Gruppo di ricerca geriatrica

Journal Club-18 Gennaio 2008

Anemia of Chronic Disease

Piera Barbisoni

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Anemia in the elderly is associated with increased mortality and hospitalization, worst quality of life and overall health/functional status, cardiovascular and pulmonary diseases, renal impairment, cognitive impairment, falls, disability and frailty.

Medical and Functional Consequences of Anemia in the Elderly. Balducci, JAGS, 2003
Anemia of Chronic Disease. Weiss et Goodnough, NEJM, 2005
Anemia in the elderly: A Public Health Crisis in Hematology. Guralnik et al. Hematology, 2005
Epidemiology of anemia in the elderly. Nardi et al. Ital J Medicine, 2007
Chronic Anemia and Fatigue in Elderly Patients: Results of s Randomized, Double-Blind, Placebo-Controlled, Crossover Exploratory Study with Epoietin Alfa. Agnihotri et al. JAGS 2007

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REVIEW

Anemia in the Elderly: How Should We Define It, When Does It Matter, and What Can Be Done?

DAVID P. STEENSMA, MD, AND AYALEW TEFFERI, MD

Mayo Clin Proc. 2007;82(8):958-966

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Definition

	maschi	femmine
-WHO* (1968)	Hb <13g/dL	Hb <12g/dL
-Timiras e Brownstein (1987)	Hct <40%	Hct <37%
-NCCN** (2002)	Hb <14g/dL	Hb <12g/dL
-National Kidney Foundation Guidelines (2006)	Hb <13.5g/dL	Hb <12.0g/dL

- GRADO 1: anemia lieve: Hb 10-WNL g/dL
- GRADO 2: anemia moderata: Hb 8.0-9.9 g/dL
- GRADO 3: anemia severa: Hb 6.5- 7.9 g/dL
- GRADO 4: anemia a rischio per la vita: Hb < 6.5 g/dL

* World Health Organization (1968)

•* National Comprehensive Cancer Network Guidelines (2002) (WHO-National Cancer Institute):
I limiti normali (WNL) di Hb sono: 12-16g/dl (donne) e 14-18 g/dl (uomini)

Italian Journal of Medicine 2007

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Definition

The WHO definition of anemia (Hb <13g/dL in men and Hb <12 g/dL in women) is the most frequently (although not universally) used criteria.

This definition in elderly patients may be "*too restrictive*", expecially in the light of recent data.

Italian Journal of Medicine 2007

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Looking at the Relationship Between Hemoglobin Concentration and Prevalent Mobility Difficulty in Older Women. Should the Criteria Currently Used to Define Anemia in Older People be Reevaluated?

Chaves et al, JAGS 2002

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Definition

Findings from the Women's Health and Aging Study I and II (WHAS I, II) in 633 disabled community-dwelling women aged 70 to 80 have shown that:

- women with Hb between 13.0 and 14.0 g/dl consistently obteined the best results in performance based tests of mobility function;
- those with Hb less than 12.0 g/dl achieved the worst results;
- and those with Hb between 12.0 and 13.0 g/dl (low-normal Hb concentrations) performed intermediately.

…….Hb 12.0 g/dl might be a suboptimal cutoff for defining anemia in older women.

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What Constitutes Normal Hemoglobin Concentration in Community-Dwelling Disabled Older Women?

Paulo H. M. Chaves, MD, PhD,[*†‡§] *Qian-Li Xue, PhD,*[*‡] *Jack M. Guralnik, MD, PhD,*[‖] *Luigi Ferrucci, MD, PhD,*[¶] *Stefano Volpato, MD, MPH,*[#] *and Linda P. Fried, MD, MPH*[*†‡]

. J Am Geriatr Soc 52:1811–1816, 2004.

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Definition

Women's Health and Aging Study I (WHAS I)

In 686 community-dwelling women aged 65 and older with moderate to severe self reported disability, Hb levels progressively lower than 11 g/dl were associated with increasingly higher risks for all-cause 5-year mortality than levels of 12.0 g/dl, whereas Hb levels of 13.0 and 14.0 g/dl were associated with a lower risk of death.

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…considerations should be given to refining the current definition of anemia in elderly.

… Hb levels higher than what is currently recommended might offer clinical advantage.

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The Definition of Anemia in Older Persons

Izaks GJ et al, JAMA 1999

The study of 755 subjects >85 years of age showed that a Hb <13g/dl in males and <12g/dl in females was associated with an increased relative risk of mortality of 1.6 in males (95% CI 1.2-2.1) and 2.3 in females (95% CI 1.6-3.3).

Disorders such as malignancy, peptic ulcer, and infection were more common in the anemic patients. However, the mortality risk in elderly anemic patients without obvious clinical disease was also increased to more than twice that of non anemic patients.

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In conclusion:

The mortality risk was increased in older persons with anemia if anemia was defined by the WHO criteria (the WHO criteria are appropriate for older persons).

Anemia in older patients is due to the disease and not aging, and that further investigation is warranted if an older person's Hb is below normal, even if no clinical disease is immediately apparent.

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Prevalence

The studies of prevalence of anemia among the elderly are notable for their extreme diversity (variability in the patient populations studied, countries in which the research was conducted, range of simple sizes, definition of anemia used, quality of the research and setting of care).

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Prevalence

Anemia is an increasingly common medical disorder in the elderly, affecting approximately 13% of people aged 70 and older.

The prevalence of anemia increases with age and this increase starts at the age of 65 and rises sharply after 80.

Am J Med 2004

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Prevalence

In addition to age, sex is a factor that has been shown to influence the prevalence of anemia in the elderly.

Anemia is generally more common in men than women perhaps because the Hb levels used to define anemia are tipically higher for men (42.8% 70-74y; 59.5% >85y)

JAGS 2003

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Prevalence

Before age 55, the prevalence of anemia is lower in men than in women (3% in men vs 6% in women aged 50-54). After this age, the trend is reversed (prevalence at 65y is 21% in men and 16% in women) (higher prevalence of underlying diseases in men).

