Chronic Kidney Disease-Key Factors in Anaemia Management

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www.PassPACES.com/kidney.htm

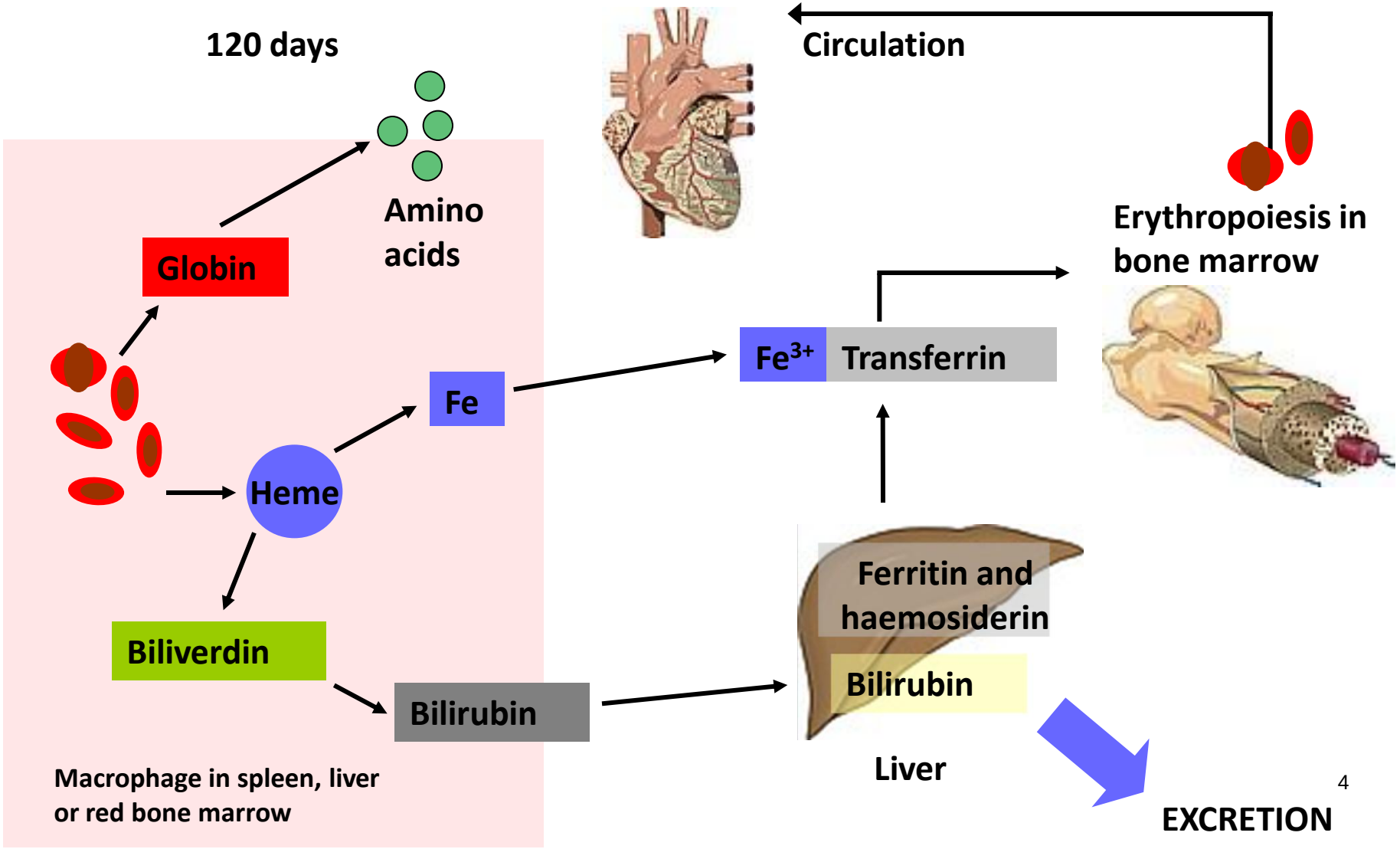
Outline

- Introduction and Pathophysiology of anaemia
- How common is anaemia in ESRD/CKD?
- Consequences of anaemia
- Investigating anaemia in CKD
- Anemia Management
- Other causes of anemia in CKD
- Conclusion

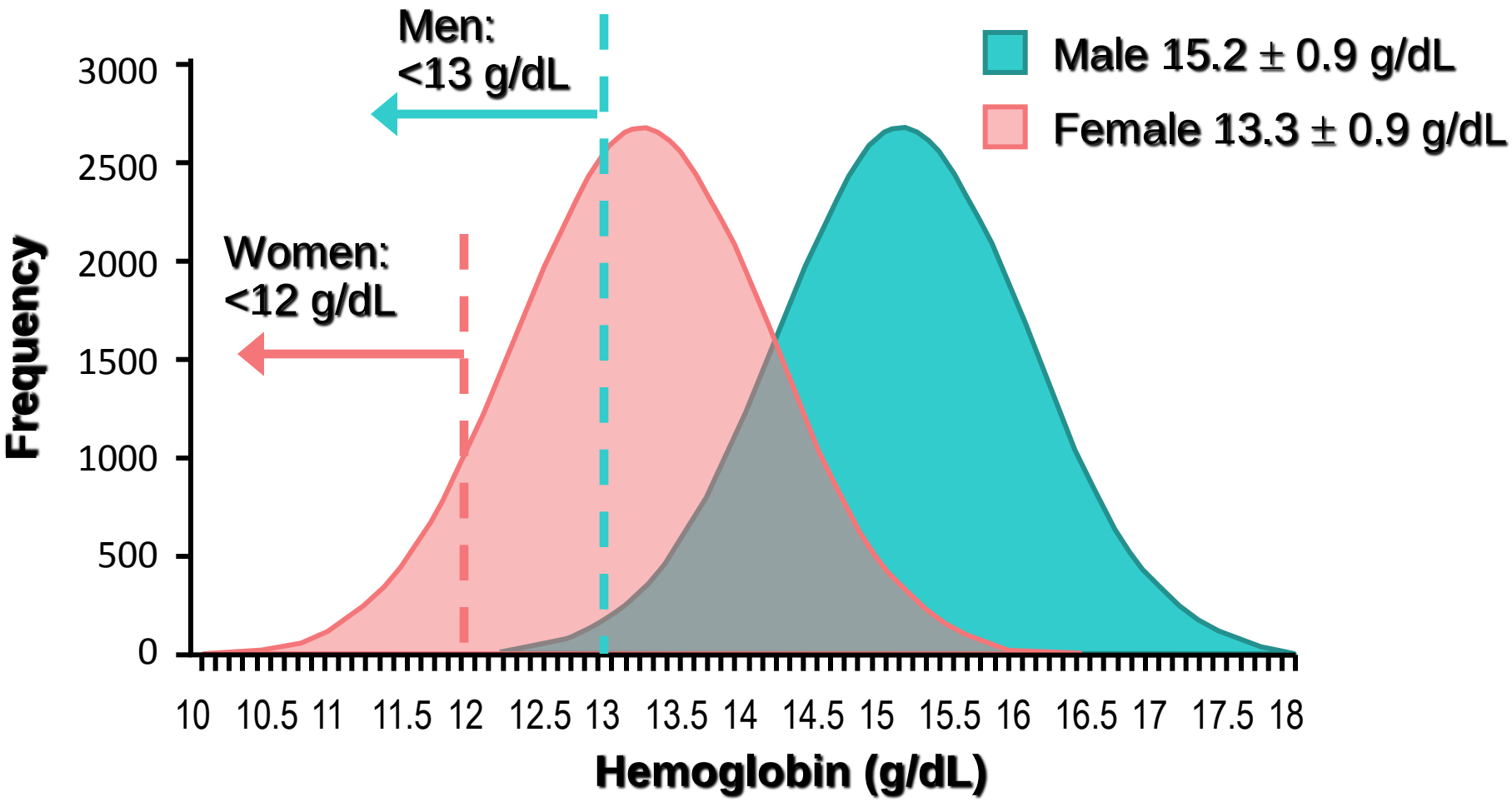
Introduction: Anaemia

- Greek term for “no blood”
- Shortage of red blood cells (RBC) or *a reduction in their haemaglobin (Hb) content.*
- Hb is a molecule in RBCs that carries oxygen.

