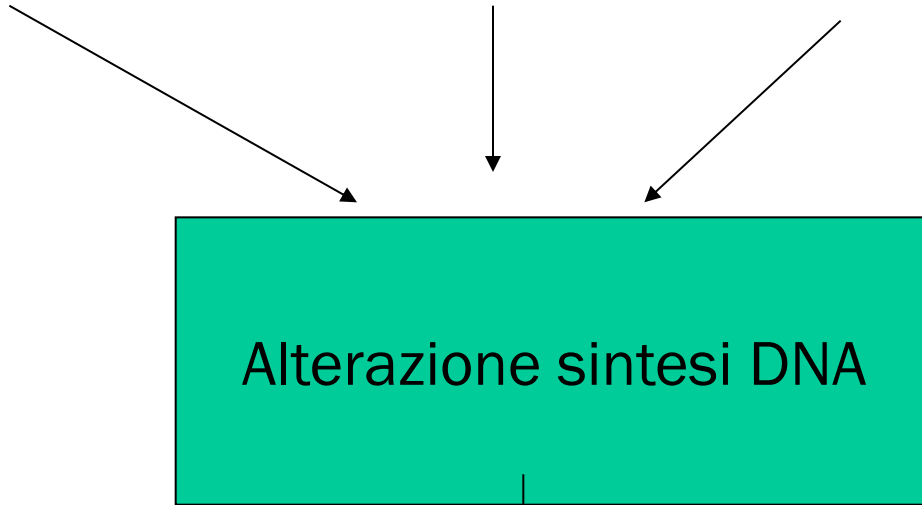


WBC	3.300
Hb	7,3
GR	1,900.000
MCV	123
MCH	26
Pst	98.000

**Carenza B12**

**carenza folati**

**patologia