

Anemias of Chronic Diseases (ACD)¹

Possibly due to blunted Ep response by RBC precursors, decreased RBC survival, defective iron absorption, or cytokines blockading iron release from RE system to developing RBCs.

See Tables 11-7, 11-8, and 11-9 and Figure 11-3.

Due To

Chronic kidney disease (BUN >70 mg/dL) and inflammation
Autoimmune disorders

- RA (anemia parallels activity of arthritis)
- SLE, connective tissue diseases
- Sarcoidosis
- Inflammatory bowel disease
- Vasculitis

Neoplasms (solid tumors, leukemias)

Subacute or chronic infections

- Bacterial (especially TB, bronchiectasis, lung abscess, empyema, infective endocarditis, brucellosis, osteomyelitis)
- Viral
- Parasitic
- Fungal

Others (e.g., chronic liver diseases, chronic adrenal insufficiency, hypothyroidism, rheumatic fever)

Laboratory Findings

- ◆ Anemia is usually mild (Hb 8–9 g/dL) but may be as low as 5 g/dL in uremia when other factors are present. Is insidious over a 3- to 4-week period, then *not progressive*. May be caused by multiple mechanisms (e.g., failure of erythropoiesis, decreased RBC survival, iron deficiency, etc).
- ◆ Anemia is normocytic, normochromic in 60% to 70% of cases. RDW and indices are usually normal. Anemia is hypochromic and/or microcytic in 30% to 40% of these patients, in which case it is always less marked than in IDA.

Moderate anisocytosis and slight poikilocytosis are present.

Low reticulocyte count.

Polychromatophilia, and nucleated RBCs are absent (may be present with severe anemia or uremia).

- ◆ Serum iron is decreased. TIBC is decreased or normal; if TIBC is elevated, presence of iron deficiency must be ruled out, but TIBC is not sufficiently sensitive or specific to distinguish ACD from IDA. Transferrin saturation is usually normal; >10% if decreased; <10% implies iron deficiency. IDA may be caused by GI blood loss due to treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) for RA.
- ◆ Serum ferritin is increased or normal in contrast to iron deficiency. *In RA, liver disease, or neoplasms, normal serum ferritin does not exclude concomitant iron deficiency, but serum ferritin <40 ng/mL indicates iron depletion.*
- ◆ sTfR is normal. Used to help differentiate from IDA.

Free erythrocyte protoporphyrin is increased.

- ◆ Hemosiderin is increased or normal; sideroblasts are decreased in bone marrow; cellular elements are generally morphologically normal. Myeloid:erythroid ratio is usually normal.

Platelet count is normal.

Increased WBC, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and other acute phase reactants (e.g., fibrinogen, ceruloplasmin) are disproportionate to anemia, and may be a useful clue to distinguish this from IDA.

RBC survival is slightly decreased in patient (80–90 days) but not in normal recipient.

¹Weiss G, Goodnough LT. Anemia of Chronic Disease. *N Engl J Med* 2005;352:1011.

Chronic Renal Disease

Blood smear frequently shows burr cells or schistocytes.

Usually normochromic, normocytic; hypochromic microcytosis may be caused by chronic disease.

Severity of anemia roughly parallels severity of renal disease, but when dialysis is required, anemia is almost always severe.

Decreased serum iron and transferrin. Serum iron, TIBC, and ferritin are often not helpful, and bone marrow stained for iron may be necessary for diagnosis of iron deficiency.

Concurrent iron deficiency caused by GI tract blood loss may be present.

Bone marrow usually shows erythroid hypoplasia.

Decreased serum erythropoietin. Anemia responds to erythropoietin therapy.

Decreased RBC survival by ^{59}Cr studies.

Hypothyroidism

◆ Occurs in 1/3 to 2/3 of patients with hypothyroidism; usually mild (Hct >35%). May be secondary to hypopituitarism.

Normochromic normocytic or macrocytic (if hypochromic, rule out associated iron deficiency). No anisocytosis or poikilocytosis.

Reticulocyte count is not increased.

Serum iron is usually decreased and responds only to treatment of hypothyroidism, unless there is concomitant iron deficiency.

Decreased total blood volume and plasma volume.

Normal RBC survival.

Concurrent iron deficiency or PA may be present.

Hypogonadism

Normochromic, normocytic anemia; only occurs in men.