(Olmsted County Study Minnesota, JAGS 2003)

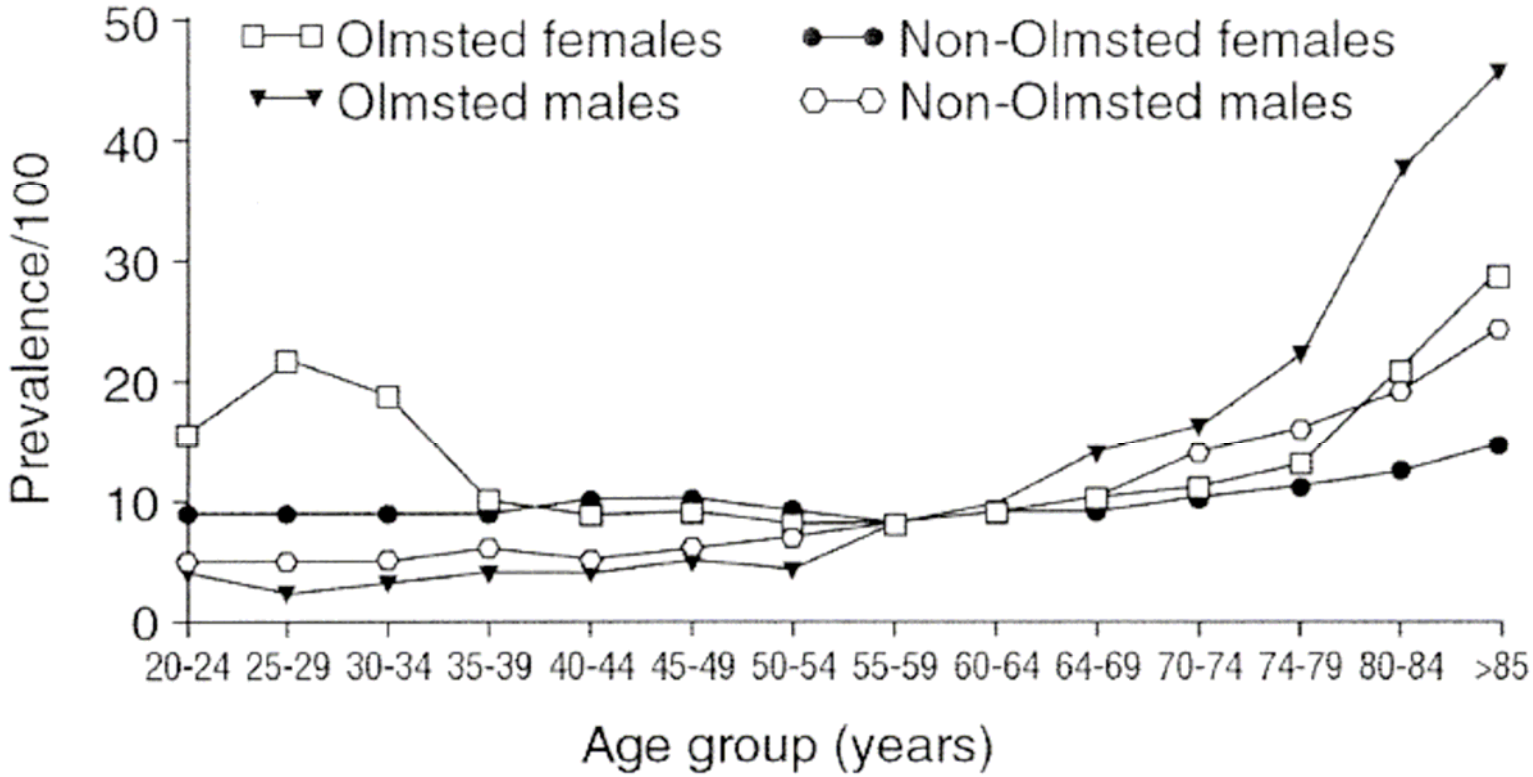

Figure 1. Prevalence of anemia in Olmsted County residents.[16]

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Prevalence

Using the WHO definition of anemia, 11% of men and 10.2% of women (≥65y) were anemic according to the NHANES III data set (Third US National Health an Nutrition Examination Survey).

Hematology, 2005

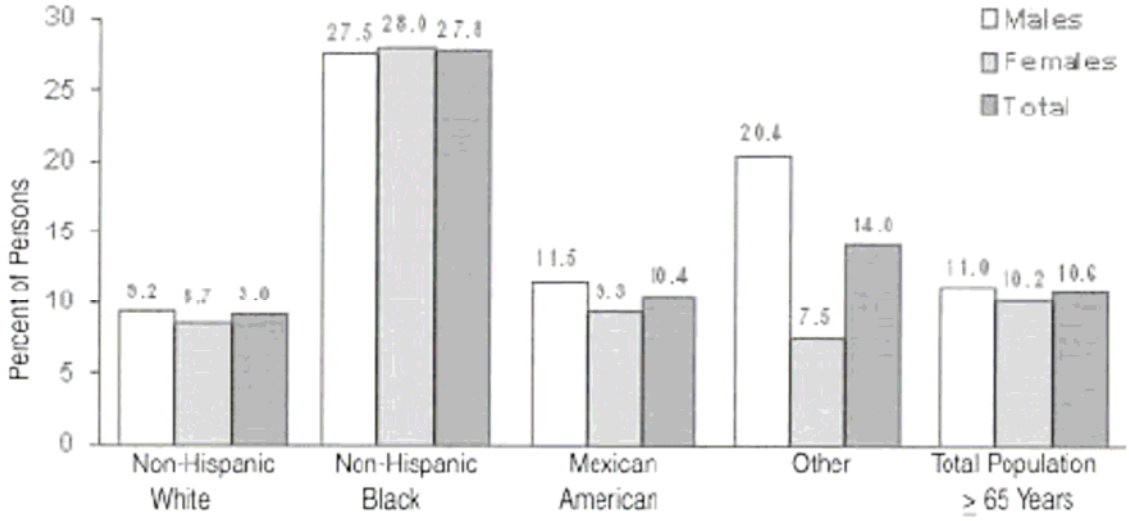

Figure 1. Percentage of persons age 65 and older who are anemic, by race/ethnicity and sex. Source: NHANES III, Phases I and II, 1988-1994: mobile examination (MEC) + home exam; sample excludes null and blank Hb values.