staminale mieloide**



Megaloblasti nel midollo

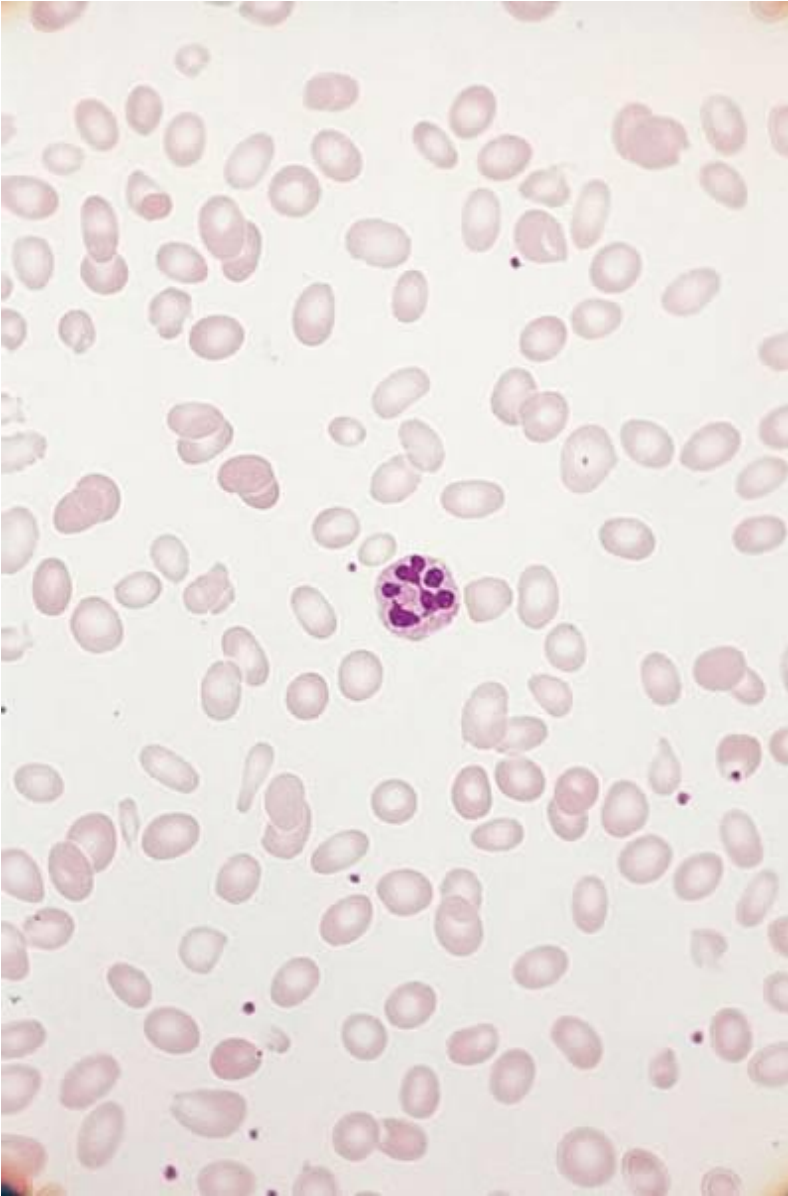
**ERITROPOIESI INEFFICACE**

**MACROCITOSI DELLE EMAZIE (MCV > 100 fl)**

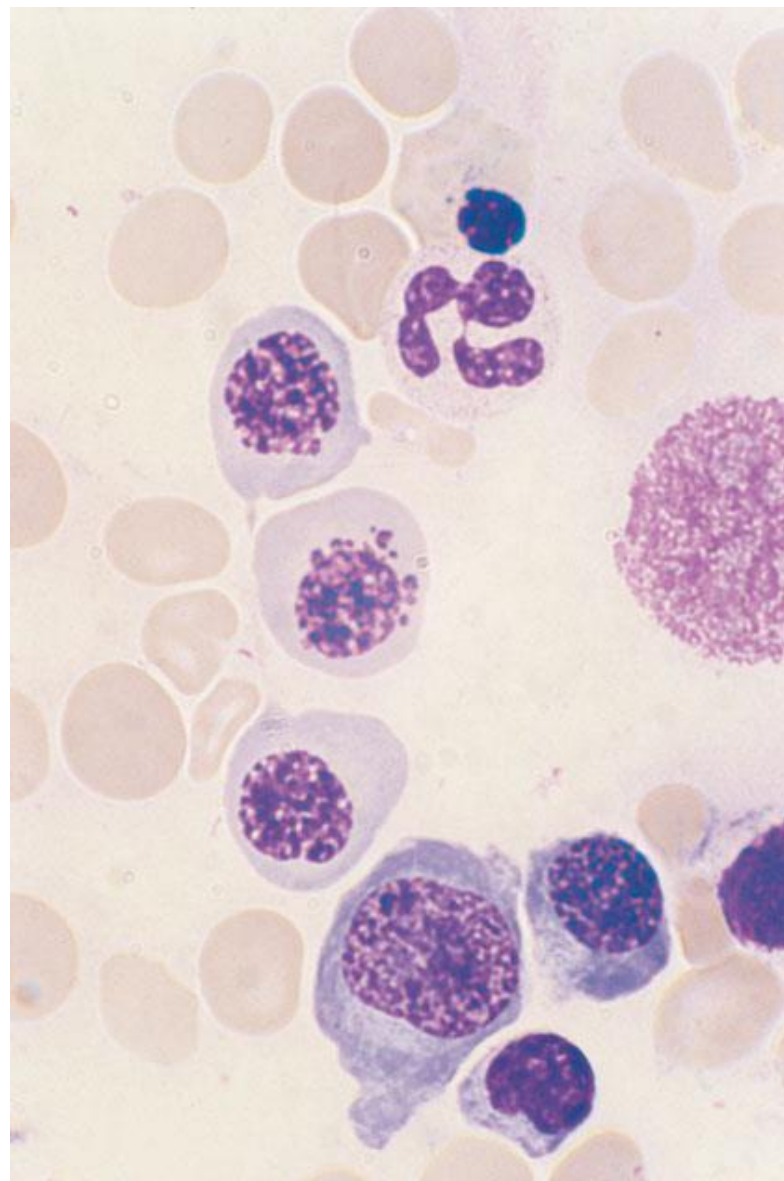
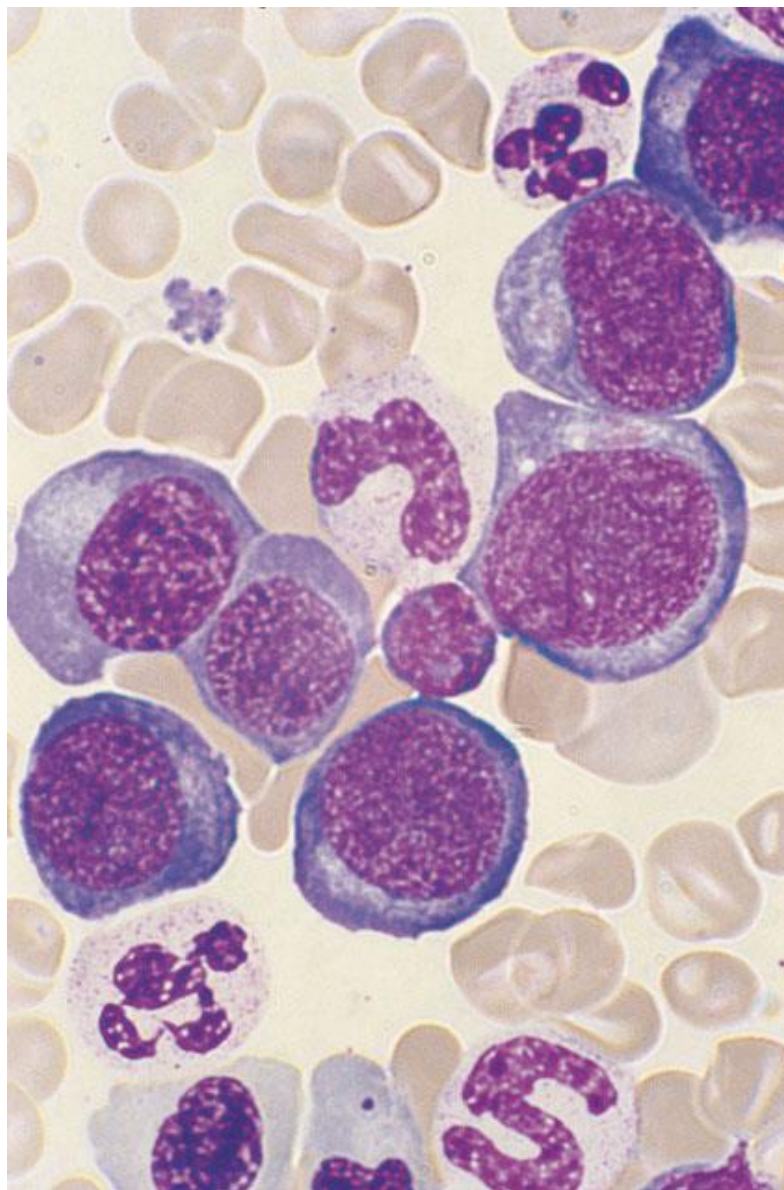
**Anemia macrocitica  
(termine generico)**