Hypoadrenalism

Hct is pseudo-normal at presentation due to plasma volume depletion; corticosteroid therapy unmasks anemia. Is corrected by 1 to 2 months of therapy.

Chronic Liver Disease

○ Increased MCV (100–125 fL) in 1/3 to 2/3 of patients. Indices resemble those in other megaloblastic anemias. Low MCHC may indicate associated iron deficiency.

◆ *Uniform round macrocytosis* is the cardinal finding. Target cells and stomatocytes may be present. The presence of hypochromic macrocytes or microcytes may suggest misleading diagnosis of iron deficiency. Spur cell (acanthocyte) hemolysis may be caused by abnormal lipid metabolism.

Hemolytic anemia or true folate deficiency is frequent in alcoholic liver disease. Reticulocyte count is usually increased.

Serum iron, TIBC, and ferritin are often not helpful, and bone marrow stained for iron may be necessary for diagnosis of iron deficiency.

Decreased RBC survival by ^{59}Cr studies.

Chiefly Macrocytic/Megaloblastic Anemias**Anemia, Megaloblastic (Pernicious Anemia [PA]; Vitamin B₁₂ Deficiency and Folate Deficiency)²**

Dyssynchronous nuclear and cytoplasmic maturation in all erythroid and myeloid cell lines due to aberrant DNA synthesis caused by deficiency of folate or vitamin B₁₂.

See Tables 11-9A and 11-9B and Figures 11-4A and 11-4B.

²Ward P. Modern approaches to the investigation of vitamin B₁₂ deficiency. *Clin Lab Med* 2002; 22:435.

Table 11-9A. Laboratory Tests in Differential Diagnosis of Vitamin B₁₂ and Folate Deficiencies

	Vitamin B ₁₂ Deficiency	Folate Deficiency	Vitamin B ₁₂ and Folate Deficiency
Serum folate	N or I	D	D
Serum vitamin B ₁₂	D	N or D	D
RBC folate	N or D	D	D
Methylmalonic acid	I	N	I
Homocysteine	I	I	I

D = decreased; I = increased; N = normal.

Hematologic picture is identical in folate or vitamin B₁₂ deficiency but neurologic findings are absent in folate deficiency. Treatment of PA with folate reverses hematologic findings but may accentuate neurologic findings.

Normochromic macrocytic anemia is a relatively late event; RBC may be as low as 500,000/ μ L. Degree of anemia does not correlate with severity of neurologic signs and symptoms which may precede hematologic abnormalities.

Hemolytic anemia *without* reticulocytosis (2%–3%) is characteristic of PA because nuclear-cytoplasmic dyssynchrony causes loss of RNA before nuclear extrusion, and also occurs in folate deficiency or iron deficiency anemia with superimposed hemolytic disease.

◆ RBC indices

- MCV is increased (95–110 fL with mild to moderate anemia but may also be due to round macrocytes due to nonmegaloblastic causes; 110 to 150 fL with more severe anemia.

MCV increases many months before onset of anemia or clinical symptoms in almost all patients. MCV >95 should prompt further study. MCV >120 fL is

Table 11-9B. Comparison of Pernicious Anemia (PA) (Vitamin B₁₂ Deficiency) and Folate Deficiency

Most Commonly Due To	Vitamin B ₁₂ Deficiency	Folate Deficiency
Defective absorption	Decreased intrinsic factor (e.g., PA, congenital deficiency of intrinsic factor, 4 years after gastrectomy) Zollinger-Ellison syndrome Pancreatitis Ileal mucosal disease (e.g., sprue, regional enteritis, surgery) Tapeworm infestation, bacterial overgrowth in blind loop Drugs (e.g., colchicine, PAS, alcoholism)	Malabsorption Jejunal mucosal disease (e.g., amyloidosis, sprue, lymphoma, surgery)
Inadequate intake	Strict vegetarian diet (rare)	Drugs (e.g., anticonvulsants, antituberculosis, oral contraceptives) Malnutrition, alcoholism
Increased need	Pregnancy, lactation	Pregnancy, lactation, infancy