Hematology 2005

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Prevalence

Although the prevalence of anemia is greater in women than men aged <75, by age 75 male prevalence surpasses female prevalence by about 5 percentage points, a disparity that continues into upper age brackets (Third US National Health an Nutrition Examination Survey).

Hematology, 2005

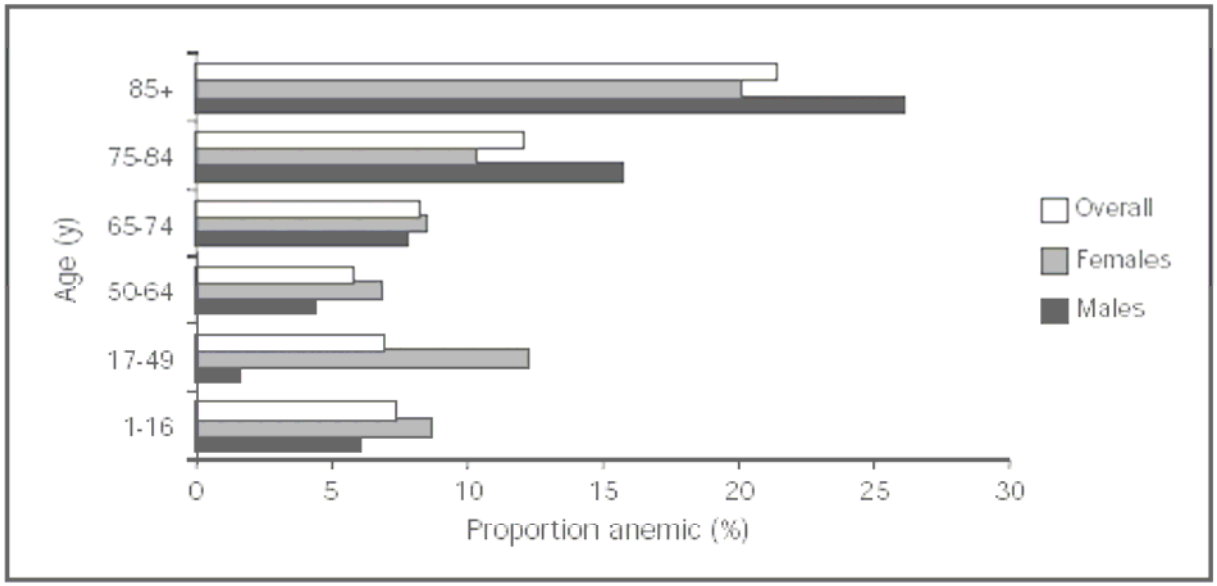

FIGURE 1. Prevalence of WHO-defined anemia (hemoglobin <13.0 g/dL for males and <12.0 g/dL for nonpregnant females) in the United States, by age and sex. SI conversion factor: to convert hemoglobin value to g/L, multiply by 10. NHANES III = Third US National Health and Nutrition Examination Survey; WHO = World Health Organization. Data from first 2 phases of NHANES III, 1988-1994.[7,8]

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Prevalence

The general prevalence of anemia in the population aged 65 and older varies greatly depending on residential status.

The prevalence is lower in community residents (2.9%-34% in men and 3.3%-25% in women) than in patients admitted to acute hospital wards or long-term care facilities (17.7%-61% in men and 8.4%-41% in women) (these patients are sicker than the general elderly population).

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Causes of anemia in the elderly: NHANES III

Type of Anemia	Percent
Blood Loss/Nutrition Related	34
Iron deficiency and iron with folate and/or B_{12} deficiency (blood loss/nutrition)	20
Folate and/or B_{12} deficiencies (nutrition)	15
Chronic Disease (EPO Deficiency)	32
CKD	8
ACD	20
CKD and ACD	4
Unexplained Anemia	34

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Causes

Table 1. Primary Causes of Anemia

Cause	Prevalence in the Acute Ward (%)[25]	Prevalence in Community-Based Outpatient Clinics (%)[2]
Chronic disease	35	17
Unexplained causes	17	36
Iron deficiency	15	8
Posthemorrhagic	7	—
Renal failure, liver, and endocrine disease	6.5	8
Myelodysplasia or acute leukemia	5.5	—
Chronic leukemia or lymphoma	5.5	—
Vitamin B_{12} or folate deficiency	5.5	—
Other hematological disease	3	8
Infection	—	23

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

MEDICAL PROGRESS

Anemia of Chronic Disease

Guenter Weiss, M.D., and Lawrence T. Goodnough, M.D.

N Engl J Med 2005;352:1011-23.

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Anemia of Chronic Disease

Anemia of chronic disease is the second most common anemia worldwide (iron deficiency) but it is the most common in elderly patients and in acute hospital wards or long-term care facilities .

It occurs in patients with acute or chronic immune activation. The condition has thus been termed “anemia of chronic inflammation”.

It was initially thought to be associated primarily with chronic disorders, infectious, inflammatory diseases, or cancer.

NEJM 2005

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Anemia of Chronic Disease

However, other observations have shown that this anemia can be seen in a variety of conditions, including severe trauma, heart disease, diabetes mellitus, and in those with acute or chronic immune activation.

