Anemia: current concepts in workup and treatment

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Anemia: grading severity

<table>
<thead>
<tr>
<th>Classification</th>
<th>Hemoglobin (g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NCI</td>
</tr>
<tr>
<td>Mild (Grade 1)</td>
<td>10-WNL</td>
</tr>
<tr>
<td>Moderate (Grade 2)</td>
<td>8.0-10</td>
</tr>
<tr>
<td>Severe (Grade 3)</td>
<td>6.5-7.9</td>
</tr>
<tr>
<td>Life threatening (Grade 4)</td>
<td>&lt;6.5</td>
</tr>
</tbody>
</table>

NCI=National Cancer Institute; WHO=World Health Organization; WNL=within normal limits.


Anemia: a problem of precise definition

- Lower limit of normal (LLN):
  - 2.5% healthy adults below LLN
  - decline in LLN in elderly males
  - causes in elderly:
    - 1/3 nutritional
    - 1/3 CKD / inflam.
    - 1/3 ? (some MDS)

- other parameters:
  - MCHC = Hb/ hct
  - MCH = Hb/ RBC #

<table>
<thead>
<tr>
<th>Value</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/dL)</td>
<td>15.7 +/- 1.7</td>
<td>13.8 +/- 1.5</td>
</tr>
<tr>
<td>Hct (%)</td>
<td>46.0 +/- 4.0</td>
<td>46.0 +/- 4.0</td>
</tr>
<tr>
<td>RBC (mil/ul)</td>
<td>5.2 +/- 0.7</td>
<td>4.6 +/- 0.5</td>
</tr>
<tr>
<td>retic (%)</td>
<td>1.6 +/- 0.5</td>
<td>1.4 +/- 0.5</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>88.0 +/- 8.0</td>
<td>same</td>
</tr>
<tr>
<td>RDW (%)</td>
<td>13.1 +/- 1.4</td>
<td>same</td>
</tr>
</tbody>
</table>

NCI=National Cancer Institute; WHO=World Health Organization; WNL=within normal limits.
Workup of anemia

An algorithm based on complete blood count (CBC) parameters and clinical features

Anemia: severity and pace of change

- The degree of anemia and the degree of associated symptoms determine the need for urgent treatment (transfusions, etc.)
- The rapidity and degree of drop in hemoglobin (Hb) determine whether rapid inpatient or methodical outpatient evaluation is required
- In general, anemia due to:
  - RBC under-production develop over weeks to months
  - bleeding or hemolysis often occur rapidly over days to weeks

Anemia: initial workup

- Clinical evaluation:
  - obvious bleeding; drug/toxin exposure; chronic or acute illness, etc.
- Reticulocyte counts
  - suggest whether patient’s bone marrow is responding adequately to anemia
  - appropriately increased: RBC loss (bleeding or hemolysis) or response to therapy (iron, folate, or cobalamin replacement)
- Iron, transferrin saturation, ferritin, folate, and cobalamin levels
  - indicate adequacy of body stores of iron and vitamins required for hematopoiesis

High reticulocyte count

- bleeding:
  - clinically evident: site specific evaluation
  - clinically occult: most often GI: EGD, colonoscopy +/- SBFT +/- capsule EGD
- hemolysis:
  - HEME referral, but send below:
    - Coombs/ Direct Antiglobulin Test (DAT) & indirect antiglobulin test (IAT)
    - LDH & indirect bilirubin
    - peripheral blood smear
    - haptoglobin
    - urine hemosiderin
Low reticulocyte count

- **High MCV:**
  - B12, folate (RBC folate); PA; ileal dz; nitrous oxide rx; food cobalamin malabsorption
  - hx: drugs (hydroxyurea, MTX), EtOH

- **Low MCV:**
  - Fe; TSAT; ferritin (soluble transferrin R): menses, pregnancy; occult GI bleeding; occult GU; intravascular hemolysis
  - hx: chronic inflammation (ex: RA), EtOH/ Pb (sideroblastic)

- **Normal MCV:**
  - hx: acute bleeding; chronic inflammation; endocrine dysfunction (TSH +/- testosterone)

- **Multi-lineage cytopenia:** often HEME (BM bx)
  - hx/imaging: viral or drug induced; cirrhosis/ hypersplenism