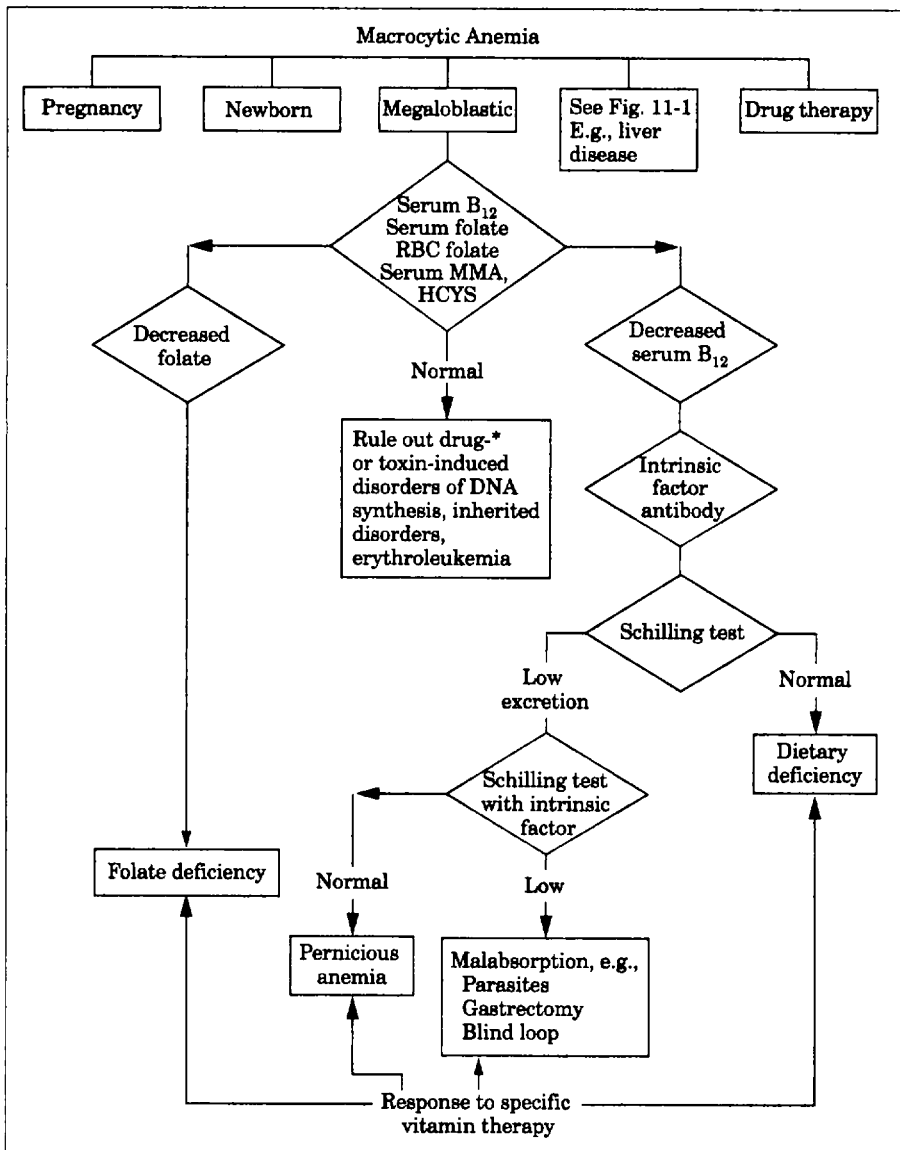


Fig. 11-4A. Sequence of laboratory tests in macrocytic anemia. (HCYS = homocysteine; MMA = methylmalonic acid.)

*E.g., valproic acid, carbamazepine, phenytoin.

most likely due to megaloblastic anemia. MCV may be normal if coexisting iron deficiency, thalassemia trait, inflammatory disease, or renal failure. MCV is normal in ~9% of megaloblastic patients.

- RDW is usually very increased due to marked aniso-poikilocytosis but may be normal.
- MCH is increased (33–38 pg with moderate anemia; ≤56 pg with severe anemia).
- MCHC is normal.