→The severity of anemia generally correlates with the severity of the underlying disease.

NEJM 2005

Table 1. Underlying Causes of Anemia of Chronic Disease.

Associated Diseases	Estimated Prevalence*
	percent
Infections (acute and chronic)	18–95[8-10]
Viral infections, including human immunodeficiency virus infection	
Bacterial	
Parasitic	
Fungal	
Cancer†	30–77[9,12-14]
Hematologic	
Solid tumor	
Autoimmune	8–71[5,9,15,16]
Rheumatoid arthritis	
Systemic lupus erythematosus and connective-tissue diseases	
Vasculitis	
Sarcoidosis	
Inflammatory bowel disease	
Chronic rejection after solid-organ transplantation	8–70[17-19]
Chronic kidney disease and inflammation	23–50[20-22]

N Engl J Med 2005;352:1011-23.

Diseases Associated with Anemia of Chronic Disease

Acute infections	Malignancy
Chronic infections	Metastatic carcinoma
Tuberculosis	Hematologic malignancies
Infective endocarditis	Leukemia
Chronic urinary tract infection	Lymphoma
Chronic fungal infection	Myeloma
Chronic inflammatory disorders	Chronic renal insufficiency
Osteoarthritis	Hypothyroidism
Rheumatoid disease	Protein-energy malnutrition
Collagen vascular disease	Decubitus ulcer
Polymyalgia rheumatica	
Acute and chronic hepatitis	
Chronic bowel disease	

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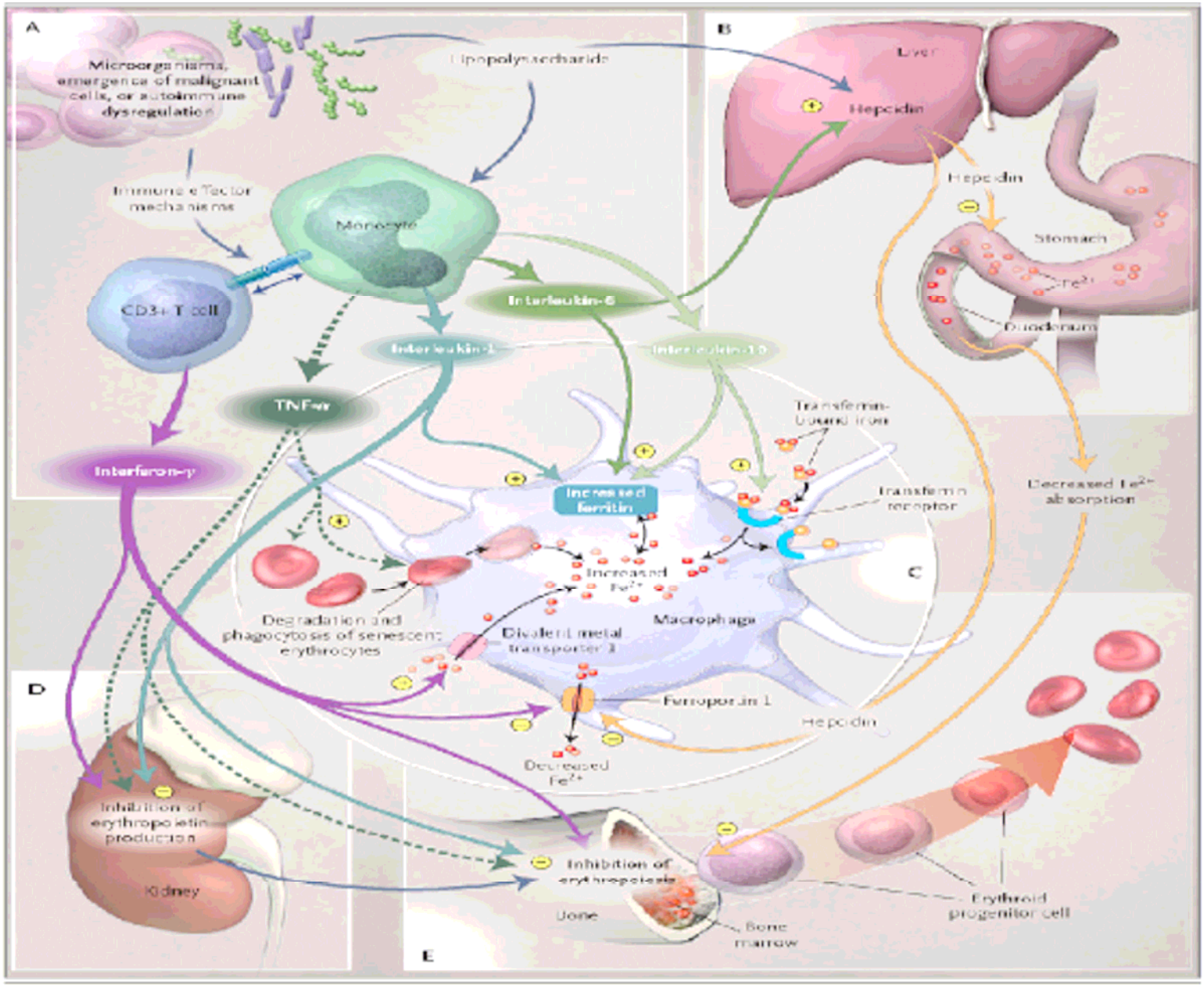
Pathophysiology

Aging itself is unlikely to be a direct cause of anemia, especially because data have shown that hemoglobin levels do not change significantly in healthy olders individuals aged between 60 and 98.

Nevertheless, experimental and clinical data have suggested that aging is associated with a progressive reduction in hematopoietic reserve, which makes older individuals more susceptible to developing anemia during hematopoietic stress.