Microcytic anemia

- **MCV < 80 fL (microcytic)**
  - **Reduced iron availability**
    - severe iron deficiency, anemia of inflammation, copper deficiency
  - **Reduced or abnormal globin chain production**
    - Thalassemias, unstable hemoglobinopathies, Hb H
  - **Reduced heme synthesis**
    - Congenital sideroblastic anemia, acquired sideroblastic anemia (MDS, lead, EtOH), toxins and drugs (INH)

Normocytic and macrocytic anemia

- **MCV > 100 fL (macrocytic)**
  - Stress erythropoiesis (reticulocytosis)
  - Liver disease
  - some MDS/ AML—M6
  - Megaloblastic maturation of RBCs:
    - Low Folate or cobalamin, Drugs that affect DNA synthesis (hydroxyurea & other anti-metabolites)

- **MCV 80-100 fL (normocytic)**
  - Bone marrow failure states
  - Acute bleeding
  - Underproduction of erythropoietin (renal failure); inflammation; deficient growth factors (T4, testosterone)
  - Low O2 affinity Hb

RBC Morphology

- normal, hypochromia, elliptocytes, target cells (in hypothyroidism), tear drops, sRBCs, immature WBCs

Blood smear evaluation

- nucleated RBC: stressed BM (hemolysis; myelophthisis)
- RBC size (MCV algorithm)
- RBC color:
  - polychromasia (RNA—retic); hypochromic (impaired Hb production); basophilic stippling (precipitated ribosomes: thalassemias, lead poisoning); no central pallor (AIHA; HS); RBC ghost (severe hemolysis—Clostridial sepsis)
- RBC shape:
  - microspherocytes (AIHA; HS); elliptocytes (HE); RBC fragments: schistocytes (TTP; HUS; DIC; mechanical (cor valve)); blister/bite cells (G6PD defic.); target cells (excess RBC membrane: Hb C; liver dz); teardrop cells (myelophthisic); sickle (Hb SS etc.)
- RBC inclusions:
  - infectious (malaria; babesia); Heinz body (ppt Hb: G6PD defic.); Howell-Jolly body (nuclear remnant—post-splenectomy)
**Definition:**
- shortened RBC survival; normal = 120 d. (shortened: t½ < 100 d.)
- 5 x increased production possible (retic 0.5 – 1.5 %; absolute retic 25-75,000/μL)

**Intrinsic vs. extrinsic:**
- **Intrinsic:** RBCs have no nucleus or RNA or ribosomes SO must use glycolysis/pentose phosphate shunt to generate ATP, 2,3 BPG (O2 affinity) & reducing capacity (glutathione, NADPH) vs. oxidant injury
  - require intact RBC membrane components (acquired PIG-A mutation: PNH; cytoskeleton) and Hb (Hb-opathies; thalassemias)
- **Extrinsic:** antibody-mediated; microangiopathic; infectious; vascular/ cor valve; trauma; burns; EtOH

**Intravascular vs. extravascular:**
- **Intravascular:** considerable structural damage to RBC membrane
- **Extravascular:** primarily spleen—phagocytosis of damaged/senescent RBCs

**Evidence for hemolytic anemia**
- **↑ lactate dehydrogenase (LDH):**
  - LD 1,2 isoforms
- **↑ total bilirubin:**
  - microsomal enzyme degraded Hb
- **↓ haptoglobin (<25 mg/dL):**
  - free Hb bound to haptoglobin and cleared by liver
- **free plasma Hb; Hb-uria**
- **hemosiderinuria:**
  - Hb dimers taken up by renal tubules then sloughed off into urine
- **brown serum:**
  - released Hb in serum oxidized to met-Hb (ABO incompatibility)

**Hemolytic Anemia: Hemolytic Anemia: smear clues**
- **Spherocytes**
  - Implies loss of membrane
  - Inherited or acquired (antibody-mediated)
- **Schistocytes**
  - Fragmentation hemolysis
  - DIC, TTP/HUS, parasites (eg, malaria), and bacteria (clostridium)
- **Bite cells**
  - Imply oxidant stress hemolysis
  - Heinz body preparation can detect oxidized RBC proteins
  - Oxidant stress produces met-hemoglobin
  - Lidocaine or dapsone can cause oxidant hemolysis
  - Stop treatment and give methylene blue or ascorbic acid