The Lifecycle of the RBC



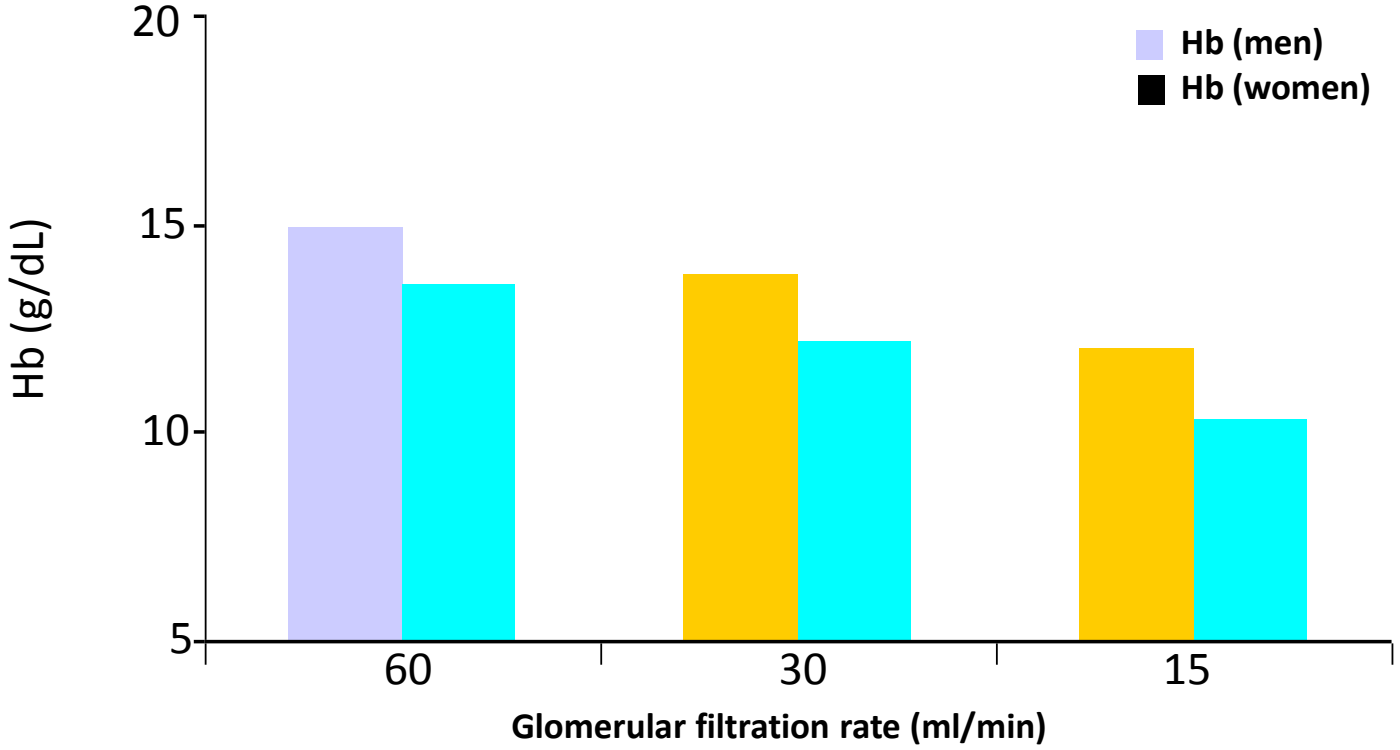
World Health Organization (WHO) Anemia Definition[1]



1. World Health Organization. Geneva, Switzerland; 2001. 2. Dallman et al. In: *Iron Nutrition in Health and Disease*. London, UK: John Libbey & Co; 1996:65-74.

Anaemia develops early in CKD

- NHANES III
  - 15,419 non-institutionalised adults over the age of 20
  - Prevalence of anaemia (KDOQI) increased from 1% at glomerular filtration rate of 60 ml/min to 9% at 30 ml/min and 33% at 15 ml/min



Astor et al, *Arch Int Med* 2002; 162: 1401-1408

Renal anaemia

- Defined as a Hb level<10g/dL.
- Affects >90% of patients undergoing dialysis.
- Starts to occur when GFR<60ml/min.
- 25% of patients when creatinine clearance is <50ml/min (Canadian multi-center study or renal anemia).

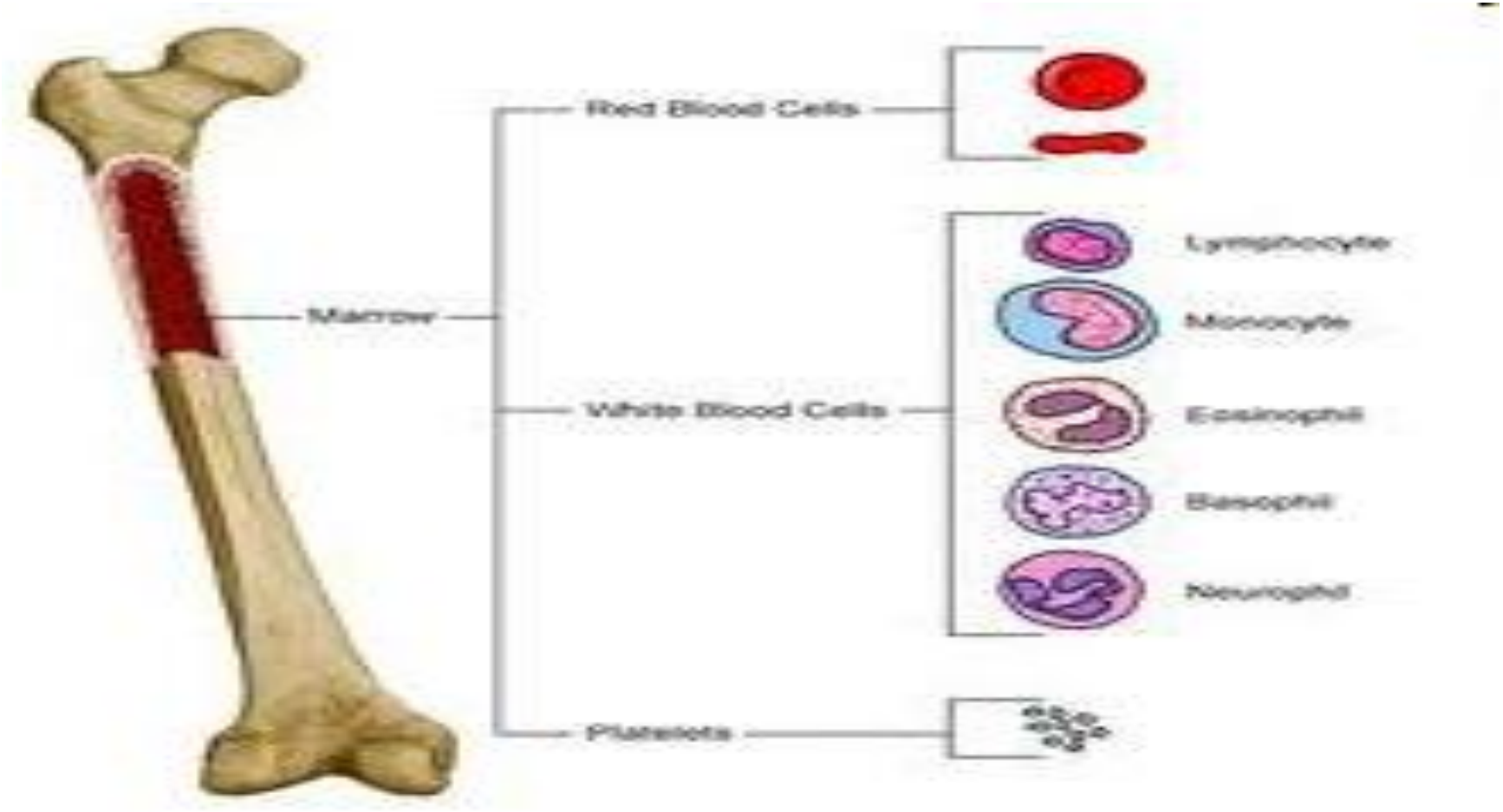
Symptoms of Anaemia

- Fatigue, reduced exercise tolerance
- Dyspnoea/Shortness of breath
- Syncope/faintness
- Palpitations. Angina if pre-existing CAD
- Cognitive impairment; memory concentration
- Loss of libido
- Altered menstrual cycles
- Erectile dysfunction