JAGS, 2003



N Eng J Med 2005

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Pathophysiology

- **L'attivazione del sistema immunitario da parte dei linfociti T e dei macrofagi in risposta ad uno stimolo infettivo, infiammatorio o neoplastico, determina la liberazione delle citochine -INFγ, IL-1, IL-6 e TNFα- responsabili dell'anemia.**

Pathophysiological mechanism features are:

NEJM 2005

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Pathophysiology

1) Impaired erythropoiesis

proliferation and differentiation of erythroid precursors are impaired (inhibitory effects of cytokines) → inability of the morphologically normal marrow to increase erythropoirsis in response to anemia

→ anemia, decreased reticulocyte count

2) dysregulation of iron homeostasis

↑ iron storage within the RES with subsequent limitation of the availability of iron for erythroid progenitor cells (hypoferremia, hyperferritinemia)

↓ iron intestinal absorption by ↑ liver production hepcidin (hypoferremia)

↑ iron uptake and inhibition of iron recirculation from erythrophagocytosis in macrophages (hypoferremia)

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Pathophysiology

3) Decreased in Erythropoietin (EPO) production (by citokines) and reduced biologic activity of EPO in response to anemic hypoxia that lead to inhibition of erythropoiesis (decreased levels of circulating EPO, anemia)

4) decreased lifespan of red blood cells

increased erythrophagocytosis during inflammation leads to a decreased erythrocyte half-life (↓10-15%)

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Pathophysiology: anemia and renal insufficiency

Anemia of renal insufficiency is primarily due to a deficiency of endogenous erithropoietin, and it has been suggested that it develops when the glomerular filtration rate falls below 50% of the normal range. It has also been suggested that a shortened red blood cell lifespan and suppressed red blood cell production aggravate the mechanism underlying this form of anemia.

NEJM 2005

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Laboratory Evaluation

Anemia of chronic disease is hypoproliferative normochromic, normocytic anemia (MCV between 80 and 100 fL) of variable severity.

Many patients have mild anemia (Hb level: 10-11g/dl). However, more severe anemia (Hb level < 8g/dl) occurs in 20% of cases.

NEJM 2005

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Laboratory Evaluation

The absolute reticulocyte count is frequently low
(reticulocyte production is impaired and not enough to compensate for the decreased red blood cell county).

Low iron serum level is a necessary condition for diagnosis (cytokines ↓ iron concentration and limited availability of iron for erythroid cell).

→ An important aspect of ACD is the inability of the patient to mobilize and use iron effectively.

NEJM 2005

Laboratory Evaluation

In both CDA and iron deficiency anemia, the serum concentration of iron and transferrin saturation are reduced, reflecting absolute iron deficiency in iron deficiency anemia and hypoferremia due to acquisition of iron by RES in anemia of chronic disease with decreased levels of serum iron**.**

In iron deficiency anemia, transferrin saturation may be even low because serum concentrations of transferrin (the iron transporter) are increased, whereas transferrin levels remain normal or decreased in anemia of chronic disease.

NEJM 2005

Laboratory Evaluation

The soluble transferrin receptor is normal (↑ in iron deficiency anemia).

The serum level of ferritin is normal or increased (>100μg/L) marker of iron storage; reflecting ↑ storage and retention of iron within the RES and ↑ ferritin levels due to immune activation). (30 μg/L cutoff – ferritin is ↓ in iron-deficiency anemia).

NEJM 2005

Table 3. Serum Levels That Differentiate Anemia of Chronic Disease from Iron-Deficiency Anemia.*

Variable	Anemia of Chronic Disease	Iron-Deficiency Anemia	Both Conditions†
Iron	Reduced	Reduced	Reduced
Transferrin	Reduced to normal	Increased	Reduced
Transferrin saturation	Reduced	Reduced	Reduced
Ferritin	Normal to increased	Reduced	Reduced to normal
Soluble transferrin receptor	Normal	Increased	Normal to increased
Ratio of soluble transferrin receptor to log ferritin	Low (<1)	High (>2)	High (>2)
Cytokine levels	Increased	Normal	Increased

* Relative changes are given in relation to the respective normal values.
† Patients with both conditions include those with anemia of chronic disease and true iron deficiency.

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Laboratory Evaluation

The soluble transferrin receptor (s-TfR) is a truncated fragment of the membrane receptor that is increased in *iron deficiency*, when the availability of iron for erythropoiesis is low.

→Negli stati ferro carenziali ha una sensibilità maggiore rispetto ad altri parametri di laboratorio.

In contrast, levels of soluble trasferrin receptors in *anemia of chronic disease* are not significantly different from normal, because transferrin-receptor expression is negatively affected by inflammatory citokines.

NEJM 2005

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Laboratory Evaluation

The ratio of the concentration of soluble transferrin receptors to the log of the ferritin level (s-TfR/log ferritina) may also be helpful:

A ratio <1 (low) suggests anemia of chronic disease

A ratio >2 (high) suggests absolute iron deficiency coexisting with anemia of chronic disease (reale fabbisogno di ferro).

