



# Anemia in Surgical Patients

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# National Anemia Action Council

[www.anemia.org](http://www.anemia.org)

*NAAC is a 501(c)(3) nonprofit organization*

# NAAC Mission



The National Anemia Action Council, Inc. (NAAC) is dedicated to raising the awareness of health care professionals and the public regarding the prevalence, symptoms, consequences, and treatment options of anemia.

*NAAC is a 501(c)(3) nonprofit organization*

# NAAC's Online Resources for Medical Professionals



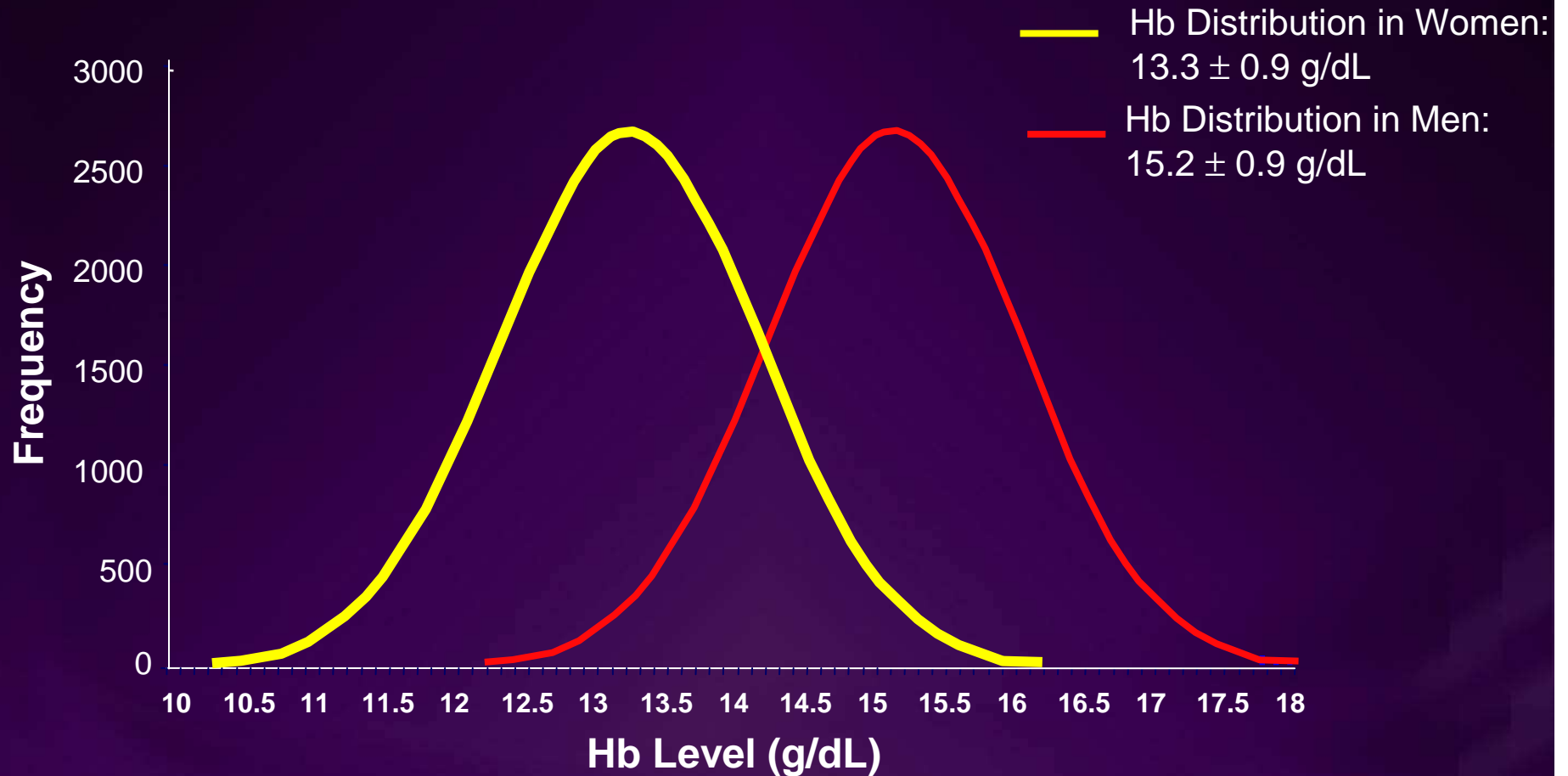
- Research Reviews - Recent clinical trials reviewed
- Ask the Expert - Your anemia questions answered
- Monograph - In-office handbook on anemia
- Feature Articles - Anemia related news and research
- Anemia Alert - Free monthly e-newsletter
- Slide Sets - Educational presentations about anemia
- We have materials for your patients too!

# Key Points



- Anemia is common among surgical patients, both pre- and postoperatively
- Preoperative anemia is often unrecognized unless hemoglobin/hematocrit (Hb/Hct) are measured prior to planned surgery
- Anemia in surgical patients has been linked to increased postoperative morbidity and mortality, and decreased quality of life
- Treatment of anemia in surgical patients can improve healthcare outcomes

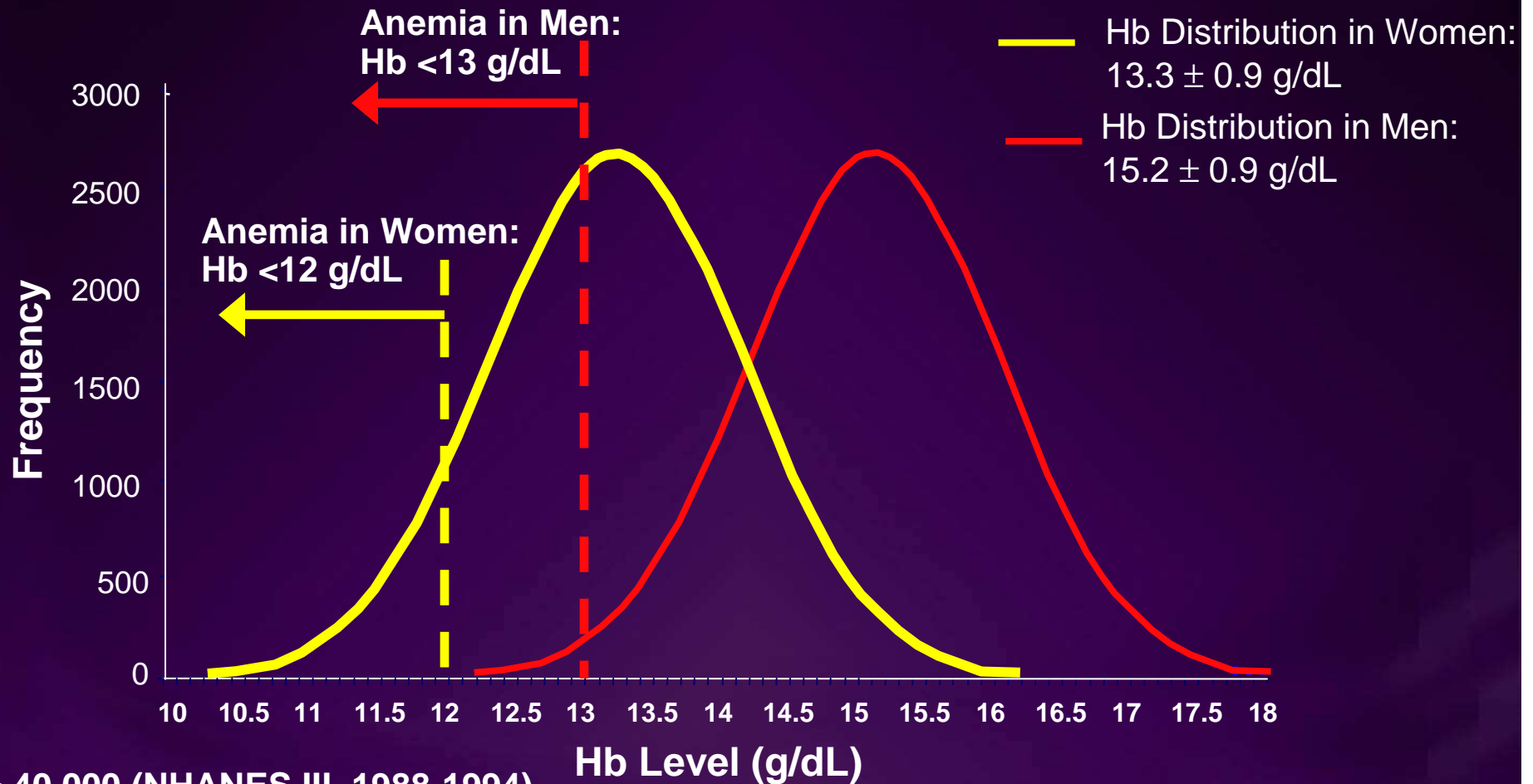
# Hemoglobin (Hb) Distribution in the General Population