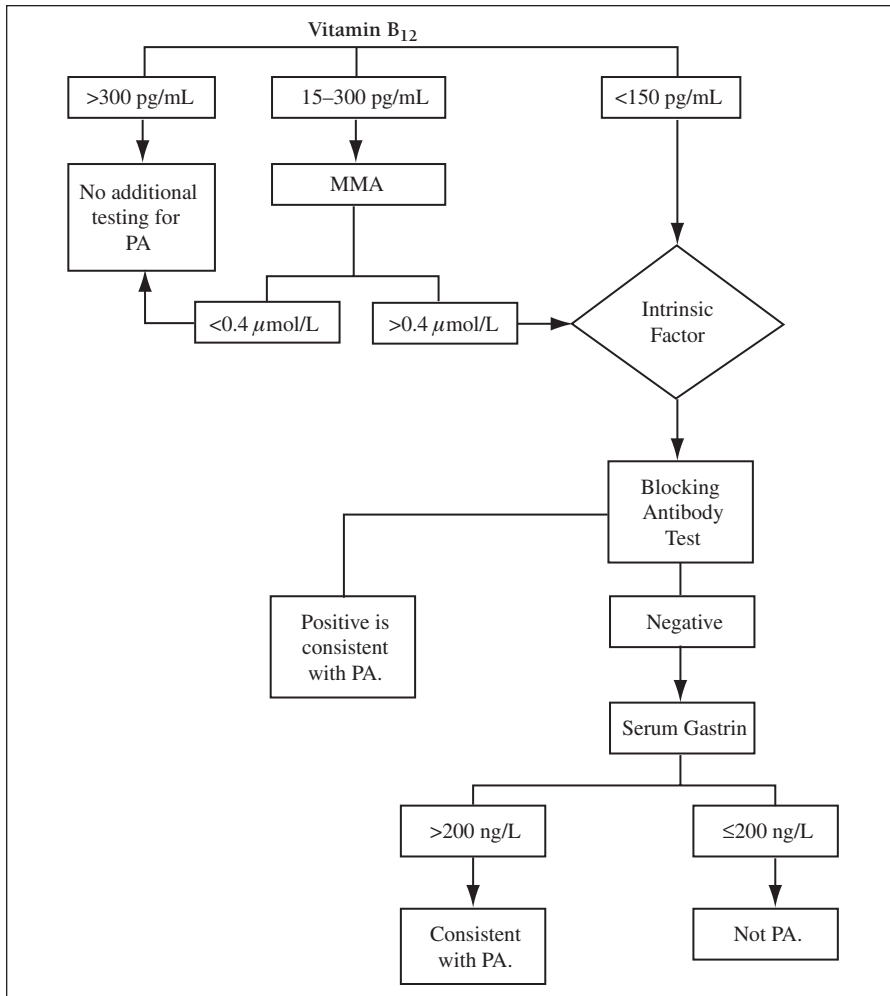


Fig. 11-4B. Algorithm for Suspected Pernicious Anemia (PA).

◆ Large hypersegmented neutrophils (≥ 5 lobes) is the earliest morphologic sign of megaloblastic anemia (rule out congenital hypersegmentation in 1% of white persons and uremia); less than two 5-lobed neutrophils is strongly suggestive and any with ≥ 6 lobes is considered diagnostic.

Occasionally there is moderate eosinophilia. Blood smear may show oval macrocytes, schistocytes, polychromatophilia, stippled RBCs, Howell Jolly bodies, Cabot's rings, etc.

Nucleated RBCs may be found with Hct $< 20\%$. Macroovalocytes are a good clue although may also be seen in myelodysplasia in contrast to round macrocytes of non-megaloblastic anemias.

◆ Large hypersegmented neutrophils with low Hb, increased MCV (95–110 fL) and macroovalocytes are considered diagnostic.

Poikilocytosis and anisocytosis are moderate to marked; always present in relapse.

Reticulocyte count is usually decreased.

Thrombocytopenia ($< 150,000/\mu\text{L}$) is present in 12% of cases; abnormal and giant forms may be seen.

Leukopenia ($< 4000/\mu\text{L}$) in 9% of cases.

- ◆ Marrow shows megaloblastic and erythroid hyperplasia and abnormalities of myeloid and megakaryocytic elements. Erythroid megaloblastosis may be masked by concomitant iron deficiency but granulocytic megaloblastic changes persist. Not indicated if diagnosis is unequivocal or treatment has been started.
 - ◆ In PA serum vitamin B₁₂ is very low, usually <100 pg/mL; 100 to 150 pg/mL usually signifies early vitamin B₁₂ deficiency even without neuropathy or macrocytosis. May occur with neurologic findings but without anemia in ≤1/3 of patients with vitamin B₁₂ deficiency especially in older persons. RBC folate is low in many patients with vitamin B₁₂ deficiency.
- Intrinsic factor is glycoprotein present in gastric secretions essential for absorption of vitamin B₁₂ in terminal ileum.