NEJM 2005

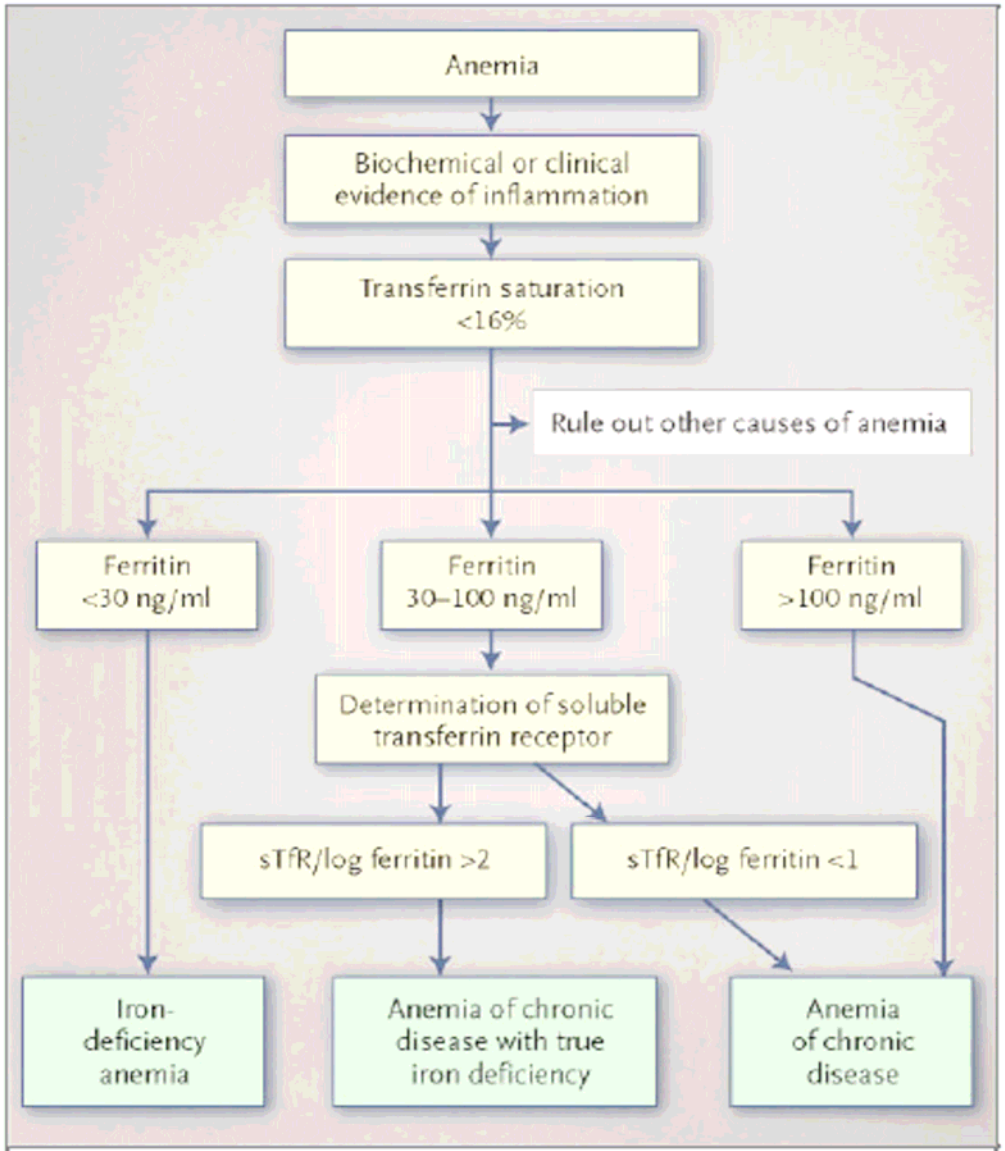

Figure 2. Algorithm for the Differential Diagnosis among Iron-Deficiency Anemia, Anemia of Chronic Disease, and Anemia of Chronic Disease with Iron Deficiency.

The abbreviation sTfR/log ferritin denotes the ratio of the concentration of soluble transferrin receptor to the log of the serum ferritin level in conventional units.

N Engl J Med 2005;352:1011-23.

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Treatment

The rationale for the treatment of anemia of chronic disease is based on two principles.

1) Anemia can be generally deleterious in itself, requiring a compensatory increase in cardiac output in order to maintain systemic oxygen delivery;

NEJM 2005

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Treatment

2) Anemia is associated with a poorer prognosis in a variety of conditions. Thus, moderate anemia warrants correction, expecially in patients older than 65y of age, those with additional risk factors (coronary artery disease, pulmonary disease, chronic kidney disease), or a combination of these factors.

In patients with renal failure who are receiving dialysis and in patients with cancer who are undergoing chemotherapy, correction of anemia up to hemoglobin levels of 12g/dl is associated with an improvement in the quality of life.

NEJM 2005

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Treatment Options

Table 4. Therapeutic Options for the Treatment of Patients with Anemia of Chronic Disease.

Treatment	Anemia of Chronic Disease	Anemia of Chronic Disease with True Iron Deficiency
Treatment of underlying disease	Yes	Yes
Transfusions*	Yes	Yes
Iron supplementation	No	Yes†
Erythropoietic agents	Yes‡	Yes, in patients who do not have a response to iron therapy

* This treatment is for the short-term correction of severe or life-threatening anemia. Potentially adverse immunomodulatory effects of blood transfusions are controversial.

† Although iron therapy is indicated for the correction of anemia of chronic disease in association with absolute iron deficiency, no data from prospective studies are available on the effects of iron therapy on the course of underlying chronic disease.

‡ Overcorrection of anemia (hemoglobin >12 g per deciliter) may be potentially harmful to patients; the clinical significance of erythropoietin-receptor expression on certain tumor cells needs to be investigated.

N Engl J Med 2005;352:1011-23.

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Treatment Options

When possible, treatment of the underlying disease is the therapeutic approach of choice for anemia of chronic disease.

In cases in which treating the underlying disease is not feasible, alternative strategies are necessary.

NEJM 2005

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Treatment: Transfusion (NEJM 2005)

Blood trasfusions are widely used as a rapid and effective therapeutic intervention. Trasfusions are particularly helpful in the context of either severe anemia (Hb <8.0g/dl) or life-threating anemia (Hb <6.5g/dl).

Blood trasfusion therapy has been associated with increased survival rates in anemic patients with myocardial infarction, but trasfusion itself has also been associated with multiorgan failure and increased mortality in patients who are in critical care. Whether blood trasfusions modulate the immune system, causing clinically relevant adverse effects, remains undetermined.

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Treatment: Transfusion (NEJM 2005)

It is important to note that existing guidelines for the management of anemia of chronic disease in patients with cancer or chronic kidney disease do not recommend long term blood transfusion therapy in their management algorithms because of the risks associated with long-term transfusion, such as iron overload and sensitization to HLA antigens that may occur in patients before renal transplantation.