**N = 40,000 (NHANES III, 1988-1994)**

Dallman PR, et al. In: *Iron Nutrition in Health and Disease*. London, UK: John Libbey & Co; 1996:65-74.

# WHO Definition of Anemia vs. Hb Distribution in General Population



N = 40,000 (NHANES III, 1988-1994)

World Health Organization. Geneva, Switzerland; 2001.

Dallman PR, et al. In: *Iron Nutrition in Health and Disease*. London, UK: John Libbey & Co; 1996:65-74.

# Laboratory Reference Ranges



| Parameter                           | Male        | Female      |
|-------------------------------------|-------------|-------------|
| Hb (g/dL)                           | 14.0 – 17.4 | 12.3 – 15.3 |
| Hct (%)                             | 41.5 – 50.4 | 36.0 – 45.0 |
| RBC count ( $10^6/\mu\text{L}$ )    | 4.5 – 5.9   | 4.5 – 5.1   |
| Reticulocyte count (% of RBC count) | 0.5 – 2.5   |             |
| Mean corpuscular volume (fL)        | 80 – 96     |             |
| Mean corpuscular Hb (MCH) (pg)      | 27.5 – 33.2 |             |
| MCH concentration (g/dL)            | 33.4 – 35.5 |             |

Hb = hemoglobin; Hct = hematocrit; RBC = red blood cell

Perkins S. In: Lee G, et al, eds. *Wintrobe's Clinical Hematology*. Vol 2. 10th ed. Baltimore, Md: Lippincott, Williams & Wilkins; 1998:2738.

# Anemia Signs and Symptoms



## Central nervous system

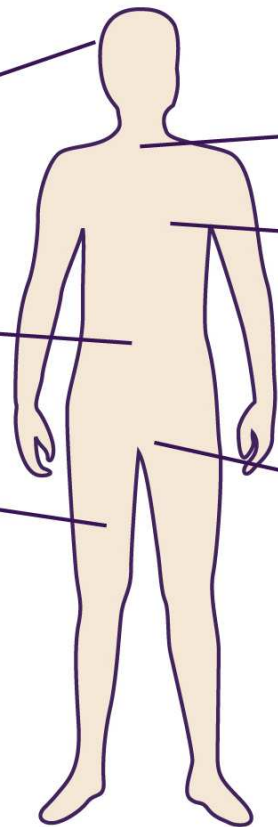
- Fatigue
- Depression
- Impaired cognitive function

## Gastrointestinal system

- Anorexia
- Nausea

## Vascular system

- Low skin temperature
- Pallor of skin, mucous membranes, and conjunctivae



## Immune system

- Impaired T-cell and macrophage function

## Cardiorespiratory system

- Exertional dyspnea
- Tachycardia, palpitations
- Cardiac enlargement, hypertrophy
- Increased pulse pressure, systolic ejection murmur
- Risk of cardiac failure

## Genital Tract

- Menstrual problems
- Loss of libido

Adapted from Ludwig H, et al. *Semin Oncol.* 2001;28(suppl 8):7-14.

# Perioperative Anemia Is Common in Surgical Patients



- Preoperative anemia prevalence: 34%<sup>1</sup>-56%<sup>2</sup>
- Preoperative anemia is often unrecognized unless Hb/Hct are measured prior to planned operation
- Postoperative anemia prevalence: 84%<sup>1</sup>-90%<sup>2</sup>

1. Clemens J, et al. *Surgery*. 1994;115:510-515.  
2. Dunne J, et al. *J Surg Res*. 2002;102:237-244.

# Multiple Factors Contribute to Anemia in Surgical Patients



- **Preoperative anemia<sup>1,2</sup>**
  - Acute or chronic blood loss
  - Iron deficiency
  - Renal insufficiency
  - Malignancy or chronic disease
  - Occult gastrointestinal (GI) bleeding
  - Reduced red blood cell (RBC) life span
- **Postoperative anemia**
  - Diminished erythropoiesis during early recovery<sup>1</sup>
  - Frequent phlebotomies<sup>2</sup>
  - Untreated bleeding episodes<sup>2</sup>

1. Kuller A, et al. *Anaesthetist*. 2002;50:73-86.

2. Eckardt KU. *Wien Klin Wochenschr*. 2001;113:84-89.

# Anemia During Early Postoperative Recovery



- Similar to anemia of chronic disease<sup>1,2</sup>
- Linked to high levels of inflammatory cytokines<sup>1,2</sup>
- Mechanisms:<sup>2</sup>
  - Erythropoietin response is blunted
  - Iron availability for erythropoiesis is reduced
  - Cytokines directly inhibit RBC formation

1. Sesti F, et al. *Gynecol Obstet Invest.* 2002;54:1-5.

2. von Ahsen N, et al. *Crit Care Med.* 1999;27:2630-2639.

# Predictors of Susceptibility to Perioperative Anemia



- African ancestry<sup>1</sup>
- Lower preoperative
- Female gender<sup>1,2</sup>
- Smaller body size<sup>2</sup>

1. Clemens J, et al. *Surgery*. 1994;115:510-515.

2. DeFoe G, et al. *Ann Thorac Surg*. 2001;71:769-776.

# Noncardiac Surgery Patients



## Anemia Linked to Increased Morbidity and Mortality

- **Preoperative anemia**
  - Increased risk of death,<sup>1-3</sup> particularly in patients with CVD<sup>2</sup>
  - Increased risk of need for blood transfusion<sup>4,5</sup>
  - Prolonged hospitalization<sup>3,4</sup>
- **Postoperative anemia**
  - Increased risk of cardiac events<sup>6,7</sup>
  - Increased risk of pneumonia<sup>5</sup>
  - Increased risk of postoperative delirium<sup>8</sup>

1. Carson JL, et al. *Lancet*. 1988;1(8588):727-729.

2. Carson JL, et al. *Lancet*. 1996;348:1055-1060.

3. Gruson KI, et al. *J Orthop Trauma*. 2002;16:39-44.

4. Dunne JR, et al. *J Surg Res*. 2002;102:237-244.

5. Faris PM, et al. *Orthopedics*. 1999;22(suppl 1):s135-s140.

6. Nelson AH, et al. *Crit Care Med*. 1993;21:860-866.

7. Hogue CW, et al. *Transfusion*. 1998;38:924-931.

8. Marcantonio ER, et al. *Am J Med*. 1998;105:380-384.

# Cardiac Surgery Patients



## Anemia Linked to Increased Morbidity and Mortality

- **After cardiac surgery<sup>1</sup>**
  - Increased risk of death
  - Increased risk of organ dysfunction
  - Increased risk of infection
  - Prolonged mechanical ventilation
  - Prolonged ICU stay
- **Decreased Hct during bypass surgery<sup>2</sup>**
  - Greater risk of in-hospital mortality
  - Greater risk of certain surgical complications