**Anemia megaloblastica  
(carenza B12 e folati)**

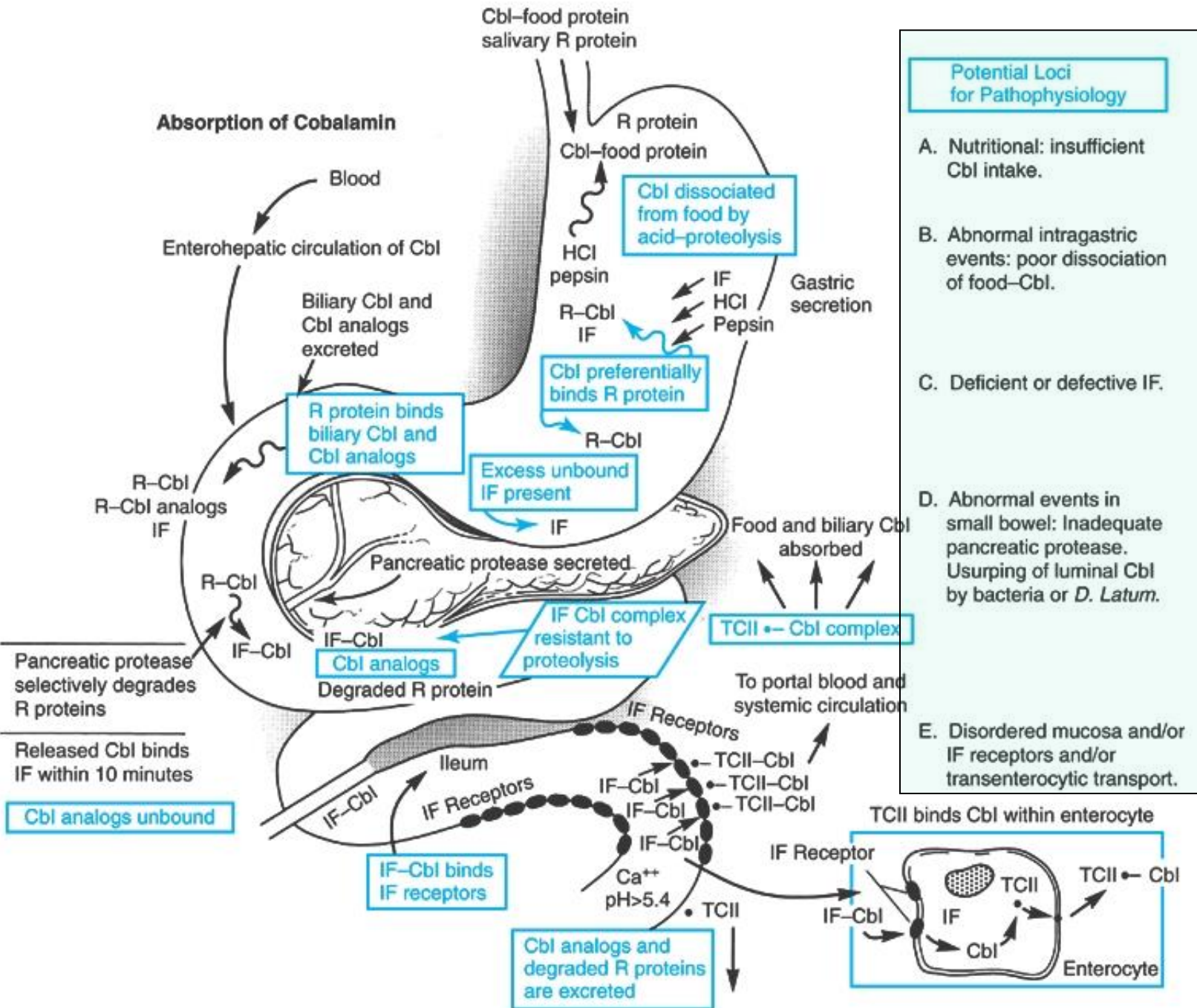
# ANEMIA MEGALOBLASTICA



# QUADRO MIDOLLARE NELL'ANEMIA MEGALOBLASTICA DA CARENZA DI B12







- Potential Loci for Pathophysiology**
- A. Nutritional: insufficient Cbl intake.
  - B. Abnormal intragastric events: poor dissociation of food-Cbl.
  - C. Deficient or defective IF.
  - D. Abnormal events in small bowel: Inadequate pancreatic protease. Usurping of luminal Cbl by bacteria or *D. Latum*.
  - E. Disordered mucosa and/or IF receptors and/or transenterocytic transport.

# Cause di anemia megaloblastica

## Carenza B12

Deficit alimentari (rari)  
dieta vegetariana

Deficiente secrezione FI:  
gastrite atrofica (atc anti  
mucosa gastrica)  
Atc anti FI  
gastrectomia totale  
irradiazione gastrica

Alterazioni intestinali  
Sprue tropicale  
estese resezioni ileali  
Crohn  
Ansa cieca  
Botriocefalo  
S Imerslund

## Carenza folati

Deficit alimentari (frequenti)  
alcolismo  
malnutrizione

Malassorbimento  
Alcolismo,  
celiachia  
Zollinger Ellison  
sprue  
estese resezioni ileali  
Crohn  
Sclerodermia

Aumentato fabbisogno  
Gravidanza  
emolisi cronica  
dermatiti esfoliative

Riduzione scorte epatiche  
cirrosi  
alcolismo

## Farmaci e altre condizioni

Inibizione diidrofolato-redutasi  
metotrexate  
pirimetamina,  
trimetoprim

Interferenza metabolismo folati  
anticonvulsivanti  
sulfamidici

Inattivazione B12  
protossido d'azoto  
metformina

Interferenze sintesi basi DNA  
5-FU  
idrossiurea  
citarabina  
azatioprina

Anemia refrattaria (SMD)