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Treatment: Iron Therapy (NEJM 2005)

Iron therapy for patients with anemia of chronic disease is controversial.

Iron is an essential nutrient for proliferating microorganism, and the sequestration of iron from microorganism or tumor cells into the RES is believed to be a potentially effective defense strategy to inhibit the growth of pathogens.

In addition, iron therapy in a setting of long-term immune activation promotes the formation of highly toxic hydroxyl radicals that can cause tissue damage and endothelial dysfunction and increase risk of acute cardiovascular events.

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Treatment: Iron Therapy (NEJM 2005)

- On the other hand, iron therapy may confer benefit:

Absolute iron deficiency accompanying the anemia of chronic disease (these patients should receive supplemental iron therapy);

Functional iron deficiency that develops under conditions of intense erythropoiesis during therapy with erythropoietic agents. Parenteral iron has been demonstrated to enhance rates of response to therapy with erytropoietic agents in patients with cancer who are undergoing chemotherapy and in patients undergoing dialysis.

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Treatment: Iron Therapy (NEJM 2005)

To achieve and maintain the target Hb levels with erythropoietin, sufficient body iron stores are required. Supplemental iron should be administered, as needed, to maintain a transferrin saturation of ≥20%, and a serum ferritin level of ≥100 ng/ml.

However, iron therapy is currently not recommended for patients with anemia of chronic disease who have a high or normal ferritin level (above 100ng/ml), owing to possible adverse outcomes in this setting.

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Treatment: Erythropoietic Agents (NEJM 2005)

The therapeutic effect involves counteracting the antiproliferative effects of cytokines, along with the stimulation of iron uptake and heme biosynthesis in erythroid progenitor cells.

Erythropoietic agents for patients with anemia of chronic disease are currently approved for use by patients with cancer who are undergoing chemotherapy, patients with chronic kidney disease, and patients with HIV infection who are undergoing myelosuppressive therapy.

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Treatment: Erythropoietic Agents (NEJM 2005)

The percentage of patients with anemia of chronic disease who respond to therapy with erythropoietic agents is 25% in myelodysplastic syndromes, 80% in multiple myeloma, and up to 95% in chronic kidney disease.

- **Three erythropoietic agents are currently available: *epoietin alfa*, *epoietin beta*, *and darbepoietin alfa* which differ in terms of their pharmacologic compounding modifications, receptor-binding affinity, and serum half life.**

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Treatment: Erythropoietic Agents (NEJM 2005)

- Current findings indicate that for patients receiving erythropoietic agents, target Hb levels should be 11 to 12g/dl. Overcorrection of anemia to normal Hb levels and insufficient treatment have each been associated with unfavorable clinical course.
- Before the initiation of therapy with an erythropoietin agent, iron deficiency should be rouled out.

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Treatment: Erythropoietic Agents (NEJM 2005)

- For monitoring the response to erythropoietic agents, Hb levels should be determined after four weeks of therapy and at intervals of two to four weeks thereafter. If the Hb level increases by less 1 g/dl, the iron status should be reevaluated and iron supplementation considered.
- The dose of erythropoietic agents should be adjusted once the Hb concentration reaches 12g/dl.
- If no response is achieved after eight weeks of optimal dosage in the absence of iron deficiency, a patient is considered nonresponsive to erythopoietic agents.

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Treatment: Erythropoietic Agents (NEJM 2005)

- EPO is given in a starting dose of 100 to 150 U/Kg subcutaneously three times weekly along with supplemental oral iron.
- However, most clinicians use 30.000-40.000 U of EPO given once a week, a single dose which is numerically equivalent to a dose of 140 to 190 U/Kg three times per week for a 70 Kg person. This dose can be increased to 60.000 U if there is no response (ie, Hb rise <1g/dl) at four weeks.
- Darbepoetin is a newer formulation of erythropoietin which has a longer in vivo half-life than erythropoietin (500 μg every 2-3 weeks).

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Treatment: Erythropoietic Agents (NEJM 2005)

Although the positive short-term effects of therapy with erythropoietic agents on the correction of anemia and avoidance of blood transfusions are well documented, few data are available on possible effects on the course of underlying disease.

Erythropoietic recetors are found on several malignant cell lines, including mammary, ovarian, uterine, prostate, hepatocellular, and renal carcinomas. A recent study (Lancet 2003) investigating the effect of therapy with epoietin on the clinical course of patients with metastatic breast carcinoma was discontinued because of a trend toward higher mortality among patients receiving the drug.