**Immune hemolysis: Coombs / Antiglobulin tests**
- **Direct antiglobulin test (DAT)**
  - pt RBCs screen for IgG or C3
  - Hemolytic Disease of the Newborn (HDN)
  - AIHA
  - drug-induced IHA
  - Delayed hemolytic transfusion reaction (DHTFR)
- **Indirect antiglobulin test (IAT)**
  - pt serum, test RBCs
  - compatibility testing

**Auto-immune hemolytic anemia (AIHA)**
- **Warm type:** ± IgG, C3; 57% IAT +; usually Rh antigen
  - Cold agglutinin: C3 only; active <30 C; usually anti-i, or I
  - Parasymal cold hemoglobinuria: C3 along; biphasic; anti-P (Donath-Landsteiner antibody)
Hemolytic anemia: specific tests

- **Direct Coombs (DAT) positive:**
  - anti-IgG: WAIHA; DHTR
  - anti-C3: cold type AIHA (anti-I, i)
  - Eluate testing (specificity of auto-Ab); differential absorption (allo-antibody identification)
  - High sensitivity Coombs (200-500 IgG/ RBC — 5-10x lower)

- **Direct Coombs negative:**
  - osmotic fragility test (HS, HE, HPP)
  - CD55/CD59 flow cytometry (PNH)
  - isopropanol instability test: unstable Hb
  - Hb electrophoresis: sickle syndromes; B thalassemia
  - alpha globin gene copy #: alpha globin mutations: alpha thal
  - O2 p50 dissociation curve: high/ low O2 affinity Hb
  - thick smear: malaria

Anemia of inflammation

- Low serum iron levels (Fe) and total iron binding capacity (TIBC) with low transferrin saturation and elevated ferritin levels (unlike pure iron deficiency)

- In inflammatory states, cytokines increase serum ferritin levels by as much as 5 to 10 fold.
  - If serum ferritin levels divided by 5 are < 20, clinicians should suspect concomitant iron deficiency in patients who have inflammatory states.

Hepcidin: a critical iron regulator

- Several regulators of body Fe have been identified:
  - HFE-1
  - transmembrane transporters (DMT-1, duodenal cytochrome b, ferroportin-1, hephaestin, TrR 2)
  - regulatory: hepcidin, hemojuvelin

- Hepcidin levels are high with inflammation and low with iron overload states

- Hepcidin mutations can potentiate iron overload with HFE mutations and cause juvenile hemochromatosis
  - HFE KO mice have low hepcidin

- Hepcidin binds ferroportin, causing decreased Fe exit from the cell (Grave T. Science. 10-28-04)
  - in GI tract, causes decreased Fe absorption
  - in other cells, decreased Fe for transport to BM
**Anemia of inflammation**

- Inflammation can contribute to anemia:
  - Increased:
    - Erythrocyte sedimentation rate
  - Levels of acute phase reactants:
    - Fibrinogen, haptoglobin, and C-reactive protein
  - Underproduction of erythropoietin (EPO)
  - Decreased responsiveness to erythroid progenitor cells to EPO
  - Blocked iron transport from macrophage storage pools to maturing erythroid cells

**Anemia of cancer**

- A special case or a subset of anemia of inflammation

**Anemia: Cancer Patients**

- Common occurrence, especially in patients receiving cytotoxic chemotherapy
- Dependent on tumor type and chemotherapy regimen
- Marker of worse prognosis
- May contribute to lower efficacy of radiation
- Leads to decreased quality of life

**Incidence of Anemia in Cancer Patients**

- Groopman and Itri. J Natl Cancer Inst. 1999;91:1616-1634. 11,000 pt; 120 studies; 1990-1996; systematic review
Anemia: Association With Cancer Survival

<table>
<thead>
<tr>
<th>Cancer</th>
<th>↑ Relative Risk of Death (%) Associated With Anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>19</td>
</tr>
<tr>
<td>Head and neck</td>
<td>75</td>
</tr>
<tr>
<td>Prostate</td>
<td>47</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>67</td>
</tr>
<tr>
<td>Overall</td>
<td>65</td>
</tr>
</tbody>
</table>

Retrospective analysis—60 studies, correlating anemia and survival in cancer patients from 1970-2000


Cancer-Related Anemias: Initial Evaluation

- Patient should be assessed for nutritional deficiencies
  - Iron (total iron-binding capacity, serum iron, ferritin)
  - Folate (serum homocysteine)
  - Vitamin B₁₂ (serum methylmalonic acid)
- Treatment must be individualized
  - Correct nutritional and metabolic deficiencies
  - Treat underlying infections or inflammatory processes
  - Manage hemolytic diseases, occult blood loss

NCCN. Available at: www.nccn.org.