1. Rady MY, et al. *Crit Care Med.* 1998;26:225-235.

2. DeFoe GR, et al. *Ann Thorac Surg.* 2001;71:769-776.

# Anemia Management Options for Surgical Patients



**Allogeneic Blood Transfusions (ABT)**

**Restrictive Hb Transfusion Threshold**

**Preoperative Autologous Donation (PAD)**

**Acute Normovolemic Hemodilution (ANH)**

**Blood Salvage**

**Erythropoietic Stimulating Proteins (eg, rHuEPO)**

# Allogeneic Red Blood Cell Transfusion (ABT)



- Two-thirds of ABTs are administered perioperatively<sup>1</sup>
- In emergency situations, ABTs do save lives
- However, ABT has risks and places demands on blood bank supply<sup>1</sup>

1. Ereth MH, et al. *Mayo Clin Proc.* 1994;69:575-586.

# Principal Risks of ABT



| <b>Blood transfusion risk</b>         | <b>Estimated frequency per unit</b> |
|---------------------------------------|-------------------------------------|
| Hepatitis C                           | 1/2,000,000                         |
| Hepatitis B                           | 1/30,000–1/250,000                  |
| Hepatitis A                           | 1/1,000,000                         |
| HIV type 1                            | 1/200,000–1/2,000,000               |
| HTLV (I, II)                          | 1/250,000–1/2,000,000               |
| Hemolytic reaction, acute             | 1/250,000–1/1,000,000               |
| Hemolytic reaction, delayed           | 1/1,000                             |
| Bacterial infection, platelets        | 1/12,000                            |
| Bacterial infection, red cells        | 1/500,000                           |
| Transfusion-related acute lung injury | 1/5,000                             |

Goodnough LT, et al. *N Engl J Med.* 1999;340:438-447.

# Additional Risks of ABT



- Febrile nonhemolytic reaction
- Allergic reactions
- Alloimmunization
- Circulatory overload — can lead to pulmonary edema
- Metabolic complications
- Hypothermia — can lead to cardiac arrhythmia, cardiac arrest
- Anaphylactoid reactions (rare)
- Graft-versus-host disease (rare)

American Red Cross. ARC Circular 1761, <http://chapters.redcross.org>. January 1999.

# Risk of Immunosuppression From ABT



- Undetermined frequency of clinically significant immunosuppression in patients treated with ABT <sup>1</sup>
- Clinical findings in cancer patients suggest exposure to ABT increases the risk of postoperative infection and cancer recurrence<sup>1-3</sup>
- ABT associated with increased risk of opportunistic infections and death in immune-suppressed HIV positive patients<sup>4</sup>

1. Goodnough LT, et al. *N Engl J Med*. 1999;340:438-447.

2. Ludwig H, et al. *Semin Oncol*. 1998;25(suppl 7):2-6.

3. Heiss MM. *Zentralbl Chir*. 2000;125:842-846.

# Infections and Other Complications of ABT

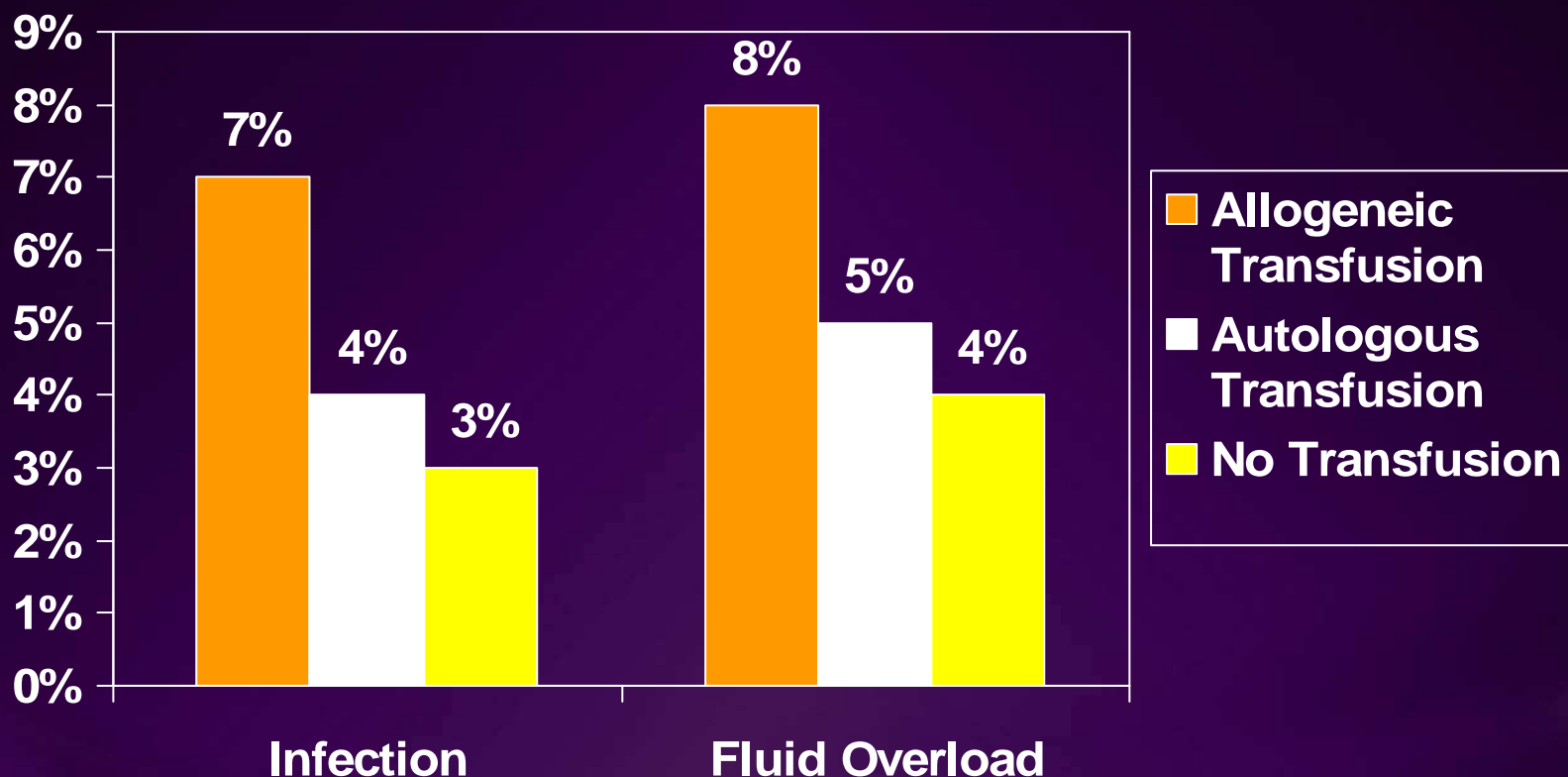


- **In 9482 orthopedic surgery patients, ABT was linked to:<sup>1</sup>**
  - Increased risk of infection, especially urinary tract infection
  - Increased risk of fluid overload
  - Prolonged hospitalization
- **In 6301 noncardiac surgery patients, ABT was linked to:<sup>2</sup>**
  - Increased risk of death
  - Increased risk of infection
  - Prolonged hospital stay