Serum Vitamin B₁₂ May Also Be Decreased In

Reference range ≥3.5 ng/mL.

Diet deficient in folic acid (low in 10%–30% of patients with simple folate deficiency; corrected by folate therapy alone). *Less than or equal to 50%* of patients with pure vitamin B₁₂ deficiency have falsely low RBC folate values.

Malabsorption

- Loss of gastric mucosa e.g., partial or complete gastrectomy, atrophic gastritis, gastric radiation. Annual assay of vitamin B₁₂ should be performed because 100% of patients with total resection and 10% with partial resection will be deficient within 5 years.
- Small bowel disease (e.g., Crohn disease, scleroderma, lymphoma, ileal resection, tropical sprue, celiac disease, chronic pancreatic insufficiency, bacterial overgrowth)
- Primary hypothyroidism. (Almost 50% of patients have serum achlorhydria with intrinsic factor failure and low vitamin B₁₂; rarely megaloblastic anemia develops.)
- Parasites (5% of persons infested with *Diphyllobothrium latum*)
- Blind-loop syndrome diagnosed by positive Schilling test that becomes normal after 2 weeks of tetracycline therapy

Drugs (e.g., chronic PAS or colchicine use, oral contraceptives, aspirin, alcohol)

Pregnancy—progressive decrease during pregnancy (*normal serum B₁₂ in megaloblastic anemia of pregnancy*)

Impaired cell utilization

- Abnormal vitamin B₁₂ carrier protein (transcobalamin II deficiency, abnormal protein)
- Enzyme deficiency (e.g., congenital methylmalonicacidemias)
- Prolonged nitrous oxide exposure

One third of patients with multiple myeloma

Others (e.g., 15%–30% of aged persons, iron deficiency, vegetarian diet, smoking, cancer, aplastic anemia, folate deficiency, hemodialysis, pregnancy, high doses of vitamin C)

Artifactual (e.g., antibiotics with microbiologic assays, diagnostic radioisotopes for other tests [with RIA assays])

Serum Vitamin B₁₂ May Be Increased In

Myeloproliferative diseases

- Leukemia—AML and CML; about 1/3 of CLL cases; some cases of monocytic. Normal in stem cell leukemia, multiple myeloma, and Hodgkin disease.
- Polycythemia vera

Leukocytosis

Some cases of carcinoma (especially with liver metastases)

Liver disease (acute hepatitis, chronic hepatitis, cirrhosis, hepatic coma)

Ingestion of vitamin A, vitamin C, estrogens, anticonvulsants

Uremia

Serum folate is normal or increased. Decreased serum folate in folate deficiency.

Decreased RBC folate in both folate and B₁₂ deficiency. (See Table 11-9A.)

Serum Folic Acid May Be Decreased In

Nutritional (may fall relatively quickly)

- Alcoholism is most common cause
- Infancy, prematurity, elderly

- Chronic disease
- Hemodialysis
- Anorexia nervosa

Increased requirements due to marked cellular proliferation

- Pregnancy
- Hyperthyroidism
- Neoplasia (e.g., acute leukemia, metastatic carcinoma)
- Hemolytic anemias (e.g., sickle cell, thalassemias, hereditary spherocytosis, PNH)
- Ineffective erythropoiesis (PA, sideroblastic anemia)
- Exfoliative dermatitis (e.g., psoriasis)

Malabsorption

- Small bowel disease (e.g., celiac disease, tropical sprue, Crohn disease, lymphoma, amyloidosis, small bowel resection, etc.)

Defect in utilization due to certain enzyme deficiencies

Drugs—folic acid antagonists (e.g., methotrexate, trimethoprim, pyrimethamine); anticonvulsants; oral contraceptives; aspirin

Decreased liver stores (e.g., cirrhosis, hepatoma)

Idiopathic

Artifactual

- Improper specimen storage (folate is labile)
- Radioactivity in blood (affects radioassays)
- Antibiotic therapy (affects microbiologic assays)

Serum folate serves to distinguish combined deficiency from vitamin B₁₂ deficiency alone. Low serum folate indicates only negative folate balance, not folate tissue deficiency for which RBC folate should be assayed.