Anemia: Association With Cancer Survival

Treatment of Anemia

RBC transfusion vs. erythropoiesis stimulating agents (ESAs)

Treatment of Anemia

<table>
<thead>
<tr>
<th>Up to 1980</th>
<th>1980s</th>
<th>1990s</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red blood cell transfusions used empirically to keep Hgb at ≥10g/dL</td>
<td>Blood supply compromised, Focus on severe anemia only (Hgb ≤8 g/dL)</td>
<td>Erythropoetin available, ↓ transfusion frequency, Focus remains on severe anemia</td>
<td>Focus on mild-to-moderate anemia</td>
</tr>
<tr>
<td>Erythropoetin ↑ QOL</td>
<td>Erythropoetin dosed once weekly</td>
<td>Darbepoetin alfa introduced</td>
<td></td>
</tr>
</tbody>
</table>

Hgb = hemoglobin; QOL = quality of life.

Blood products

- **RBC**
  - pRBC: 250-300 cc; store <42 days
  - WBC-depleted, deglycerolized, frozen (rare blood type; IgA deficiency); washed (PNH)
- WBC-depleted RBC
  - 5x10^-8 WBC/unit—filter 2-3 log depletion
  - Less fever, HLA allo-immunization (1/3), CMV
- FFP (all clotting factors, etc.)
  - solvent-detergent treated; cryoprecipitate-poor
- Cryoprecipitate (I, VIII, XIII, vW ag)
- Platelets
  - Single donor (SD)= 6-10 random donor (RD) units
  - WBC contamination: SD=5x10^-8; RD=5x10^-7

Risks of blood transfusion

- **Infection**
  - Viral (HBV, HCV: 10/mil.; HIV, HAV: 1/mil.)
  - Bacterial (RBC: 2/mil.; platelet: 100/mil.)
- **Acute hemolytic reactions** (ABO: 4/mil.)
- **Delayed hemolytic reactions (DHR)**
  - 1000/mil. (ex.:Rh—cde, Kell, Duffy, Kidd, MNSs)
- **Transfusion related acute lung injury (TRALI)**
  - 1/5000: ARDS type
- **Transfusion related graft versus host disease (tGVHD)—irradiated blood products to prevent**
  - BMT: heme malignancy under rx; congenital immunodeficiency; organ transplant; donor is 1st, 2nd or 3rd degree relative

additional drawbacks to pRBC transfusion

- inconvenience and cost
  - infusion centers/ hospital; RN time
- potential allergic reactions
  - buffy coat/ proteins
- iron overload with chronic transfusions
  - 50-100 units
- blood supply limited (particularly O -)
- patient refusal of transfusion (Jehovah’s witness)
- transient benefit
  - BM failure often 1-2 units/ week


Physiology of Red Blood Cell Development

The erythropoiesis stimulating agents (ESAs): darbepoetin (Aranesp) and erythropoietin (Procrit; Epogen)

Epoetin alfa  Aranesp™

N-linked carbohydrate chains  Sialic acids
Static acid  Static acid
Molecular weight (daltons)  38,400  37,100
Carbohydrate  49%  51%


EPO Receptor 1  EPO Receptor 2
Carbohydrate chains with sialic acids

The efficacy of erythropoiesis stimulating agents (ESAs) in the treatment of chemo-induced anemia

rHuEPO and transfusion needs in chemotherapy induced anemia (CIA)

QOL in epo rx of CIA: improves with increasing Hb

Overall HRQOL LASA Score (mm)

Demetri  Glaspy

Combined Estimate
Effect of increasing Hb on transfusions and QOL in darbopoietin-treated patients

- Based on repeated measures LR modeling.
- Based on repeated measures ANOVA.

Note: Hb target range (blue box and white dotted line) per NCCN guidelines (Sabbatini et al., 2004), ASH/ASCO guidelines (Rizzo et al., 2002), and prescribing information for darbepoetin alfa are indicated.