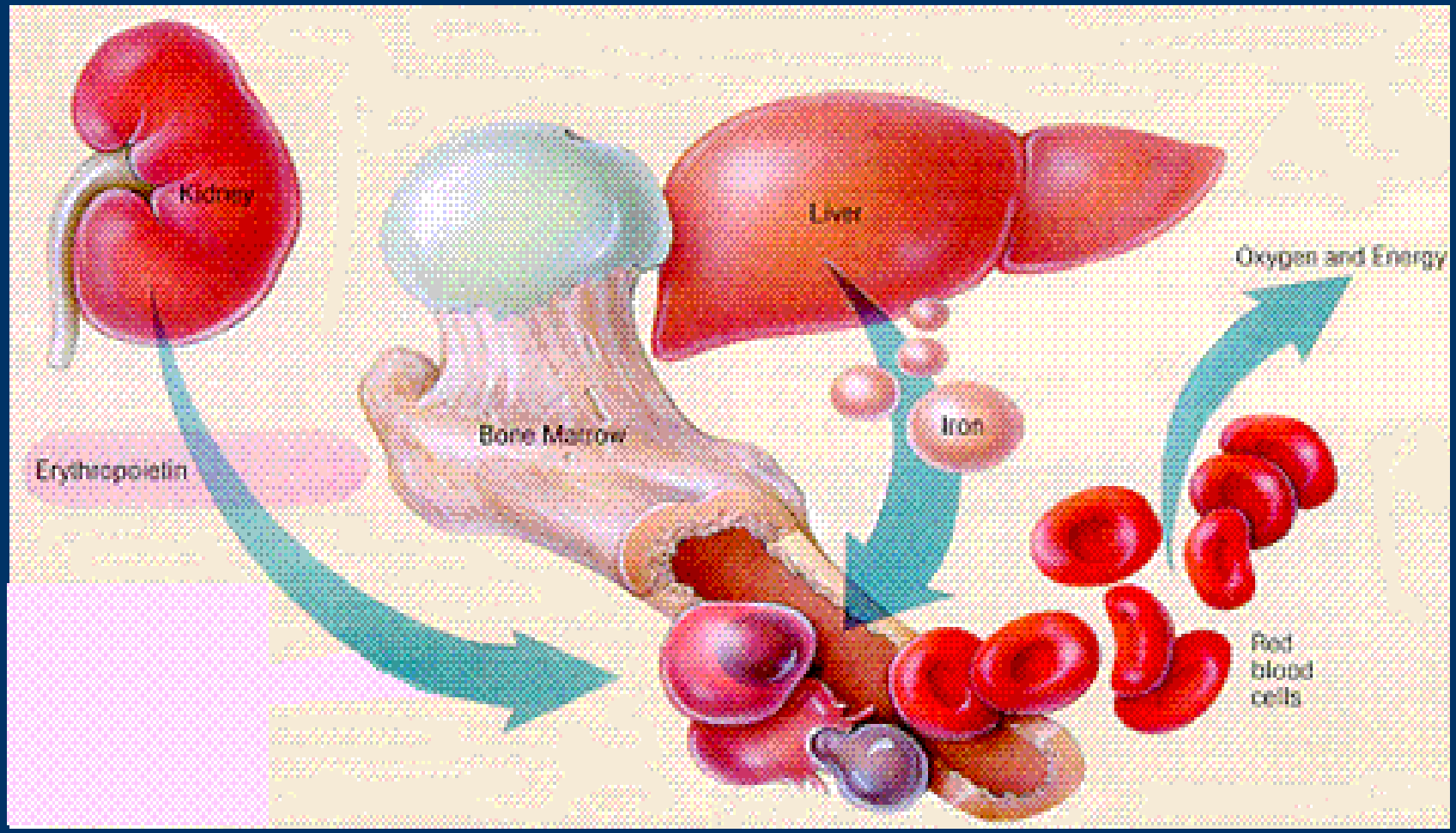
Signs

- May be absent
- Pallor – eg. Conjunctivae
- Hyperdynamic circulation
  - Tachcardia
  - flow murmur (ESM, loudest over apex)
  - cardiomegaly
- Later, heart failure may occur.

Physiology

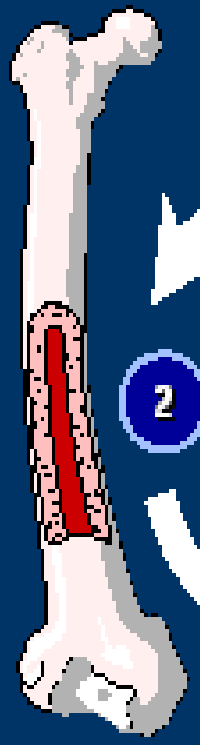

Red Blood Cells
Marrow
White Blood Cells
Platelets
Lymphocyte
Monocyte
Eosinophil
Basophil
Neutrophil

Normal Erythropoiesis



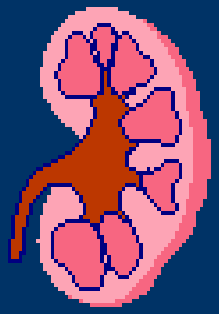
Adapted from Schott et al. US Pharmacist, 1997;22:HS5-HS12