## SINTOMI

- legati all'anemia  
(a lenta insorgenza)
- specifici

**Table 34-4 Similarities of Clinical Manifestations and Megaloblastic Sequelae of Folate and Cobalamin Deficiency\***

System	Manifestations
Hematologic	Pancytopenia with megaloblastic marrow
Cardiopulmonary	Congestive heart failure
Gastrointestinal	Beefy-red tongue and added stigmata of broad spectrum malabsorption in folate deficiency <sup>†</sup>
Dermatologic	Melanin pigmentation and premature graying
Genital	Cervical or uterine dysplasia
Reproductive	Infertility or sterility
Psychiatric	Depressed affect and cognitive dysfunction
Neuropsychiatric <sup>‡</sup>	Unique to cobalamin deficiency with cerebral, myelopathic, or peripheral neuropathic disturbances, including optic and autonomic nerve dysfunction

\* However, the neurologic spectrum of dysfunction in cobalamin deficiency is distinct. Inadequate hemoglobinization (from inadequate iron stores or globin synthesis) can mask the expected erythroid megaloblastic morphology in the bone marrow and peripheral smear, and only specific therapy (i.e., iron) can unmask classic megaloblastic manifestations (i.e., masked megaloblastosis). Megaloblastic leukopoiesis is unchanged.

<sup>†</sup>If folate deficiency is uncorrected for 2 to 3 years, cobalamin deficiency will supervene.

<sup>‡</sup>Dorsal tract involvement is earliest manifestation in more than 70% of patients with cobalamin deficiency. Neuropsychiatric manifestations are not associated with megaloblastosis in up to 30% of patients.



# Diagnosi

Emocromo (anemia, possibile leucopiastrinopenia)

- a megaloblastica
- Neutrofili ipersegmentati

Dosaggio B12 e folati (ridotto)

Bilirubinemia (aumento bil indiretta – eritropoiesi inefficace)

Sideremia (elevata - emolisi intramidollare, mancato utilizzo)

LDH (aumento che riflette espansione eritroide intramidollare)

Aspirato midollare (midollo Blu)

Escludere altre cause di megaloblastosi

Ex-adjuvantibus (crisi reticolocitaria dopo 5-7 gg di terapia)



**Table 34-5 Clinical Conditions Not To Be Confused with Megaloblastosis**

***Macrocytosis\* without Megaloblastosis†***

- Reticulocytosis ←
- Liver disease ←
- Aplastic anemia ←
- Myelodysplastic syndromes (especially 5q) ←
- Multiple myeloma
- Hypoxemia
- Smokers

***Spurious Increases in MCV without Macro-ovalocytosis‡***

- Cold agglutinin disease ←
- Marked hyperglycemia
- Leukocytosis
- Older individuals

## Differential diagnosis

**MDS: check for neutropenia, cytogenetics, ex adjuvantibus**

**Aplastic Anemia: BM aspiration**

**Liver disease: think about it!**

**Pancytopenia due to BM infiltration**

\*The central pallor that normally occupies about one third of the normal red blood cell is decreased in macro-ovalocytes. This contrasts with the finding of thin macrocytes, in which the central pallor is increased.

†Although megaloblastosis implies that a bone marrow test has been performed, with the addition of highly sensitive tests for the specific diagnosis of cobalamin and folate deficiency, the need for a bone marrow test is often dictated by the urgency to make the diagnosis.

‡When the Coulter counter readings of a high MCV are not confirmed by looking at the peripheral smear.

MCV, mean corpuscular volume.

## Treatment

Administer B12 vitamin (IM) and folate

Never folate alone (neurologic damage may worsen)

Check for reticulocytosis after 5-7 days

Check for Hb increase (at least 1-2 gr/dL after 20 days)

Check for correction of anemia after 1-2 months

### Table 34-6 Causes of Megaloblastosis Not Responding to Therapy with Cobalamin or Folate

Wrong diagnosis

Combined folate and cobalamin deficiencies being treated with only one vitamin

Associated iron deficiency

Associated hemoglobinopathy (e.g., sickle cell disease, thalassemia)

Associated anemia of chronic disease

Associated hypothyroidism