RBC Folate

Reflects folate status at time RBCs were produced; therefore more reliable indicator of tissue folate deficiency as not subject to daily variation due to diet, etc. Decreased in folate or vitamin B₁₂ deficiency. *RBC folate does not fall below normal until all body stores are depleted. Thus, all three parameters should be measured simultaneously in suspected cases of megaloblastic anemia. RBC folate should always be measured in suspected cases of megaloblastic anemia when serum folate and vitamin B₁₂ are assayed (see Table 11-9A).*

Usual normal range is 5 to 15 ng/mL; is associated with normal hematologic findings.

Borderline range is 3 to 5 ng/mL; is associated with variable hematologic findings.

Less than 3 ng/mL is associated with positive hematologic findings.

Serum Folic Acid May Be Increased In

PA (or may be normal)

Period following folic acid administration or eating

Vegetarians

Blood transfusion

Some cases of blind loop syndrome (due to folate synthesis by bacteria in gut)

False elevation in hemolyzed specimens (due to folate in RBCs)

Falsely increased to normal in some patients with severe iron deficiency (for unknown reason)

◆ *Iron deficiency is present in 1/2 of patients with folate deficiency and 1/3 with vitamin B₁₂ deficiency. If iron deficiency is more severe than folate deficiency, results of serum and RBC folate tests are normal, and diagnosis cannot be made from these tests; hypersegmentation of PMNs in blood smear is the only clue.*

◆ Increased serum methylmalonic acid (MMA) and homocysteine (HCYS) are the most sensitive tests to detect early vitamin B₁₂ deficiency and become increased before hematologic evidence of vitamin B₁₂ deficiency. Levels should be measured in patients with borderline vitamin B₁₂ levels (100–300 pg/mL).³ MMA is also increased in urine.

³Elin RJ, Winter WE. Methylmalonic acid. A test whose time has come. *Arch Pathol Lab Med* 2001;1125:824.

- Patients with folate deficiency usually increase only HCYS although some may have mild increase of MMA.
- Should be positive in acute neurological disease due to vitamin B₁₂ deficiency even when hematologic changes are absent. Remain positive for at least 24 hours after onset of vitamin B₁₂ therapy in cases where therapy is begun before blood was drawn for vitamin B₁₂ levels.
- Urine MMA may be useful when serum MMA is falsely high in renal insufficiency or in hypovolemic states.
- Tests should always be requested in cases of unexplained hematologic or neuropsychiatric abnormalities with low or borderline serum vitamin B₁₂ levels. (Reference ranges: MMA = 70–279 nmol/L, HCYS = 5–15 μmol/L; HCYS may be increased in renal failure and smoking).⁴

◆ Serum antibodies:

Intrinsic factor (IF) antibody

- Type I autoantibodies block binding of vitamin B₁₂ to intrinsic factor; found in serum in 40% to 50% of PA patients.
- Type II autoantibodies bind to site remote from vitamin B₁₂-binding site; found in ~40% of PA patients; rarely occur in absence of Type I antibodies. Should be performed in patients with low serum B₁₂; presence of Type I blocking antibodies combined with low serum B₁₂ very strongly favors diagnosis of PA and obviates need for Schilling test; however, a negative test does not rule out PA. More often found in gastric juice than serum. False positive results are rare (high serum B₁₂ may cause false positive results).

Parietal cell antibodies

- Directed against ATPase pump in parietal cells is specific for type A gastritis, not for PA.
 - Found in 90% of patients with PA but frequency decreases with duration of PA.
 - Found in ~30% of their non-anemic first-degree relatives and in patients with autoimmune endocrinopathies; occur frequently in chronic gastritis.
 - Found in 2% of normal population (third decade) increasing to >9% in eighth decade. Intrinsic antibodies are more specific but less sensitive.
- ◆ Schilling test is diagnostic of PA (shows very decreased absorption of radiolabeled B₁₂ which is corrected only by simultaneous administration of gastric intrinsic factor with B₁₂).
- Now performed very infrequently.

Differentiates PA from other causes of vitamin B₁₂ deficiency (*commonplace injection of vitamin B₁₂ may make serum level temporarily normal for many weeks*) and can establish the functional absence of intrinsic factor before serum B₁₂ deficiency or anemia are present or after patient has received vitamin B₁₂ treatment (Table 11-9C).