Erythropoiesis



Bone Marrow

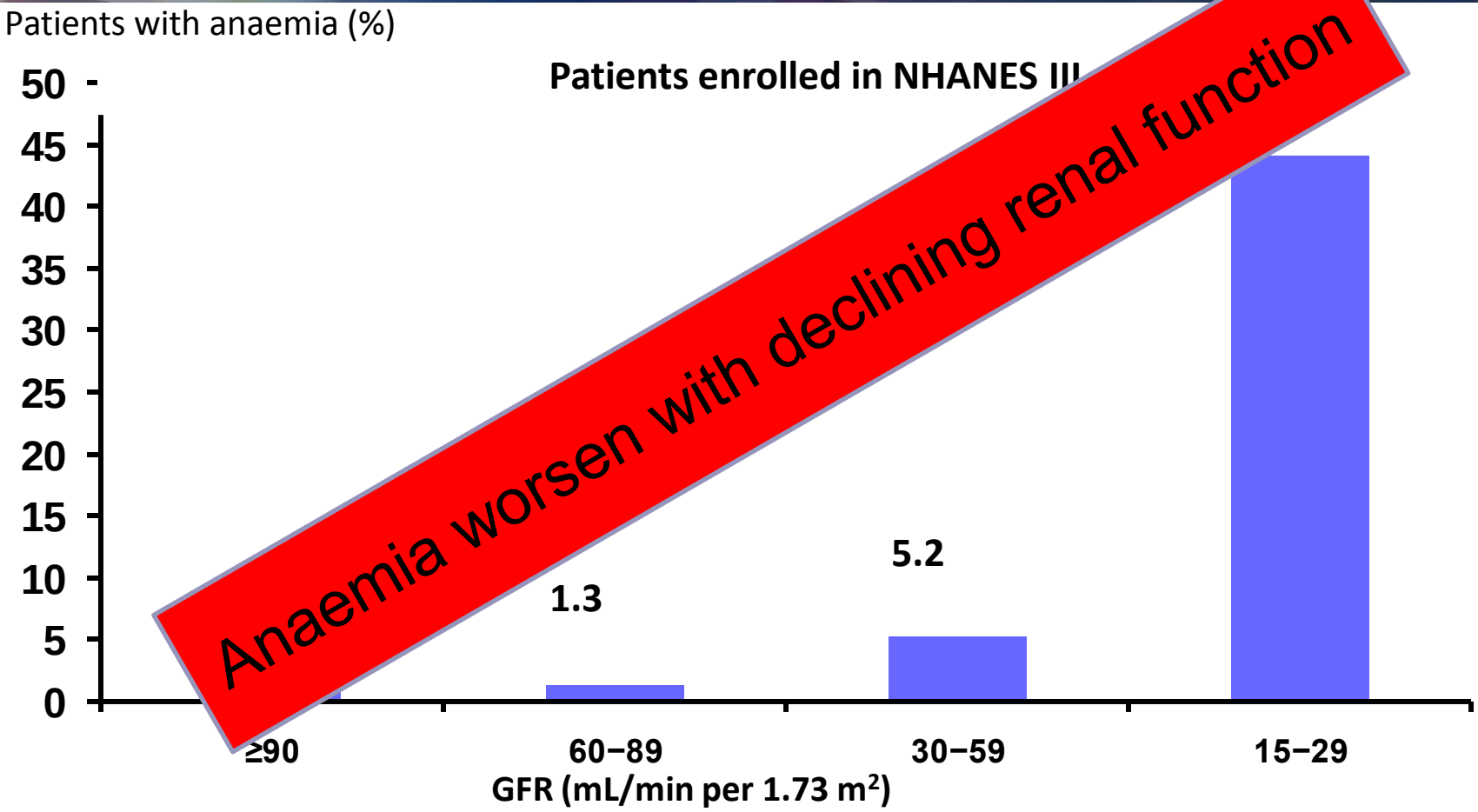
1. Kidney senses hypoxia (anemia) and increases endogenous erythropoietin production
2. Erythropoietin acts on the E-progenitor cells in the bone marrow to produce new red blood cells
3. Kidney senses increased tissue oxygenation
4. Kidney decreases erythropoietin production



Kidney

How common is anaemia in ESRD/CKD?

Increased Presence of Anaemia with Declining Kidney Function



Anaemia defined as Hb <12 g/dL in men, <11 g/dL in women; NHANES=National Health and Nutritional Survey

Astor et al. *Arch Intern Med.* 2002;162:1401-1408

Anaemia develops early in CKD

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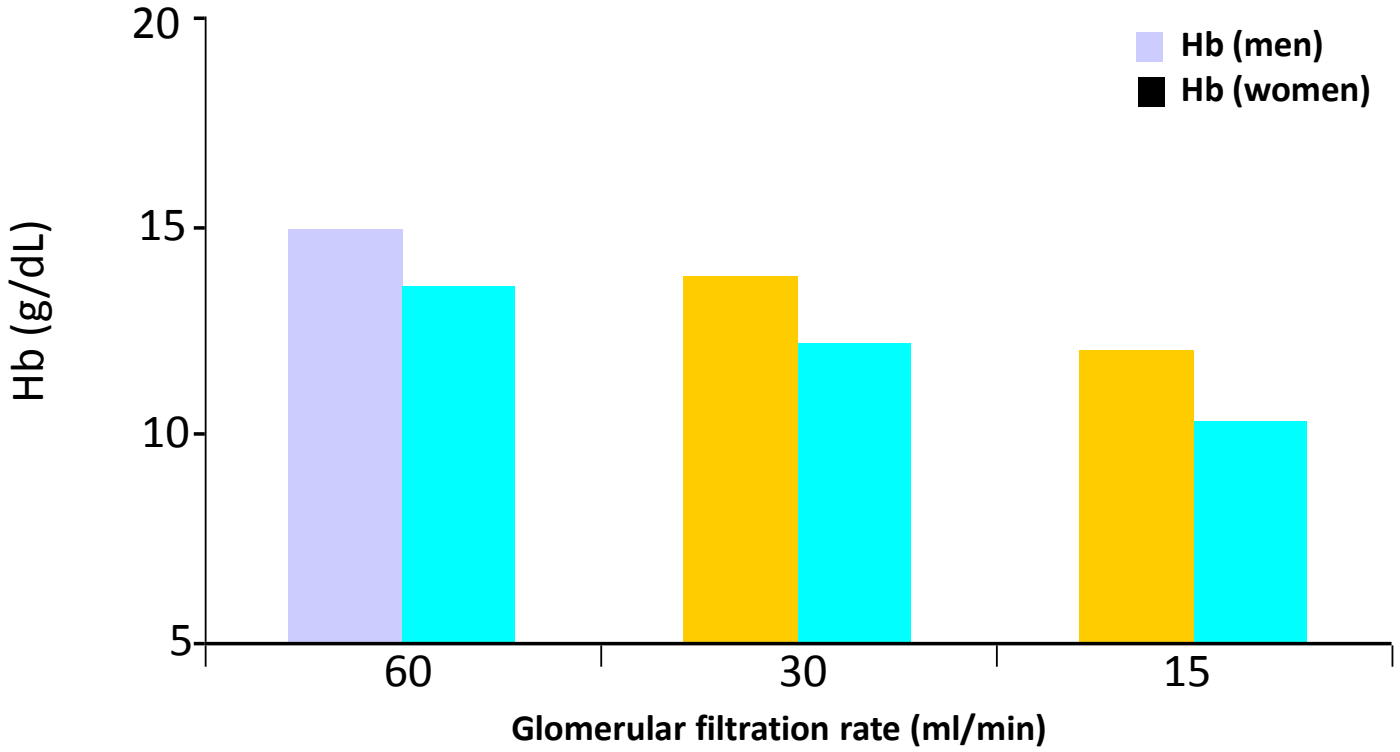
  - 15,419 non-institutionalised adults over the age of 20
  - Prevalence of anaemia (KDOQI) increased from 1% at glomerular filtration rate of 60 ml/min to 9% at 30 ml/min and 33% at 15 ml/min