Risks of ESAs in treating anemia

- Hypertension
  - rare; mainly in dialysis pts
- Thrombosis
  - meta-analysis: RR = 1.67 (borderline p value—225 RCT, 9307 pt; mainly a meta)
- Pure RBC aplasia
  - rare; seen in dialysis pts, epo (particularly Eprex); recently darbo
- Impaired survival?
  - controversial; mainly with high Hgb; only a few trials in chemo-induced anemia (CIA); worse with anemia of cancer (AoC)

Summary of Venous Thromboembolism (VTE) Data From Published Systematic Reviews

<table>
<thead>
<tr>
<th>VTE</th>
<th>RR/HR</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cochrane (all cancer patients)</td>
<td>1.67 RR</td>
<td>1.35 – 2.06</td>
</tr>
<tr>
<td>AHRQ*</td>
<td>1.68 RR</td>
<td>1.36 – 2.08</td>
</tr>
</tbody>
</table>

Absolute Risk | NNH* |
<table>
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<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>2%</td>
<td>75</td>
</tr>
<tr>
<td>5%</td>
<td>30</td>
</tr>
</tbody>
</table>

* The adverse event has always been noted in the ESA prescribing information.
* Overall, the incidence of thrombotic events was 6.2% for Aranesp® and 4.1% for placebo (AHRQ).

AHRQ: Agency for Healthcare Research and Quality.

NNH: Number needed to harm.

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Summary of Venous Thromboembolism (VTE) Data From Published Systematic Reviews
Randomized, Controlled Trials with Decreased Survival and/or Decreased Locoregional Control

<table>
<thead>
<tr>
<th>Study / Tumor / Substudy</th>
<th>Hemoglobin Target</th>
<th>Achieved Hemoglobin (Median 21 SD)</th>
<th>Primary Endpoint</th>
<th>Adverse Outcome for ESA-Containing Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer Study 1, Chemotherapy</td>
<td>13.1 g/dL</td>
<td>12.0–13.8 g/dL</td>
<td>Decreased 3 yr. relapse-free survival</td>
<td>Hemoglobin response not available</td>
</tr>
<tr>
<td>Cancer Study 2, Chemotherapy</td>
<td>12.5 g/dL, 13.7 g/dL</td>
<td>12.5–13.0 g/dL</td>
<td>Decreased overall survival</td>
<td>Hemoglobin target not available</td>
</tr>
<tr>
<td>Cancer Study 3, Lymphoid malignancy</td>
<td>13.5 g/dL</td>
<td>13.0–13.9 g/dL</td>
<td>Decreased overall survival</td>
<td>Hemoglobin target not available</td>
</tr>
<tr>
<td>Cancer Study 4, Cervical Cancer</td>
<td>12.7 g/dL</td>
<td>12.1–13.3 g/dL</td>
<td>Decreased overall survival</td>
<td>Hemoglobin target not available</td>
</tr>
<tr>
<td>Cancer Study 5, Head and neck cancer</td>
<td>12.9 g/dL</td>
<td>12.2–13.3 g/dL</td>
<td>Decreased overall survival</td>
<td>Hemoglobin target not available</td>
</tr>
<tr>
<td>Cancer Study 6, Head and neck cancer</td>
<td>12.7 g/dL</td>
<td>12.0–13.3 g/dL</td>
<td>Decreased overall survival</td>
<td>Hemoglobin target not available</td>
</tr>
<tr>
<td>Cancer Study 7, Non-small cell lung cancer</td>
<td>12.9 g/dL</td>
<td>12.2–13.3 g/dL</td>
<td>Decreased overall survival</td>
<td>Hemoglobin target not available</td>
</tr>
</tbody>
</table>

Cochrane Meta-Analysis of Controlled Clinical Trials Looking at Overall Survival (Bohlius et al)

- This meta-analysis includes BEST, ENHANCE and Wright et al studies
- OR 1.08 (95% CI 0.99, 1.18) (42 trials and 8187 patients)

Summary of Overall Survival by Target Hemoglobin Stopping Level (AHRQ)