1. Bierbaum B, et al. *J Bone Joint Surg.* 1999;81-A:2-10.

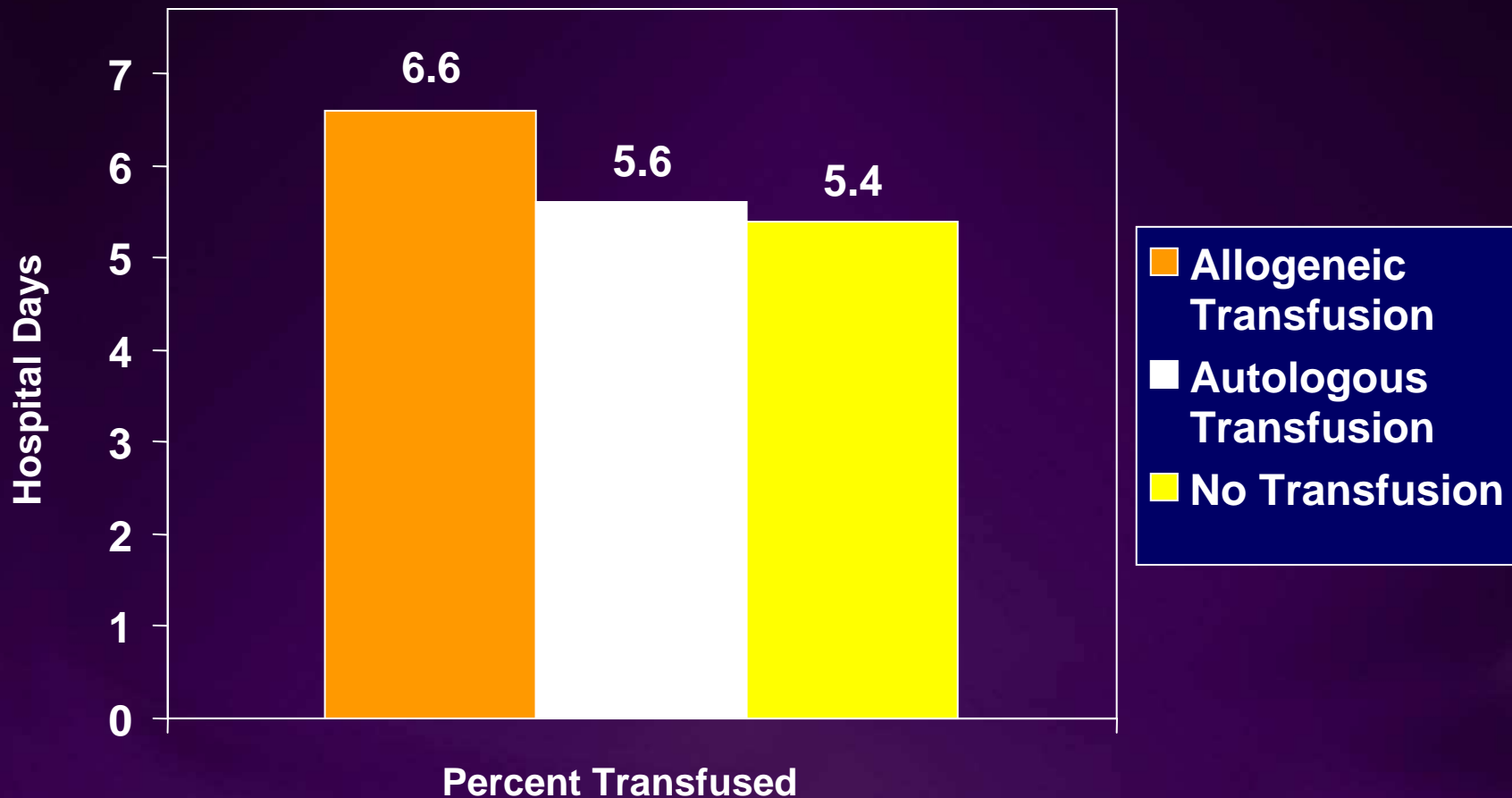
2. Dunne J, et al. *J Surg Res.* 2002;102:237-244.

# Complications of ABT in Orthopedic Surgery Patients



Bierbaum BE, et al. *J Bone Joint Surg* 1999;81-A:2-10.

# Complications of ABT in Orthopedic Surgery Patients



Bierbaum BE, et al. *J Bone Joint Surg* 1999;81-A:2-10.

# ABT Current Guidance



Red-cell containing components should not be used to treat anemia that can be corrected with specific medications such as iron, vitamin B12, folic acid, or recombinant erythropoietin, except when the patient's symptoms require immediate enhancement of oxygen-carrying capacity.

American Association of Blood Banks, America's Blood Centers, and the American Red Cross

# Blood Conservation Strategies To Decrease ABT Rates



**Strategies  
can be used  
alone or  
combined**

**Restrictive Hb Threshold for ABT**

**Preoperative Autologous Donation**

**Acute Normovolemic Hemodilution**

**Blood Salvage**

**Erythropoietic Stimulating Proteins (eg, rHuEPO)**

**Meticulous Surgical Technique**

# Hb Threshold for ABT Noncardiac Surgery



- Historically, physicians have followed the 10/30 rule  
**Hb = 10 g/dL or Hct = 30% → ABT**
- Professional groups have published guidelines with lower ABT thresholds
- Most organizations recommend ABT trigger of Hb 6 g/dL to 8 g/dL

Corwin HL, et al. *Chest*. 1995;108:767-771.

# Hb Thresholds for ABT: Published Guidelines



| Organization   | Year | Trigger Hb (g/dL)     |
|--|------|-----------------------|
| NIH Consensus Conference <sup>1</sup>                      | 1988 | 8                     |
| American College of Physicians <sup>2</sup>                | 1992 | 7                     |
| American Society of Anesthesiologists <sup>3</sup>         | 1996 | 6                     |
| Canadian Medical Association <sup>4</sup>                  | 1997 | Insufficient evidence |
| Association of Anaesthetists of Great Britain <sup>5</sup> | 2001 | 8 (a)                 |
| Scottish Intercollegiate Guidelines Network <sup>6</sup>   | 2001 | 7 (b)                 |

(a) Applies even to patients with significant cardiorespiratory disease

(b) 9 g/dL for patients with CVD or likely covert CVD

1. National Institutes of Health. *JAMA*. 1988;260:2700-2703.

2. American College of Physicians. *Ann Intern Med*. 1992;116:403-406.

3. American Society of Anesthesiologists. *Anesthesiology*. 1996;84:732-747.

4. Canadian Medical Association. *Can Med Assoc J*. 1997;156(suppl 11):S1-S24.

5. Association of Anaesthetists of Great Britain & Ireland. *Blood Transfusion and the Anaesthetist: Red Cell Transfusion*. 2001.