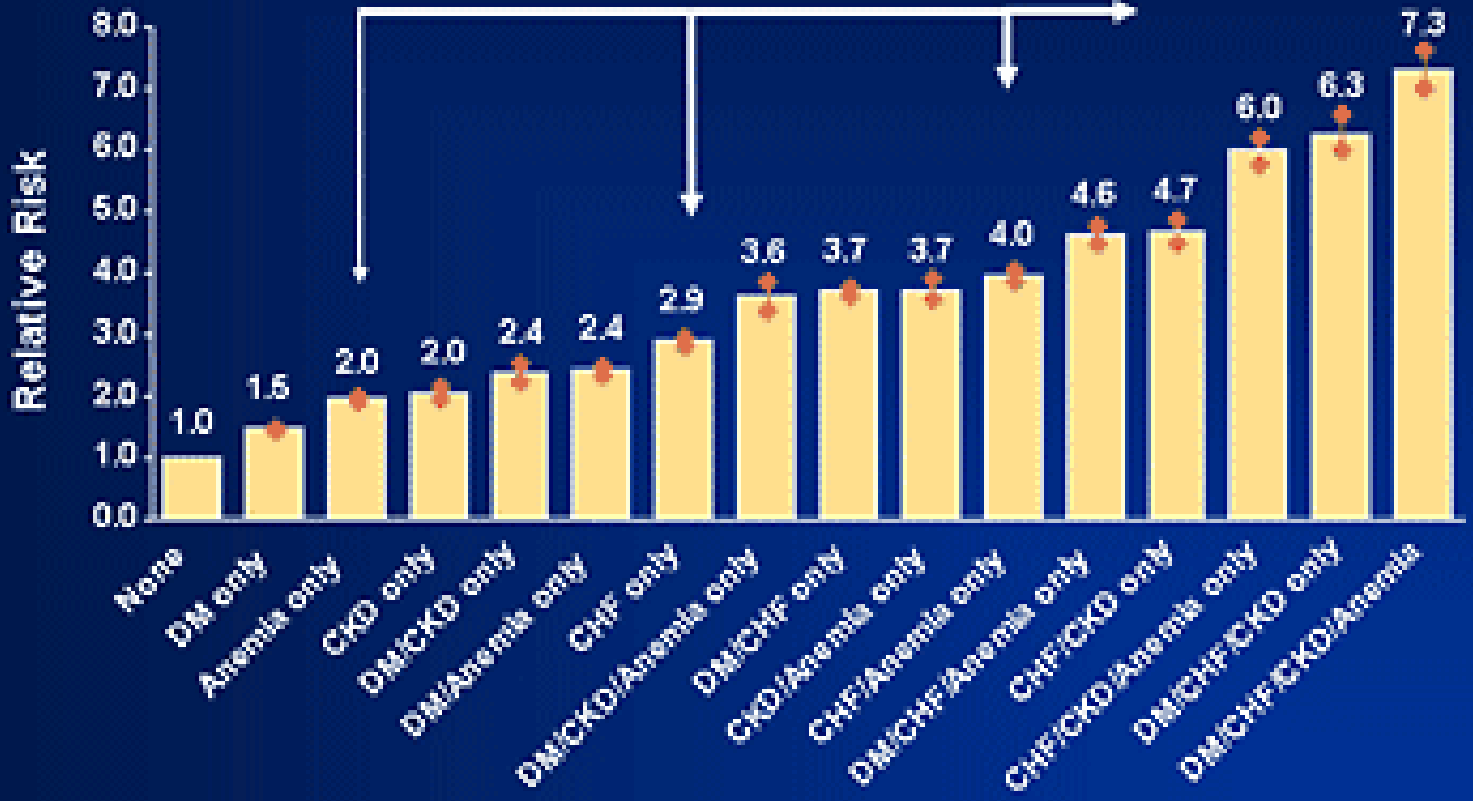
Astor et al, *Arch Int Med* 2002; 162: 1401-1408

Consequences of anaemia

Detrimental effects of anaemia in ESRD patients

- Decreased
  - Exercise capacity
  - Skeletal muscle oxidative capacity
  - Coagulation
  - Immune response
  - Cognitive function
  - Sexual function
  - Appetite/nutrition
  - Quality of life
  - Growth in children
- Increased
  - Depression
  - Sleep/awake pattern
  - Cardiac output
  - Angina
  - LVH
  - Cardiac failure
  - Myopathy
  - Morbidity
  - Mortality

Anemia Is a Mortality Multiplier



DM = diabetes mellitus.
Medicare sample (5%) follow-up from 1996 to 1997 of enrollees aged ≥65 years, adjusted for age, sex, and race.

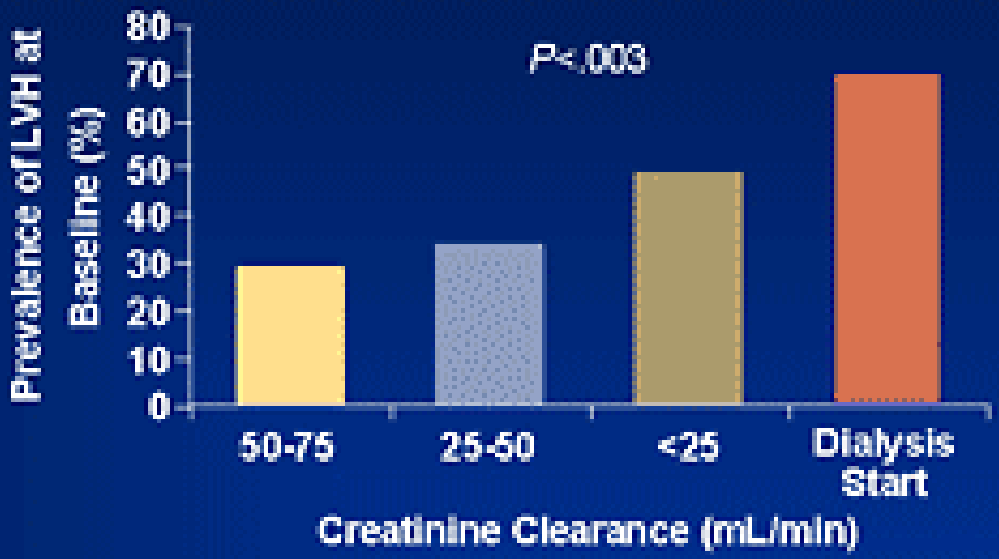
Collins AJ. *Adv Stud Med.* 2003;3(3C):S194-S197.

Cardiovascular Care Is Suboptimal in Patients With CKD

Predictors of LVH

Risk Factors	↑ Risk of LVH
Decrease in Hb by 1.0 g/dL	6%
Increase in systolic BP by 5 mm Hg	3%

Prevalence of LVH in CKD

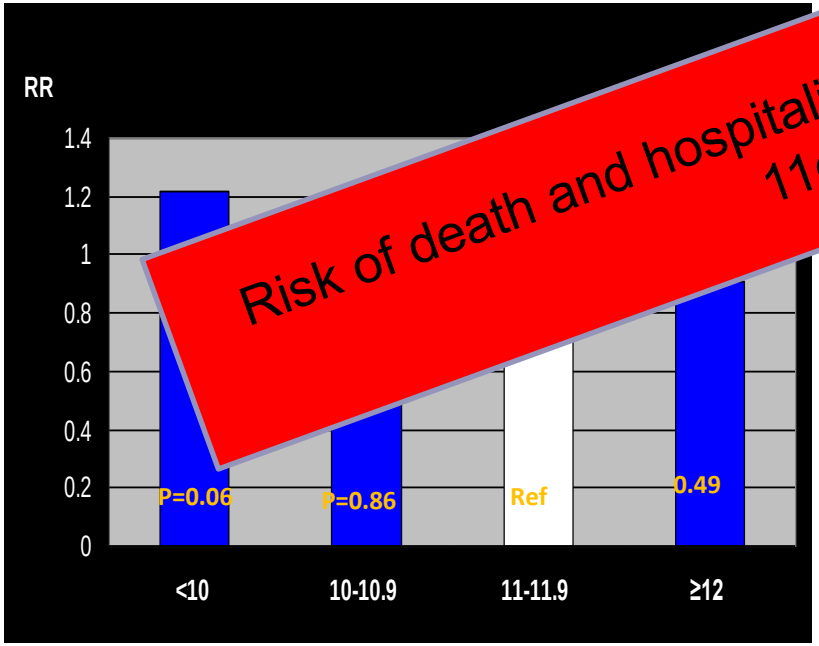


- LVH is an independent risk factor for death in patients with ESRD
- 11% of patients with CKD on BP medication have optimal levels

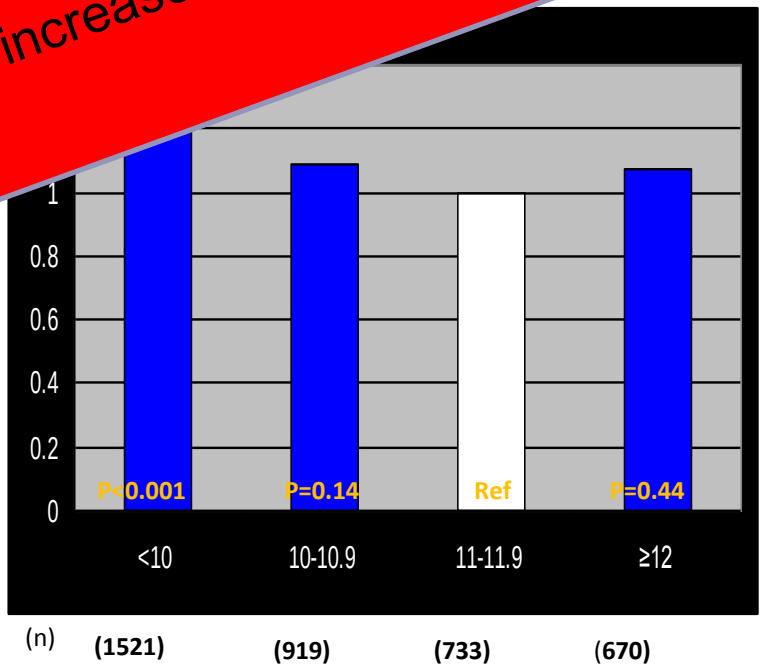
Coresh J, et al. *Arch Intern Med*. 2001;161:1207-1216; Levin A, et al. *Am J Kidney Dis*. 1996;27:347-354; Levin A, et al. *Am J Kidney Dis*. 1999;34:125-134.

