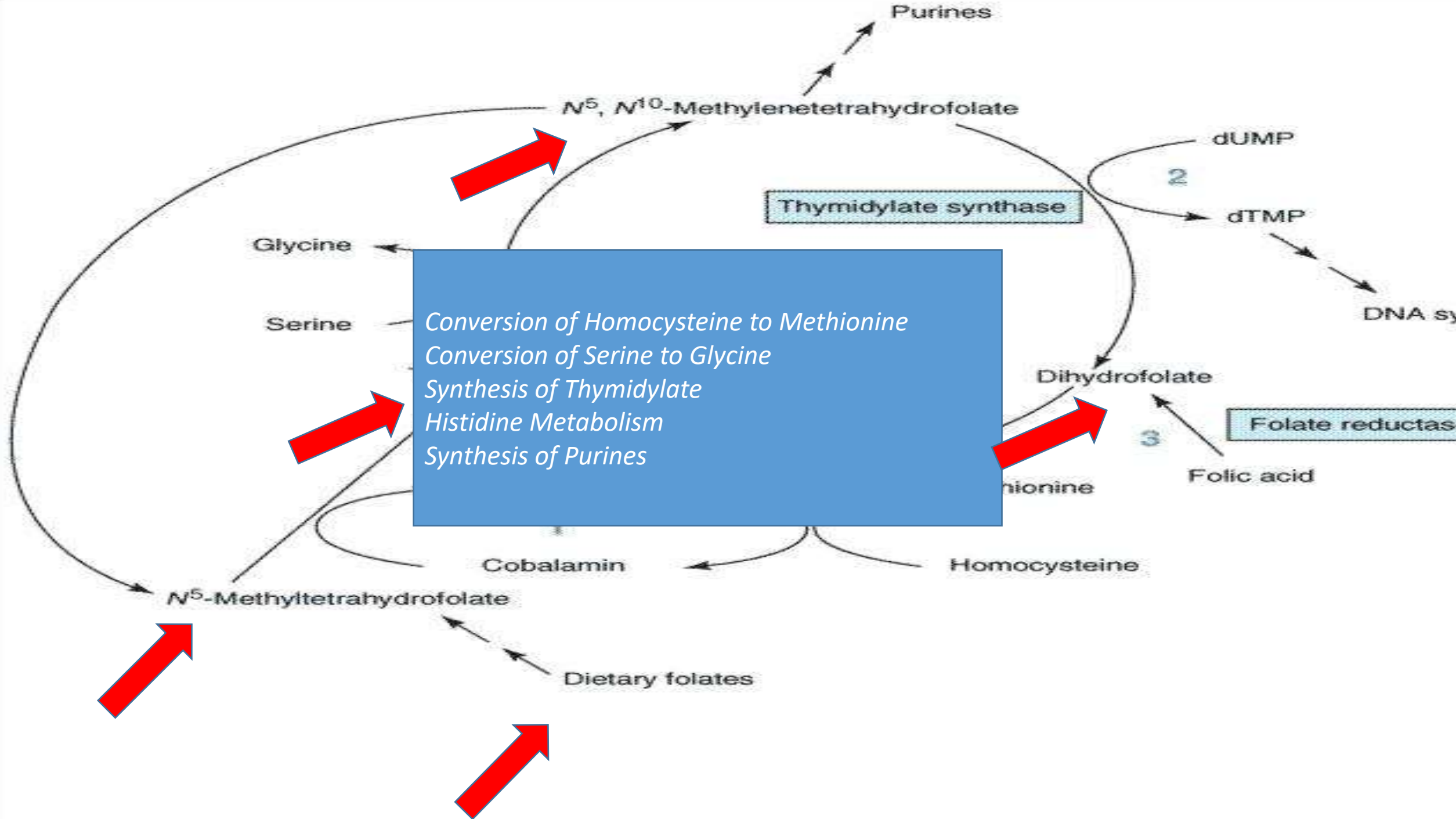
once monthly (cyanocobalamin)

once every two to three months (hydroxocobalamin)