6. Scottish Intercollegiate Guidelines Network. 2001.

# Preoperative Autologous Donation (PAD)



- Significantly decreases the need for ABT<sup>1,2</sup>
- Eligible patients<sup>1</sup>:
  - Hemoglobin  $\geq 11$  g/dL or
  - Hematocrit  $\geq 33\%$ <sup>3</sup>
  - Potential for bacteremia is nonexistent
  - No underlying medical condition that would make phlebotomy hazardous<sup>4</sup>

1. Ereth MH, et al. *Mayo Clin Proc.* 1994;69:575-586.

2. Bierbaum BE, et al. *J Bone Joint Surg.* 1999;81-A:2-10.

3. Cazzola M, et al. *Blood.* 1997;12:4248-4267.

4. Walpoth B, et al. *Semin Hematol.* 1996;22(2 suppl 2):75-77.

# PAD Not Feasible for Some Patients



- Limiting factors<sup>1-4</sup>
  - Low initial Hb
  - Small body size (small RBC mass)
  - Short time to surgery (3-5 weeks usually required)
  - Severe cardiac disease
  - Consent issues (logistical problems, religious beliefs)

1. Ereth MH, et al. *Mayo Clin Proc.* 1994;69:575-586.
2. Bierbaum BE, et al. *J Bone Joint Surg.* 1999;81-A:2-10.
3. Cazzola M, et al. *Blood.* 1997;12:4248-4267.
4. Walpoth B, et al. *Semin Hematol.* 1996;22(2 suppl 2):75-77.

# Limitations of PAD



- Prohibited in US when Hct <33% and Hb <11 g/dL<sup>1</sup>
- Risk of breakthrough ABT due to undercollection of PAD or perioperative anemia<sup>2-5</sup>
- Transfusion risks<sup>6</sup>
- Wastage of blood due to over-collection of PAD<sup>1,2,7</sup> or storage time exceeded (PAD blood should not be added to general supply<sup>8</sup>)
- PAD cost higher than ABT<sup>2,4</sup>

1. *Standards for Blood Banks and Transfusion Services*. 21st ed. Bethesda, Md: American Association of Blood Banks; 2002.

2. Bierbaum BE, et al. *J Bone Joint Surg*. 1999;81;A:2-10.

3. Cazzola M, et al. *Blood*. 1997;89:4248-4267.

4. Goodnough LT, et al. *N Engl J Med*. 1999;340:525-533.

5. Kanter MH, et al. *JAMA*. 1996;276:798-801.

6. Armas-Loughran B, et al. *Med Clin N Am*. 2003;87:229-242.

7. Ereth MH, et al. *Mayo Clin Proc*. 1994;69:575-586.

8. Blum LN, et al. *Transfusion*. 1998;38:891-895.

# Why Consider Alternatives to Transfusions (PAD or ABT)?



- Transfusions not documented to improve outcomes<sup>1</sup>
- Risks of transfusion<sup>2</sup>
  - Infections
  - Immunological impact
  - Administrative errors
  - Volume overload
- Physiological limitations of stored blood<sup>3-7</sup>

1. Spence PK. *Clin Ortho*. 1998;357:19-29.

2. Goodnough LT, et al. *NEJM*. 1999;340:525-533.

3. Corwin HL, et al. *Crit Care Med*. 1999;27:2346-2350.

4. Carson J. *JAMA*. 2002;288:2884-2886.

5. Marik PE, et al. *JAMA*. 1993;269:3024-3029.

6. Lorente JA, et al. *Crit Care Med*. 1993;21:1312-1317.

7. Gramm J, et al. *Shock*. 1996;5:190-193.

# Physiological Limitations of Stored Blood



- Storage of RBCs can lead to<sup>1,2</sup> :
  - Impaired ability of RBCs to distribute oxygen
  - Microcirculatory occlusion
- Greater age of blood has been linked to increased risk of death,<sup>2</sup> pneumonia, and splanchnic ischemia<sup>2,3</sup>
- In patients with sepsis, transfusion does not appear to increase oxygen uptake<sup>3-5</sup>

1. Corwin HL, et al. *Crit Care Med.* 1999;27:2346-2350.

2. Carson J. *JAMA.* 2002;288:2884-2886.

3. Marik PE, et al. *JAMA.* 1993;269:3024-3029.

4. Lorente JA, et al. *Crit Care Med.* 1993;21:1312-1317.

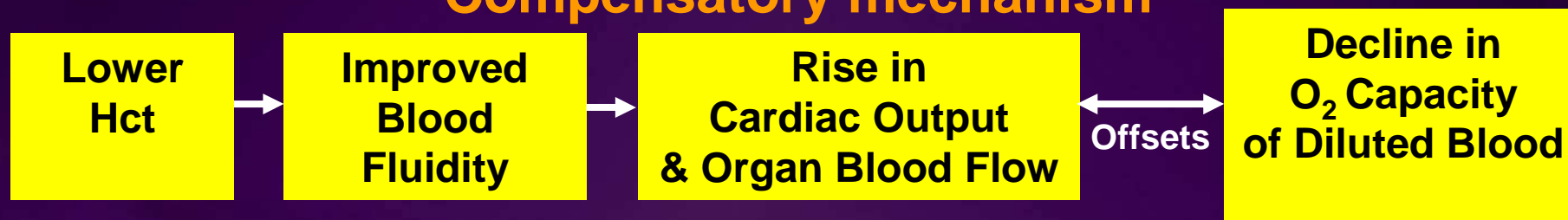
5. Gramm J, et al. *Shock.* 1996;5:190-193.

# Acute Normovolemic Hemodilution (ANH)



- ANH = withdrawal of whole blood immediately before surgery, with concurrent colloid/crystalloid replacement
- Considered when expected blood loss is >20% blood volume and preoperative Hb is >10 g/dL, except in the presence of severe myocardial disease<sup>1</sup>
- Goal: Decrease RBC mass by lowering Hct<sup>2</sup>

## Compensatory mechanism<sup>2</sup>



1. Napier JA, et al. *Br J Anaesth*. 1997;78:768-771.

2. Messmer K, et al. *Eur Surg Res*. 1986;18:254-263.

# ANH Versus PAD



- ANH has the same risk of ABT as PAD<sup>1,2</sup>
- ANH Advantages
  - Lower cost<sup>1,2</sup>
  - Eliminates risk of bacterial contamination and administrative error<sup>3</sup>
  - Patient relieved of the inconvenience of predonation<sup>3</sup>

1. Monk TG, et al. *Transfusion*. 1995;35:559-565.

2. Goodnough LT, et al. *Transfusion*. 2000;40:1054-1057.

3. Goodnough LT, et al. *N Engl J Med*. 1999;340:525-533.

# Blood Salvage



- Blood salvage = intraoperative or postoperative collection and reinfusion of RBCs lost during surgery
- Used most commonly in cardiac surgery<sup>1</sup>
- Reduces ABT in cardiac and orthopedic surgery<sup>2-4</sup>
- Acceptable to many Jehovah's Witnesses<sup>1</sup>