Relationship between Hb level and relative risk of death or hospitalisations

Relative risk of death



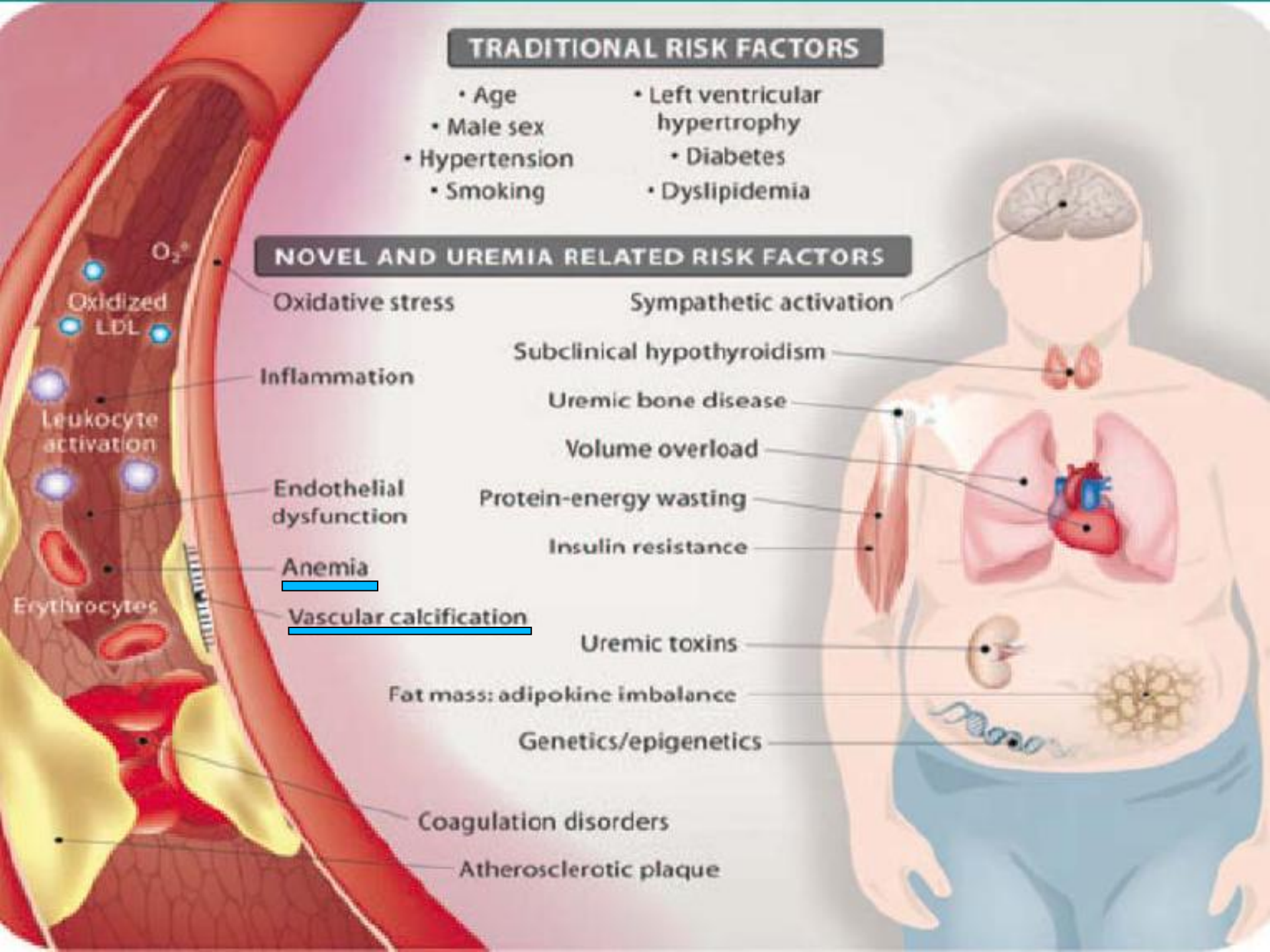
Relativ tion



Risk of death and hospitalisation increases with Hb < 11gm/dl

Hb g/dl at study entry

Locatelli et al *NDT* 2004


TRADITIONAL RISK FACTORS
• Age
• Male sex
• Hypertension
• Smoking
• Left ventricular hypertrophy
• Diabetes
• Dyslipidemia
NOVEL AND UREMIA RELATED RISK FACTORS
Oxidative stress
Sympathetic activation
Subclinical hypothyroidism
Inflammation
Uremic bone disease
Volume overload
Protein-energy wasting
Endothelial dysfunction
Insulin resistance
Anemia
Vascular calcification
Uremic toxins
Fat mass: adipokine imbalance
Genetics/epigenetics
Coagulation disorders
Atherosclerotic plaque
O_2^-
Oxidized LDL
Leukocyte activation
Erythrocytes

If a cure is not achieved, the kidneys will pass on the disease to the heart

Huang Ti Nei Ching Su Wen
The Yellow Emperor's Classic of Internal Medicine
~2000 B.C.

Benefits of Increased Haemoglobin in ESRD

- Improved quality of life
- Improved cognitive function
- Improve exercise capacity
- Improved sexual function
- Improved systemic haemodynamics and cardiac function
- Regression of LVH
- Decreased mortality risk
- Decreased hospital stay

Investigating anaemia in CKD

Investigations

- **FBC**
  - Hb
  - WCC
  - Platelets
  - MCV
  - RCC
  - Htc
- B12
  - necessary for rapid synthesis of DNA during cell division
- Folate
  - Required for cell division in bone marrow to produce RBC's