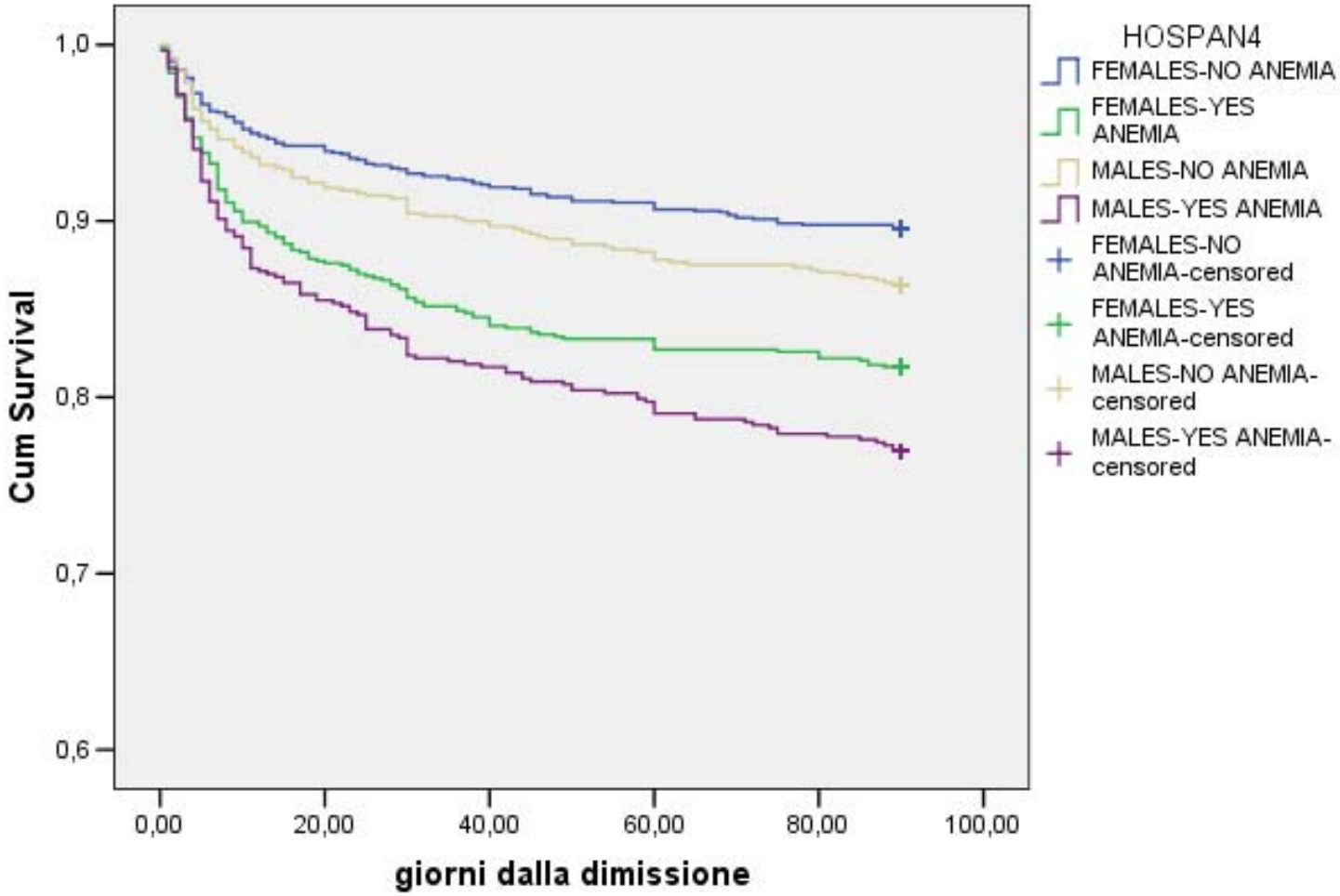
Conclusioni

1. Anemia in the elderly is an extremely common problem that is associated with increased mortality and poorer health-related quality of life.
2. It may represent a sign of serious underlying disease and may be itself a cause of dysfunction of multiple organ systems from chronic hypoxiemia.
3. Future research is needed to define the optimal Hb levels for health, to refine diagnostic testing to sort out the etiology of the unexplained anemias, and to evaluate rigorously therapies designed to augment erythropoiesis.

Prevalenza di anemia in anziani spedalizzati

	Femmine	Maschi	Totale
	N=2086	N=1294	N=3380
Anemia	464 (22,2)	215 (16,6)	679 (20,1)

Mortalità a tre mesi di una popolazione di pazienti anziani ospedalizzati e stratificati per valori di emoglobina (anemia) e sesso



Anemia and Recovery from Disability in Activities of Daily Living in Hospitalized Older Persons

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JAGS 54:632–636, 2006

OBJECTIVES: To evaluate the predictive value of hemoglobin levels upon hospital admission on recovery from activity of daily living (ADL) disability during hospital stay in older patients.

DESIGN: Longitudinal observational study.

SETTING: Geriatric and internal medicine acute care units.

PARTICIPANTS: Data are from 5,675 patients aged 65 and older enrolled in the Italian Group of Pharmacoepidemiology in the Elderly Study with ADL disability upon hospital admission.

MEASUREMENTS: ADL disability was defined as inability to perform or need for assistance in performing one or more ADLs. Recovery from ADL disability was defined as independence in ADLs upon hospital discharge. Anemia was defined according to the World Health Organization criteria. Sociodemographic and clinical characteristics were considered as potential confounders.

RESULTS: Mean age was 80.5 years; 57.7% of subjects were female. Prevalence of anemia was 46.8%. A total of 536 (9.4%) participants regained independence in all six ADLs at hospital discharge. Patients with anemia had a lower rate of recovery from ADL disability than those with normal hemoglobin levels (7.0% vs 11.6%; $P < .001$). Adjusted analyses confirmed that anemia was inversely associated with the likelihood of ADL recovery (odds ratio = 0.71, 95% confidence interval = 0.57–0.88). The probability of ADL recovery in anemic patients was higher at higher hemoglobin concentrations.

CONCLUSION: In older hospitalized patients, anemia is inversely associated with the likelihood of regaining ADL independence during a hospital stay. J Am Geriatr Soc 54:632–636, 2006.

EORTC Guidelines for the use of Erythropoetic Proteins in Anemic Patients with Cancer (Eur J Cancer 2007)

- Il trattamento con Eritropoietina va intrapreso per valori di Hb compresi tra 9 e 11 g/dl in base ai sintomi correlati, avendo come obiettivo il raggiungimento di valori di 12-13 g/dl o un miglioramento della sintomatologia.
- La dose raccomandata è di 30.000/40.000 UI settimanali (per eritropoietina beta e alfa) o 500 μg ogni 2-3 settimane (darbepoietina).
- La risposta alla terapia migliora se viene eseguita una integrazione di ferro ev. Alcuni autori raccomandano di mantenere la saturazione della transferrina > il 20% e la ferritina >100 ng/ml.
- L'unico fattore predittivo di risposta sembra essere un basso valore di eritropoietina sierica all'esordio.