1. Ereth MH, et al. *Mayo Clin Proc.* 1994;69:575-586.

2. McGill N, et al. *BMJ.* 2002;324:1299-1305.

3. Shenolikar A, et al. *Transfus Med.* 1997;7:277-280.

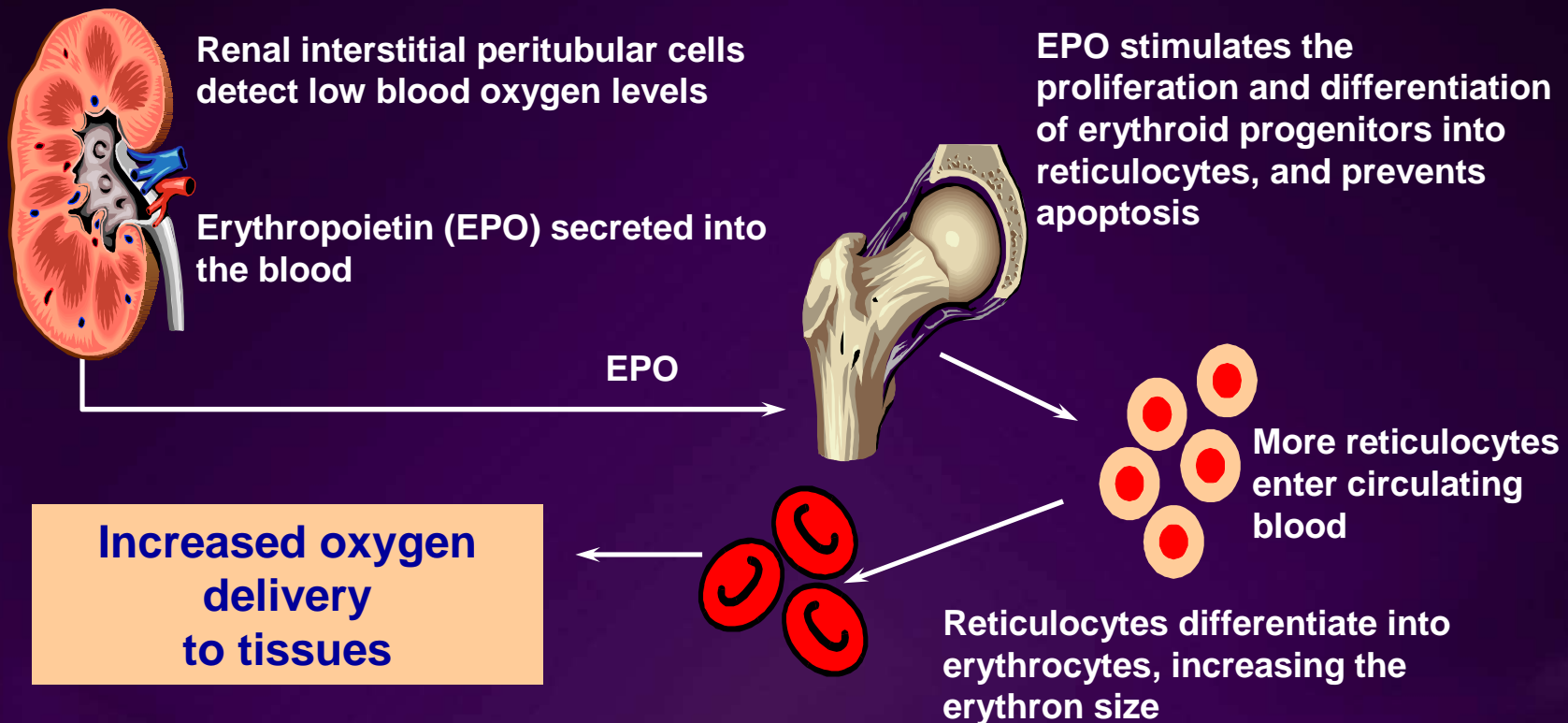
4. Thomas D, et al. *Br J Anaesth.* 2001;86:669-673.

# Erythropoietic Stimulating Proteins



- Peptide hormones and their derivatives, manufactured by recombinant DNA technology, which stimulate the production of red blood cells
  - Recombinant human erythropoietin (rHuEPO)
    - Eg, epoetin alfa, epoetin beta, epoetin omega
  - Darbepoetin alfa

# Erythropoietin Regulates Red Blood Cell Production



Bunn H. In: Isselbacher K, et al, eds. *Harrison's Principles and Practice of Internal Medicine*. 13th ed. New York, NY: McGraw-Hill; 1994:1717–1721.

Dessypris E. In: Lee G, et al, eds. *Wintrobe's Clinical Hematology (Vol. 1)*. Baltimore, Md: Lippincott, Williams & Wilkins; 1998:169–192.

# Recombinant Human Erythropoietin (rHuEPO)



- An amino-acid glycoprotein manufactured by recombinant DNA technology
- Identical in structure and biological activity to native erythropoietin
- Used for more than a decade to manage anemia in patients with CKD and cancer

1. Epogen® package insert. Amgen. Thousand Oaks, Calif., USA

# rHuEPO Uses in Surgical Patients



- Facilitate PAD
- Increase perioperative Hb
- Decrease ABT

# rHuEPO

## Use Varies by Country



- United States: Approved for reduction of the need for ABT in anemic surgical patients, except those eligible for PAD<sup>1</sup>
  - Elective noncardiac, nonvascular surgery
  - Hb >10 to ≤13 g/dL
  - High risk of significant perioperative blood loss
- Canada: Approved for the above, for facilitating PAD, and for limiting the decline in Hb with PAD<sup>2</sup>
- Europe: Approved for facilitating PAD<sup>3</sup>

1. Epogen® package insert. Amgen. Thousand Oaks, Calif., USA.

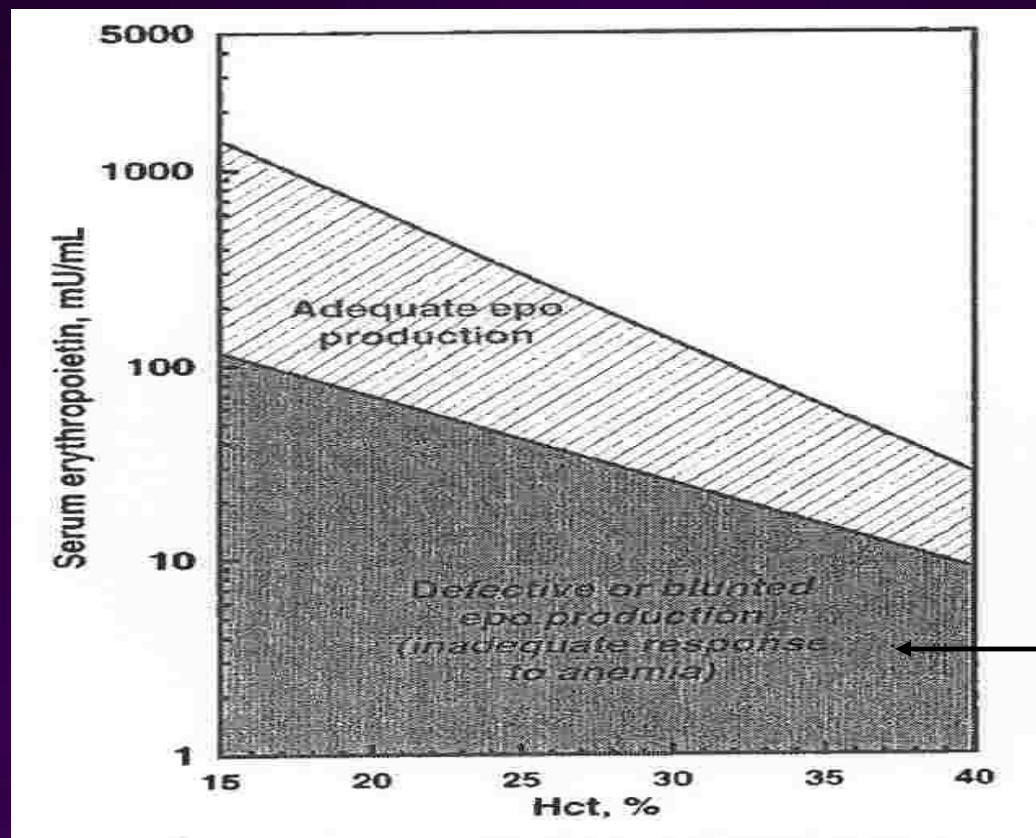
2. Eprex® package insert. Janssen-Ortho Inc. Toronto, Ontario, Canada.