FOLATE

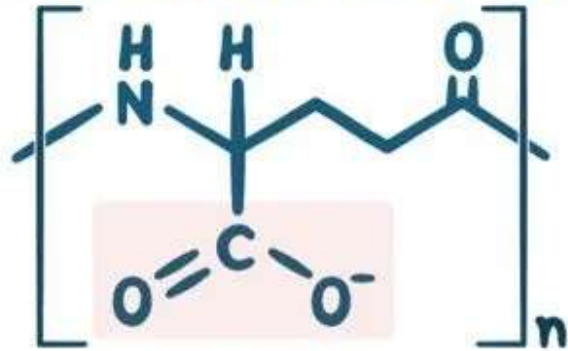


Position	Radical	Congener	
N ⁵	—CH ₃	CH ₃ H ₄ PteGlu	Methyltetrahydrofolate
N ⁵	—CHO	5-CHOH ₄ PteGlu	Folinic acid (citrovorum factor)
N ¹⁰	—CHO	10-CHOH ₄ PteGlu	10-Formyltetrahydrofolate
N ^{5,10}	=CH—	5,10-CHH ₄ PteGlu	5,10-Methenyltetrahydrofolate
N ^{5,10}	—CH ₂ —	5,10-CH ₂ H ₄ PteGlu	5,10-Methylenetetrahydrofolate
N ⁵	—CHNH	CHNH ₄ PteGlu	Formiminotetrahydrofolate
N ¹⁰	—CH ₂ OH	CH ₂ OH ₄ PteGlu	Hydroxymethyltetrahydrofolate



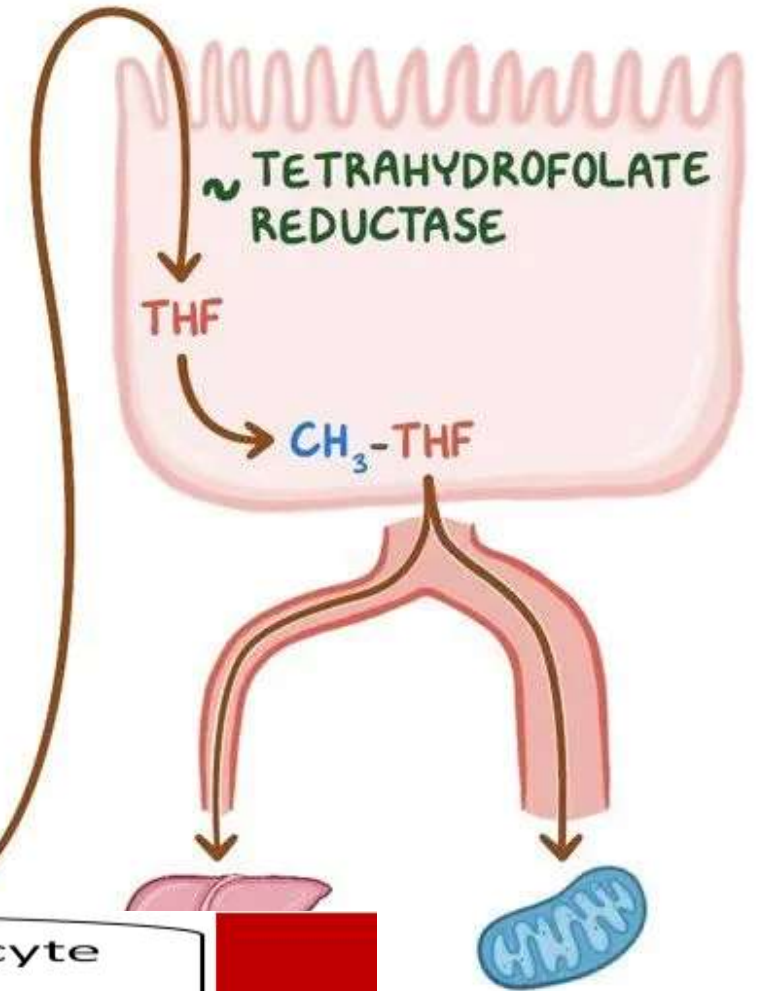
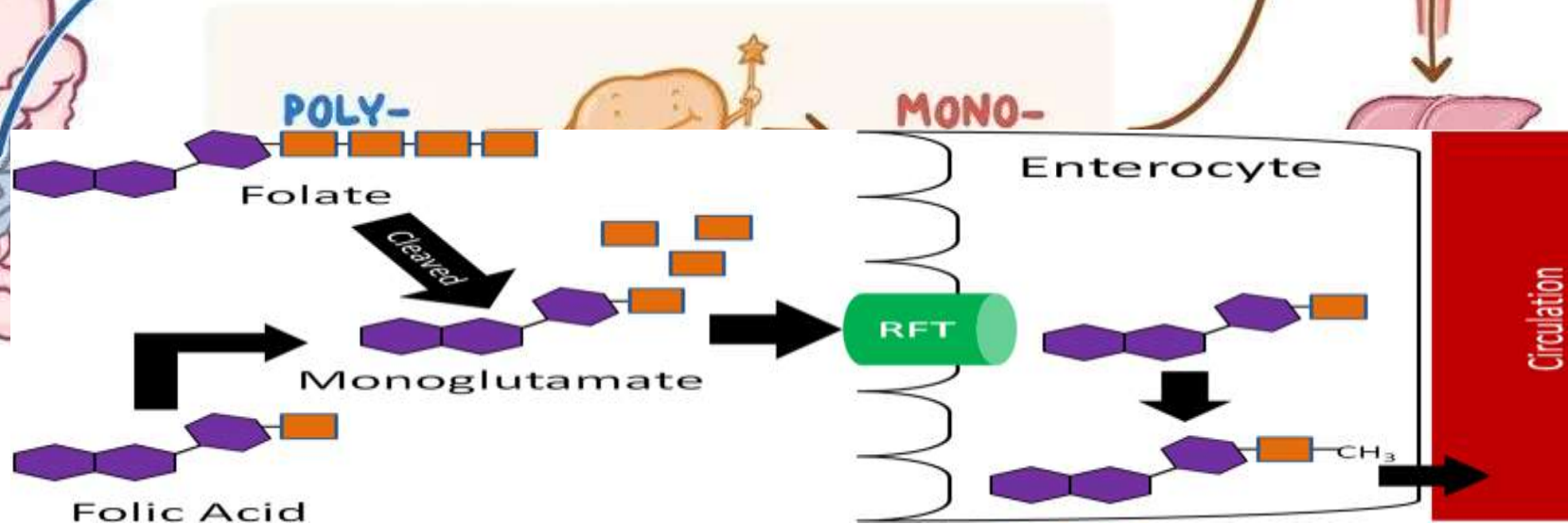
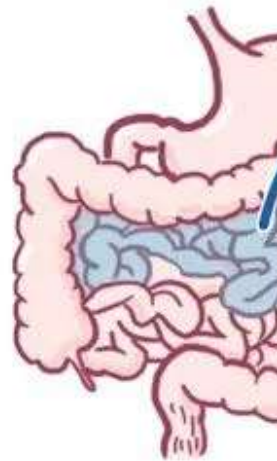
FOLIC ACID in