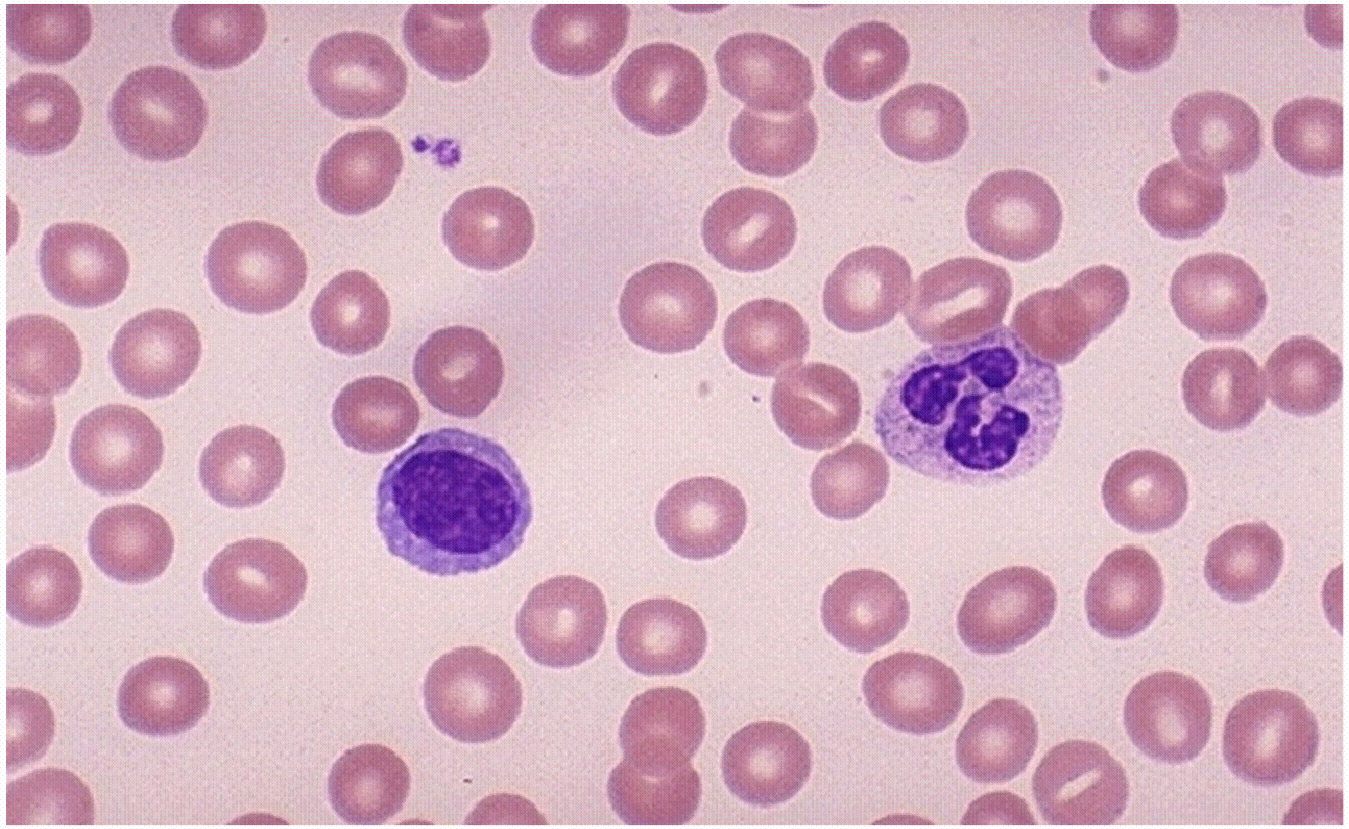
- **Iron studies**
- Iron
- Ferritin
- Transferrin
- Transferritin saturation (TSAT)

- CRP
- Inflammatory marker

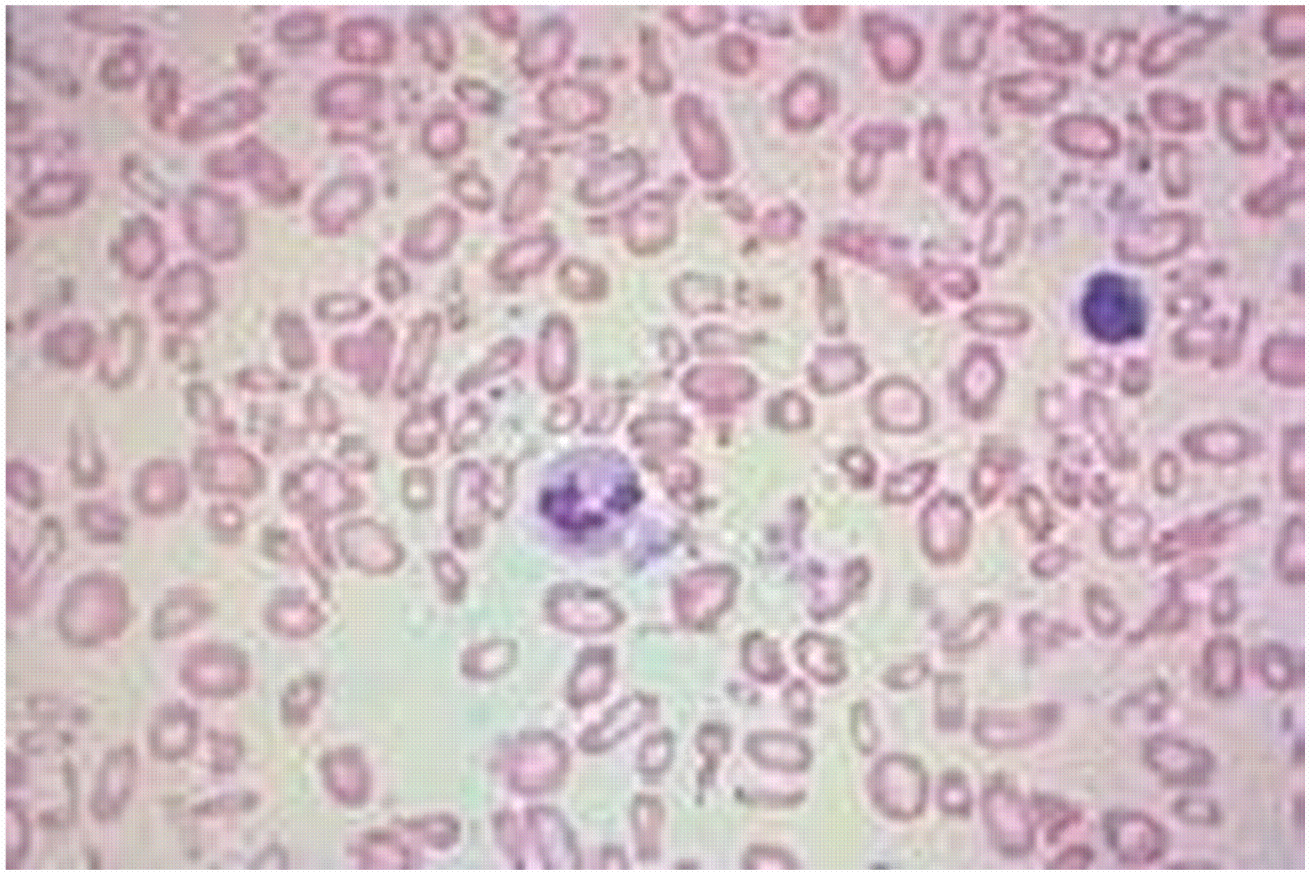
Classification of anaemia

- Mean cell volume (MCV)
  - average size of one RBC
- Microcytic MCV < 80
- Normocytic 80 - 100
- Macrocytic > 100

Normocytic RBCs



Microcytic hypochromic RBCs



Factors That Cause or Contribute to Anemia

- Insufficient production of endogenous erythropoietin
- Iron deficiency
- Acute/chronic inflammatory conditions
- Severe hyperparathyroidism
- Aluminum toxicity
- Folate deficiency
- Decreased red-blood-cell (RBC) survival
- Hypothyroidism
- Hemoglobinopathies (eg, α-thalassemia, sickle-cell anemia)

NKF. *Am J Kidney Dis*. 2001;37(suppl 1):S182.

Management of Anemia in CKD

Management

- **Look for loss**
  - Blood loss, malignancy

- **Correct RBC precursors**
  - Iron deficiency
  - B12, folate deficiency

- **Correct EPO deficiency**
  - with erythropoiesis stimulating agent (ESA)

- **Blood transfusions**
  - very cautiously

Types of Erythropoiesis Stimulating Agent

First generation:

- Epoetin alfa: Eprex
- Epoetin beta: Recormon

Second generation

- Darbopoietin

Third generation

- Continuous erythropoietin receptor activator : Mircera

Erythropoiesis Stimulating Agent (ESA)

- Before commencing ESA, make sure adequate
  - Iron stores *** likely an ongoing requirement
  - red cell folate
  - Vitamin B12

Key Management 2: How to Initiate ESA?