3. NeoRecormon® product information. Roche Registration Ltd. Hertfordshire, UK.

# How rHuEPO Facilitates PAD



Limited Erythropoiesis  $\Rightarrow$  Anemia  $\Rightarrow$  Undercollection



Relationship between serum EPO levels and Hct in reference subjects.<sup>1</sup>

Defective or blunted EPO production (inadequate response to anemia)

1. Cazzola M, et al. *Blood*. 1997;89:4248-4267. (Figure)

2. Kickler TS, et al. *JAMA*. 1988;260:65-67.

# PAD Outcomes With rHuEPO in Noncardiac Surgery



- Increases the number of units collected<sup>1-4</sup>
- Improves the percentage of patients able to donate sufficient blood<sup>1,3,5</sup>
- Reduces the need for ABT<sup>2,3</sup>

1. Goodnough LT. *Int J Cell Cloning*. 1990;8(suppl 1):203-210.

2. Mercuriali F, et al. *Transfusion*. 1993;33:55-60.

3. Adamson J. *Semin Hematol*. 1996;33(2 suppl 2):15-16.

4. Price T, et al. *Transfusion*. 1996;36:29-36.

5. Hyllner M, et al. *Obstet Gynecol*. 2002;99:757-762.

# IV Iron Enhances Hb Response in PAD



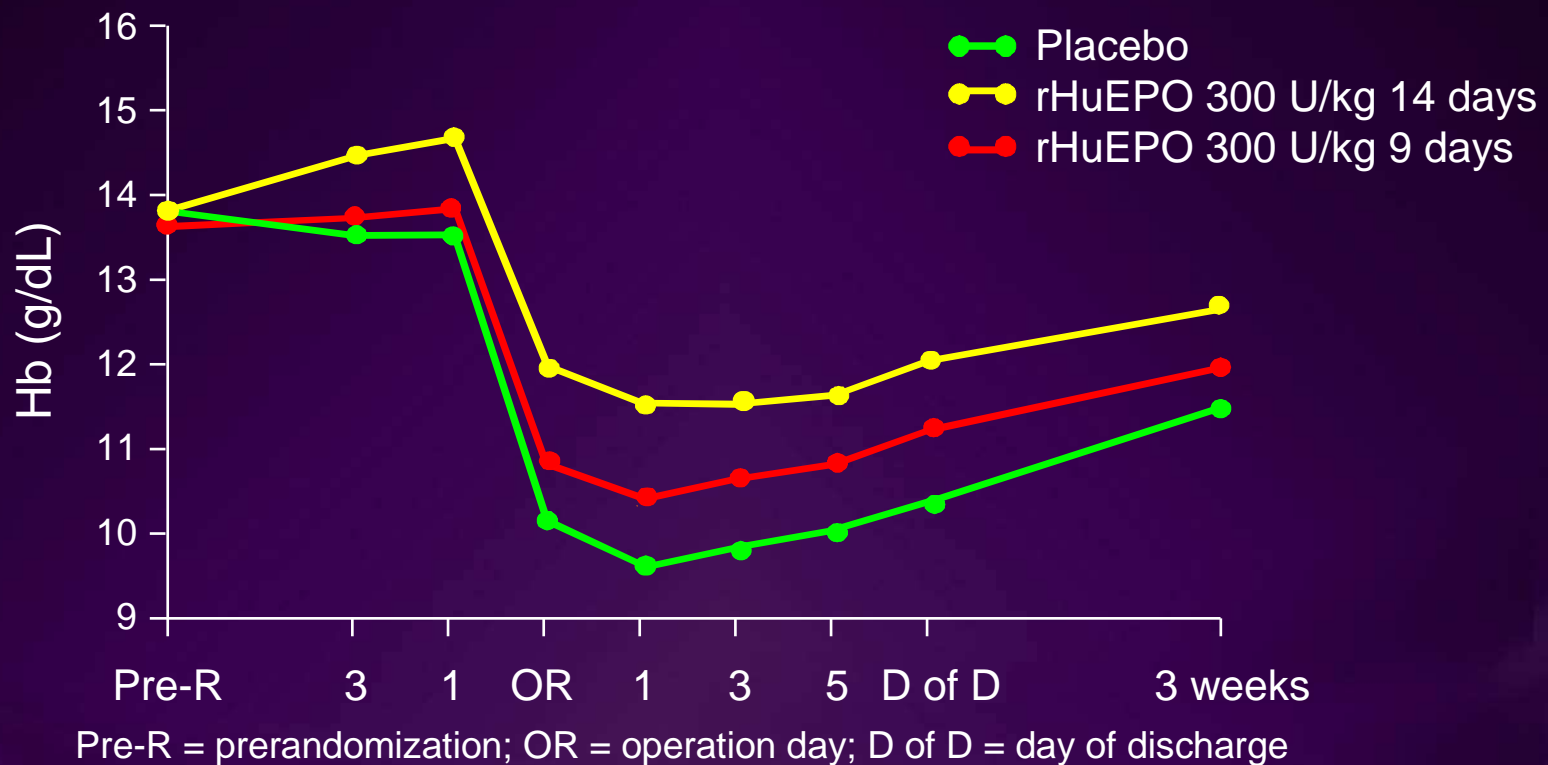
- During PAD, the effect of rHuEPO can be restricted by iron depletion despite oral iron<sup>1,2</sup>
- IV iron produces a more adequate iron supply<sup>2,3</sup>
  - Increases Hb response to same rHuEPO dose
  - Allows reduction of rHuEPO dose

1. Biesma DH, et al. *Eur J Clin Invest*. 1994;24:426-432.

2. Goodnough LT, et al. *Transfusion*. 2003;43:668-676.

3. Cazzola M, et al. *Blood*. 1997;89:4248-4267.

# rHuEPO Improves Perioperative Hb in Noncardiac Surgery



1. Canadian Orthopedic Perioperative Erythropoietin Study Group. *Lancet*. 1993;341:1227-1232.
2. Qvist N, et al. *World J Surg*. 1999;23:30-35.

# Benefits of rHuEPO in PAD Cardiac Patients



| Study                              | N   | Effect on Hb  | Effect on ABT   |
|------------------------------------|-----|---|---|
| Kyo et al., 1992 <sup>1</sup>      | 205 | Hb ↑ with rHuEPO vs placebo. Best with rHuEPO+ iron                           | ABT rate significantly less with rHuEPO +iron vs rHuEPO, placebo ( $P = .001, .003$ ) |
| Kulier et al., 1993 <sup>2</sup>   | 24  | Hb ↑ more with rHuEPO vs iron alone   | ABT rate reduced with rHuEPO vs iron alone ( $P = < .001$ )                           |
| Walpoth et al., 1996 <sup>3</sup>  | 31  | Hb ↓ less with rHuEPO vs placebo ( $P < .05$ )                                | No difference in ABT rate with rHuEPO vs placebo                                      |
| Cazenave et al., 1997 <sup>4</sup> | 80  | Number donating $\geq 4U$ greater with rHuEPO vs placebo ( $P = .011, .032$ ) | No difference in ABT rate with rHuEPO vs placebo                                      |
| Kiyama et al., 1999 <sup>5</sup>   | 32  | Hb ↑ more with rHuEPO vs iron alone   | 25% of rHuEPO group needed ABT vs 100% of controls                                    |