* **POLYGLUTAMATE FORM** ~ CHAINS of GLUTAMIC ACID

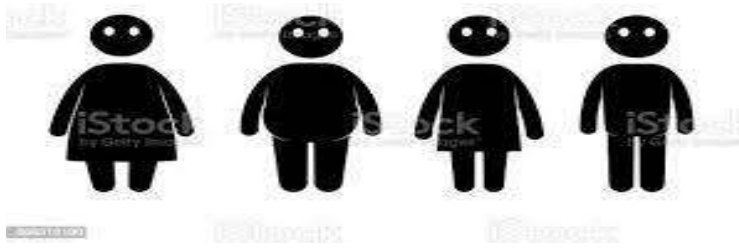


- ~ POLAR & SOLUBLE in WATER
- ~ **NOT** SOLUBLE in LIPIDS
- ∴ NON-ABSORBABLE from GI TRACT

JEJUNUM
* ABSORBABLE

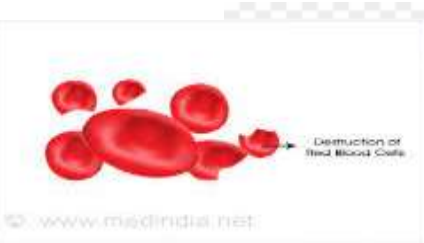


METABOLIC ACTIVITY in CELLS



400

3 mcg/kg/day.



500-600 or more



80 to 400 mcg



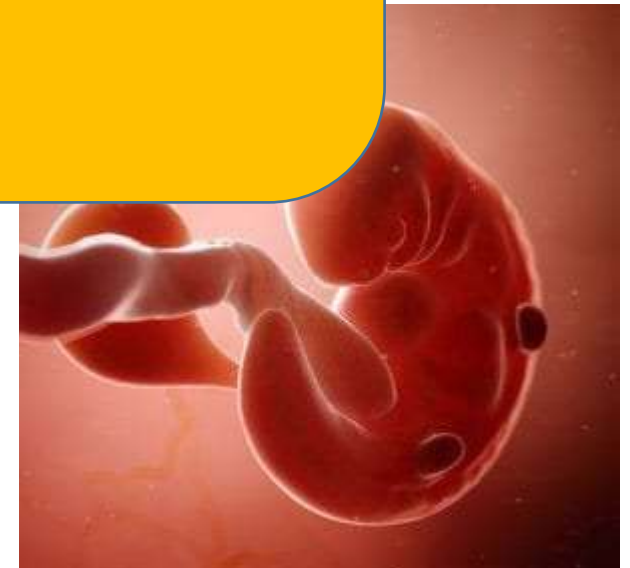
65 mcg

Prevention of folate deficiency

- ☐ inadequate dietary supply
- ☐ small intestinal disease
- uremia, alcoholism, or hepatic disease
- ☐ the concentration of folate-binding proteins in plasma
- ☐ the folate enterohepatic cycle
- ☐ “trap” folate



www.medindia.net



Treatment of folate deficiency

- 1 to 5 mg daily
- administration of folic acid to an individual with vitamin B12 deficiency can potentially mask untreated vitamin B12 deficiency or even worsen the neurologic complications