- Fasting patient is given oral ⁵⁸Co B₁₂ and ⁵⁷Co B₁₂ bound to intrinsic factor. In 1 to 2 hours, a flushing dose of 1 mg of nonradioactive B₁₂ is injected to saturate B₁₂ binding sites, and a 24-hour urine specimen is collected.
- In PA, the ⁵⁸Co in urine is low (usually <5% of the administered dose) but the ⁵⁷Co B₁₂ bound to IF is normally absorbed and excreted (>10% of the administered dose). Failure of IF to correct malabsorption indicates small intestinal lesion (e.g., primary mucosal, bacterial overgrowth, tapeworm infestation).
- In intestinal malabsorption, ⁵⁷Co and ⁵⁸Co in the urine are equally low (<5%). Both become normal if underlying cause is treated (e.g., antibiotic treatment in patients with bacterial overgrowth, administer exogenous pancreatic enzyme in patients with pancreatic insufficiency).
- For test to be valid, patient must have: Normal renal function, normal intestinal mucosal absorption, and complete 24-hour urine collection.

⁴In children, see Monsen AB, et al. Cobalamin status and its biochemical markers methylmalonic acid and homocysteine in different age groups from 4 days to 19 years. *Clin Chem* 2003;49:2067.

Table 11-9C. Interpretation of Schilling Test

Disorder	Without Intrinsic Factor	With Intrinsic Factor
Pernicious anemia	No	Yes
Congenital deficiency of intrinsic factor	No	Yes
Gastrectomy	No	Yes
Intestinal malabsorption (e.g., ileal diseases, bacterial overgrowth, pancreatic disease, fish tapeworm)	No	No
Renal failure	No	No
Incomplete urine collection	No	No
Folate deficiency	Yes	Yes

- *Some patients (e.g., after partial gastrectomy or vagotomy cannot absorb dietary vitamin B₁₂ but can absorb crystalline vitamin B₁₂ used in test giving false normal result.*

○ Increased serum gastrin (may be very high) in >80% of patients but poor specificity. With low serum vitamin B₁₂ suggests PA. Vitamin B₁₂ level does not predict either degree of anemia or MCV.

Serum pepsinogen (derived from fundic mucosa) is low but specificity is poor.

◆ Achlorhydria occurs even after administration of pentagastrin; this is virtually essential for diagnosis of PA; presence of gastric acid rules out PA. Decreased volume of gastric juice, high pH (>3.5), and decreased or absent pepsin and rennin are also found. Achlorhydria and gastric changes are rarely found in children.

◆ Serum holotranscobalamin (circulating protein carries 30% of vitamin B₁₂ but enters all body cells) falls before those of vitamin B₁₂; presently available in research laboratories.

Less than 50 pmol/L: Unlikely to have vitamin B₁₂ deficiency; <25 pmol/L: Likely to have vitamin B₁₂ deficiency; 25 to 50 pmol/L requires further evaluation.

◆ Deoxyuridine (dU) suppression test: Patient's marrow cells are cultured with radio-labeled thymidine; in normal marrow, labeled thymidine uptake is suppressed on addition of unlabeled dU because dU can be converted to deoxythymidine but suppression does not occur when patient is folate or B₁₂ deficient due to inability to convert deoxyuridine; adding either folate or B₁₂ to the medium indicates specific cause. May be useful when other test results are masked by recent therapy or are equivocal. Limited availability.

Serum iron, TIBC, ferritin and marrow iron are almost always increased during relapse unless there is complicating iron deficiency.

Serum ALP is decreased; increases after treatment.

Serum cholesterol is moderately decreased.

Cholinesterase activity in RBC, plasma, and whole blood is decreased.

Laboratory findings due to hemolysis

- RBC survival is decreased.
- Serum LD is markedly increased (principally LD-1 and LD-2 with 1 > 2).
- Serum indirect bilirubin is increased (<4 mg/dL).
- Urine urobilinogen and coproporphyrin I are increased.
- Stool urobilinogen is increased.

Fifty percent of PA patients have thyroid antibodies.

Increased frequency of gastric adenocarcinoma and gastric carcinoids.

◆ **Characteristic Response of Laboratory Tests to Specific Treatment of PA or Folate Deficiency**

RBC count reaches normal between eighth and 12th week regardless of severity of anemia; Hb concentration may rise at a slower rate, producing hypochromia with microcytosis.

Peripheral blood is normal in 1 to 2 months.

Characteristic reticulocyte response is proportional to severity of anemia. Reticulocyte count begins to rise by fourth day after treatment and reaches maximum on eighth to ninth day; returns to normal by the 14th day. Daily injection of 200 μg of folic acid or citrovorum factor causes a reticulocyte response in patients with folate deficiency but not in those with B_{12} deficiency.