# rHuEPO Also Useful for Non-PAD Cardiac Patients



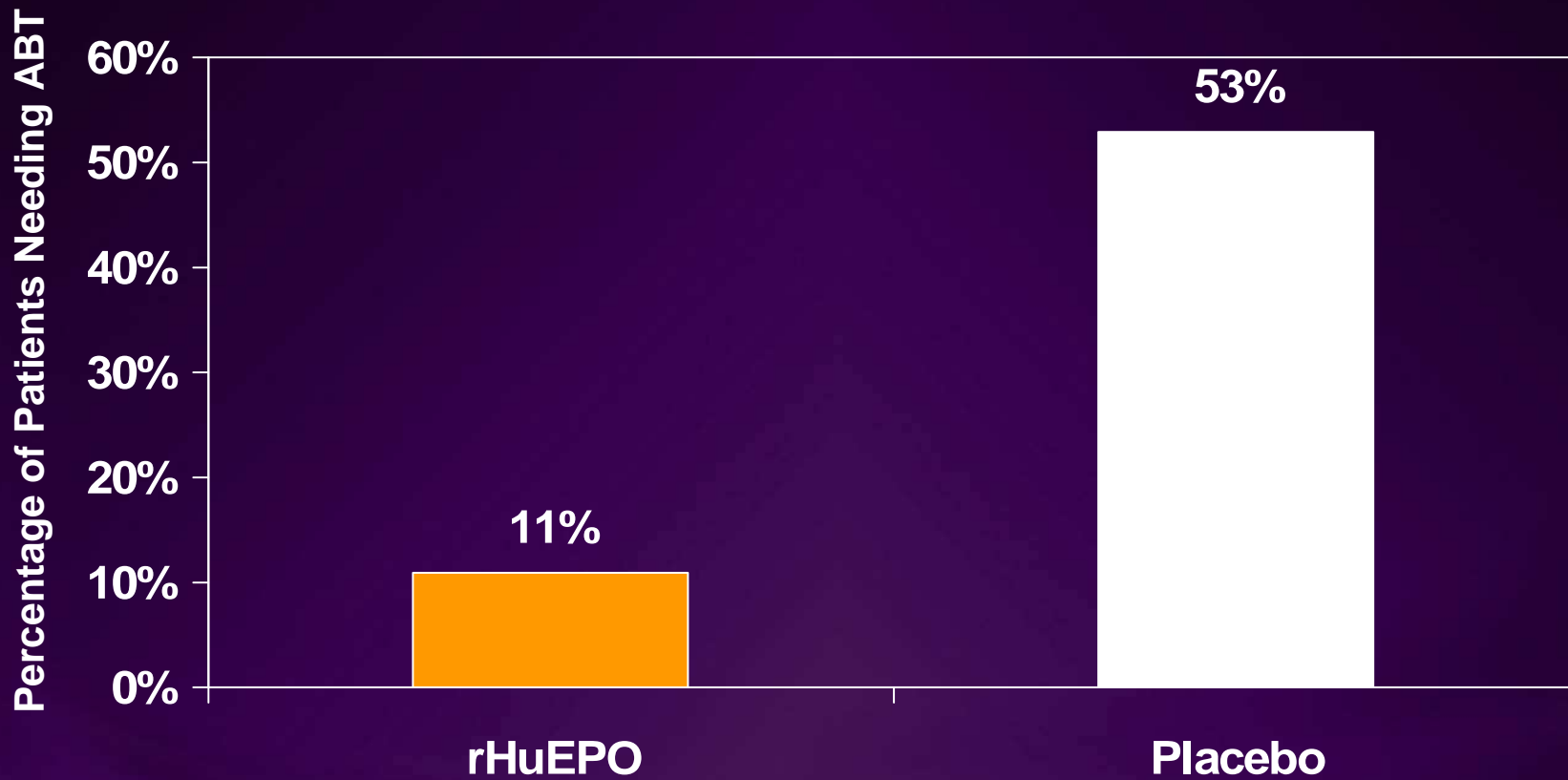
- Study design** Double-blind RCT of 76 open-heart surgery patients<sup>1</sup>
- Intervention** rHuEPO or placebo for 14 days preoperatively
- Findings**
- With rHuEPO:
    - Significant reduction in need for ABT<sup>1</sup> ( $P = .0003$ )
    - Greater increase in extractable oxygen<sup>2</sup>
  - Lower rate and severity of lactic acidosis<sup>2</sup>
  - No difference between groups in mortality, frequency of specific adverse events, hemostatic values, or BP<sup>1</sup>
  - No good evidence for thrombosis or thromboembolic disease<sup>3</sup>

1. Sowade et al. *Blood*. 1997;89:411-418.

2. Sowade et al. *J Lab Clin Med*. 1997;129:97-105.

3. Sowade et al. *J Lab Clin Med*. 1997;129:376-383.

# Reduced Need for ABT in Cardiac Surgery Patients Receiving rHuEPO



Sowade O, et al. *Blood*.1997;89:411-418.

# Many Strategies Contribute to Blood Conservation<sup>1</sup>



| Options  | No. of Units           |
|--|------------------------|
| <b>PREOPERATIVE</b>  |                        |
| Tolerance of anemia (reduce level at which transfusion is performed) | 1-2 <sup>2</sup>       |
| Increase preoperative RBC mass                                       | 2 <sup>3,4</sup>       |
| Preoperative autologous donation                                     | 1-2 <sup>3</sup>       |
| <b>INTRAOPERATIVE</b>  |                        |
| Meticulous hemostasis and operative technique                        | 1 or more <sup>5</sup> |
| ANH  | 1-2 <sup>6,7</sup>     |
| Blood salvage  | 1 or more <sup>8</sup> |
| <b>POSTOPERATIVE</b>   |                        |
| Restricted phlebotomy  | 1 <sup>9</sup>         |
| Blood salvage  | 1 <sup>10</sup>        |

1. Goodnough LT, et al. *Trans.* 2003;43:668-676.

2. Goodnough LT, et al. *N Engl J Med.* 1999;340:525-533.

3. Hébert PC, et al. *N Engl J Med.* 1999;340:409-417.

4. Goodnough LT, et al. *Blood.* 2000;96:823-833.

5. Goodnough LT, et al. *Trans.* 1992;32:441-445.

6. Spence RK, et al. *Curr Probl Surg.* 1993;30:1101-1180.

7. Goodnough LT, et al. *Trans.* 1998;38:473-476.

8. Monk TG, et al. *Trans.* 1995;35:559-565.

9. Goodnough LT, et al. *J Vasc Surg.* 1996;24:213-218.

10. Smoller BR, et al. *N Engl J Med.* 1986;314:1233-1235.

# Emerging Approaches to Blood Conservation



- Oxygen-carrying solutions
- Darbepoetin alfa

# Oxygen-Carrying Solutions



- Still investigational
- Two types:
  - Hemoglobin-based oxygen carriers (HBOC)
  - Perfluorocarbon emulsions
- Some may not require refrigeration<sup>1</sup>
- Could be used with or without ANH<sup>1</sup>
- Could be used as bridge to erythropoietin therapy<sup>2</sup>

1. Goodnough LT, et al. *Lancet*. 2003;361:161-169.

2. Gannon CJ, et al. *Crit Care Med*. 2002;30:1893-1895.

# Darbepoetin Alfa



- Genetically engineered protein
- Compared with rHuEPO, contains more sialic acid, which increases serum half-life and biological activity
- Half-life is about threefold that of rHuEPO
  - Early and sustained erythropoietic effect
  - Less frequent dosing
- Approved in the US for treatment of anemia associated with chronic kidney disease (CKD) and cancer chemotherapy

Aranesp® package insert. Amgen Inc. Thousand Oaks, Calif., USA.

# Summary



- One-third to one-half of surgical patients may be anemic preoperatively and up to 90% have postoperative anemia
- Anemia in surgical patients has been linked to increased postoperative morbidity and mortality, and decreased quality of life
- Preoperative anemia is often unrecognized unless Hb/Hct are measured prior to planned surgery
- Decisions about transfusion and blood conservation should no longer be based on perceived risks of the blood supply, but rather on patient-specific factors
- Multiple blood conservation strategies are available, which can be used alone or in combination
- Oxygen-carrying solutions and darbepoetin alfa may be added to potential future treatment strategies

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