<table>
<thead>
<tr>
<th>Target stop hemoglobin (g/dL)</th>
<th>Relative Risk (RR)</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤12</td>
<td>Not estimable</td>
<td>Not available</td>
</tr>
<tr>
<td>&gt;12 – ≤13</td>
<td>0.91</td>
<td>0.47 – 1.78</td>
</tr>
<tr>
<td>&gt;13 – ≤14</td>
<td>1.16</td>
<td>1.00 – 1.35</td>
</tr>
<tr>
<td>&gt;14 – ≤15</td>
<td>1.03</td>
<td>0.90 – 1.19</td>
</tr>
<tr>
<td>&gt;15 – ≤16</td>
<td>1.67</td>
<td>1.13 – 2.48</td>
</tr>
</tbody>
</table>

ESA treatment and survival

- worse in anemia of cancer (AoC); no effect in chemo-induced anemia (CIA)—epo meta-analysis HR = 1.08 (NS) (Bohlius.JNCI. 5/06) not seen with darbo (JCO 10-1-05)
- epoR expression in some CA—possible stimulus to CA progression; questionable clinical relevance and accuracy of in-vitro assessment, but provocative
- increased death with higher Hgb in chronic kidney disease (CKD): CHOIR & meta-analysis of 9 RCT in ESRD, 5143 pt. (Lancet 2.3-4/05)
**ESA treatment: summary**

- Both epo (P) and darbo (A) have demonstrated efficacy in increasing hemoglobin, decreasing transfusions, and improving quality of life.
- Extended dosing intervals of darbo (A), and possibly epo (P), maintain efficacy and allow synchronization with chemo treatments.
- Parenteral iron supplementation appears to improve response to epo (P) rx.
- Side effects are rare, but possible compromised survival in certain situations (RT alone?; high Hb targets?; epoR in CA?; anemia of cancer!).

**Anemia workup and treatment summary**

- The severity and pace of Hb fall dictates the location and rapidity of workup.
- The initial CBC provides guidance for the focus of additional workup (other WBC/platelet abnormalities) and MCV (low, nl, high).
- Primary care workup involves clinical evaluation for bleeding, other acute illnesses or change in chronic conditions, and drug/toxin exposures AND a limited additional blood test evaluation (retic count; Fe, TSAT, ferritin; B12; folate).
- HEME referrals are clearly indicated for multi-lineage abnormalities (WBC/platelet # as well), unexplained underproduction anemias and suspected hemolytic anemias.
- Both RBC transfusions and erythropoiesis stimulating agent (ESA) rx have potential significant risks that should be considered and discussed with the patient.

**Patient’s functional status: a critical component of evaluating cancer therapy**

**Performance status scales**

Correspondence between ECOG and Karnofsky scales

<table>
<thead>
<tr>
<th>ECOG</th>
<th>Karnofsky %</th>
<th>Performance status</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>Normal activity; no special care is needed</td>
</tr>
<tr>
<td>1</td>
<td>80</td>
<td>Most patients work; able to live at home; could be certain degree of assistance; needs occasional supervision; unable to do strenuous activity; neurologic disease may be present</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>In bed &lt;50% of time; may be unable to work; able to dress; a varying amount of assistance needed; can complete daily activities</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>In bed &gt;50% of time; unable to walk; requires assistance for most personal needs; may be hospitalized or institutionalized; inability to carry on normal activity</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>100% bedridden; unable to carry on normal activity; may be institutionalized; senile dementia or delirium may be present</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>Dead; unable to carry on normal activity; generally unconscious.</td>
</tr>
</tbody>
</table>

**THANK YOU**
**Anemia: QOL in CA Patients**

- Fatigue is the most prevalent symptom reported by cancer patients
  - Patients report that fatigue has more impact on daily living than does nausea, depression, or pain
- Patients more concerned about gaining relief from fatigue; oncologists more concerned about treating pain
- QOL improves with every gram rise in hemoglobin concentration (greatest gain: 11 to 12 g/dL)

**Possible Mechanisms of Decreased Survival by Anemia**

- **Effects on the tumor**
  - Increased angiogenesis
  - Decreased p53
  - Resistance to apoptosis
- **Effects on the treatment**
  - Radiation therapy - oxygen radicals
  - Chemotherapy - oxygen radicals and resistance mutations
- **Effects on the host**
  - Reduced tolerance of therapy
  - Reduced QOL
  - Reduced immune function

QOL = quality of life.