Megaloblasts disappear from marrow in 24 to 48 hours followed by reversal of megaloblastic changes in myeloid cells a few days later.

Serum folate decreases (in PA) at the same time reticulocytosis takes place.

Serum iron decreases to normal or less than normal at the same time reticulocytosis takes place.

Serum uric acid increases; peak precedes maximum reticulocyte count by about 24 hours; remains increased as long as rapid RBC regeneration goes on.

Serum LD decreases but is not yet normal by eighth day.

Serum bilirubin becomes normal.

Serum ALP increases to normal.

Serum cholesterol rises to greater than normal levels; most marked at peak of reticulocyte response.

Increased urinary urobilinogen and coproporphyrin I immediately revert to normal, preceding reticulocyte response.

Achlorhydria persists.

RBC cholinesterase activity increases.

In Children

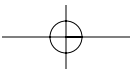
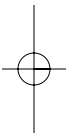
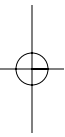
Adult type PA (very rare condition of gastric atrophy with lack of IF production at birth; antibodies to IF are present; parietal cell antibodies in 50% of cases; corrected by administration of IF; frequent endocrine dysfunction such as hypoparathyroidism and hypoadrenalism)

Congenital absence of IF (PA develops at age 12–18 months; corrected by exogenous gastric IF)

Normal gastric mucosa and acid secretion, no antibodies to IF or parietal cells, no associated endocrine deficiency)

Imerslund-Gräsbeck syndrome (rare autosomal recessive defective ileal receptor of B_{12} prevents absorption; ileum is normal histologically; normal gastric and endocrine function; proteinuria and renal tubular dysfunction are present; decreased folate and normal B_{12} concentrations; responds to parenteral B_{12} therapy).

Reader: Continue with "Atransferrinemia" subsection page 404.



Note to the reader: Insert on page 402 with the following pages:

Table 11-8. Comparison of Iron-Deficiency Anemia (IDA) Alone and Combined with Thalassemia Minor or Anemia of Chronic Disease (ACD)

	IDA Alone	ACD Alone	IDA + ACD	Thalassemia Minor Alone	IDA + Thalas. Minor
MCV	D	N or D	D	Very D	Very D
RDW	I	I or N	I	D	I
RBC count	V	D	D	N or I	N or D
Serum iron	D	D	D	N	D
Serum ferritin	D	N or I	N or D	N	D
Marrow iron	D to 0	N to I	D to 0	N	D to 0
TIBC	I	D	I or N	N	I
sTfR	I	N	I	N	I
Hb electrophoresis	N	N	N	Ab	Ab

0, absent; Ab, abnormal; D, decreased; I, increased; N, normal; V, varies.

MCV, mean corpuscular volume; RDW, red blood cell distribution width; TIBC, total iron-binding capacity; sTfR, serum soluble transferrin receptor. Bold type and larger font indicate most useful differences.

Hb electrophoresis is abnormal in β -thalassemia but not in α -thalassemia.

Measurement of globin chain synthesis ratios for confirmation of α - and β -thalassemias.

DNA analysis can detect gene deletions and point mutations, which detect most types of α - and β -thalassemia.

In the United States, median Hb is about 1 g/dL lower in blacks without iron deficiency than in whites.

Laboratory finding may disclose causative factors (e.g., GI bleeding).

Table 11-9. Comparison of Anemia of Chronic Disease (ACD) Alone, Iron-Deficiency Anemia (IDA) Alone, and Combined IDA + ACD

	ACD Alone	IDA Alone	IDA + ACD
MCV	N or D	D	D (tends to be lower)
RDW	I or N	I	I
RBC count	D	V	D (tends to be lower)
Serum iron	D	D	D
Serum ferritin	N or I	D	N or D
Transferrin	I	D or N	D
Transferrin saturation	D	D	D
Marrow iron	N to I	D to 0	D to 0
TIBC	D	I	I or N
sTfR	N	I	I or N
Ratio sTfR to log ferritin	<1	>2	>2

0, absent; Ab, abnormal; D, decreased; I, increased; N, normal; V, varies.

MCV, mean corpuscular volume; RDW, red blood cell distribution width; TIBC, total iron-binding capacity; sTfR, serum soluble transferrin receptor. Bold type and larger font indicate most useful differences.