	EBPG	NKF-K/DOQI
Recommended start dose of epoetin	50-150 IU/kg/week	80-120 IU/kg/week SC 120-180 IU/kg/week IV
Preferred route of administration	SC	SC
Dose indicating an inadequate response	300 IU/kg/week	300 IU/kg/week SC 450 IU/kg/week IV

International Guidelines

Dosing Protocol

- Start when Hb persistently <11g/dl
- Start with 4,000u/week @ 50-150Iu/kg/week
- Aim for Hb100 – 110 g/L

OR (MICERA)

For naïve patients, the recommended starting dose is 0.6ug/kg, administered (IV or sc) once every week

After correction is achieved, double the dose for the once-monthly maintenance

Previously Calculated weekly ESA dose

	Micera
<8000 u	120 mcg/month
8000-16000	200 mcg/month
>16000	360mcg/month

Available strength :50,75,100,150,200mcg

Concern with EPO

- Hypertension, especially if Hb ↑rised too fast
  - Ideally < 180mmHg systolic.

  HPT may be indicative of fluid overload

  Seziures
  - Up to 3% in first 3/12 of Rx

- Pure red cell aplasia (PRCA)

Causes of EPO not working

- Iron deficiency ** *most common* **
- B12 & Folate deficiency
- Inflammation
- ACE inhibitors
- Hyperparathyroidism – bone marrow fibrosis
- Aluminium toxicity
- Inadequate dialysis
- Malignancies, including multiple myeloma

Iron Studies

- **Ferritin**
  - Iron storage protein, giving an indirect measurement of stored iron
  - ↓ ferritin always Iron def, but high in inflammation (inflammatory marker)
- **Transferrin**
  - Transports iron from stores to the bone marrow.
- **Transferrin saturation**
  - Gives a measure of the iron available to bone marow
  - Useful to detect functional iron deficiency

Iron Deficiency

- TSAT < 20%
- Ferritin < 100ng/mL (not on EPO)
- Ferritin < 300ng/mL (on EPO)

- Aim
  - ferritin around 200-500ng/ml if on EPO
  - TSAT 30-40%

Iron Supplement

- Oral
  - Suboptimal,limited absorption,side effects
- IM
  - Painful,discolouration,muscle sarcomas,variable absorption
- IV
  - Ideal. Single and maintenance dosing (500mgs)
  - Iron dextran/Sucrose

Optimal Hb Target?

- Since the introduction of rHuEPO in 1989, the level of anaemia correction has been debated.

- The clinical benefits of correcting Hct to >30% have shown improved ex capacity, cognitive function, better QoL, improved cardiac function, and improved sexual function.

- Study by Besarab et al showed no benefit of achieving Hct of 39 to 42% in patients with NYHA class I to III cardiac disease.

Old School Of Thought

- NKF-DOQI guidelines:

- recommend a target Hct of between 33% and 36% or a Hb conc of between 11 and 12g/dl.

- EBPG

- recommend that the target Hb should be >11g/dl (Hct >33%). No upper limit is specified.

New School of Thought

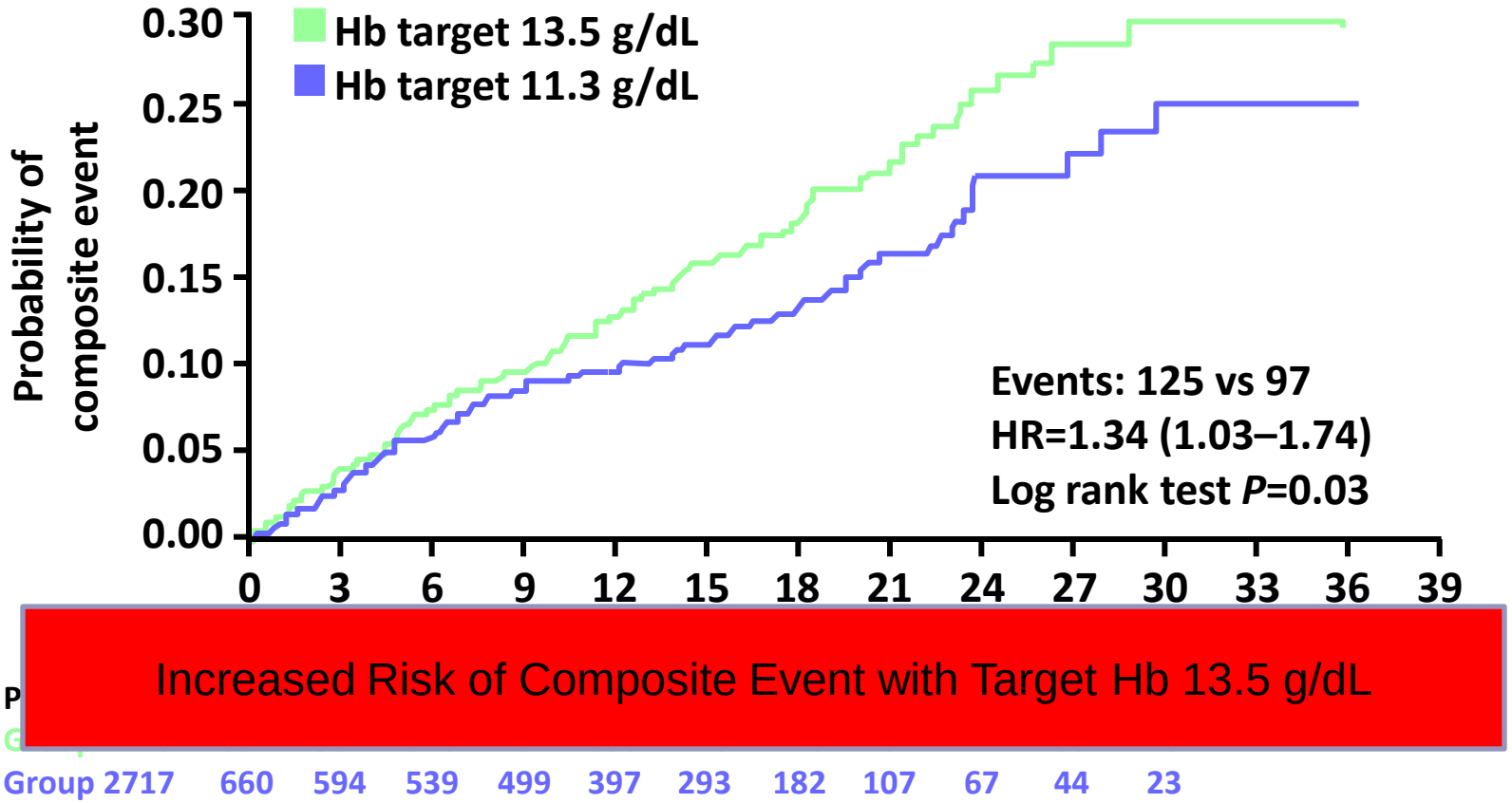
- Higher is necessary better!

	Normal Hematocrit Study (NHS) (N = 1265)	CHOIR (N = 1432)	TREAT (N = 4038)
Time Period of Trial	1993 to 1996	2003 to 2006	2004 to 2009
Population	CKD patients on hemodialysis with coexisting CHF or CAD, hematocrit 30 ± 3% on epoetin alfa	CKD patients not on dialysis with hemoglobin < 11 g/dL not previously administered epoetin alfa	CKD patients not on dialysis with type II diabetes, hemoglobin ≤ 11 g/dL
Hemoglobin Target; Higher vs. Lower (g/dL)	14.0 vs. 10.0	13.5 vs. 11.3	13.0 vs. ≥ 9.0
Median (Q1, Q3) Achieved Hemoglobin Level (g/dL)	12.6 (11.6, 13.3) vs. 10.3 (10.0, 10.7)	13.0 (12.2, 13.4) vs. 11.4 (11.1, 11.6)	12.5 (12.0, 12.8) vs. 10.6 (9.9, 11.3)
Primary Endpoint	All-cause mortality or non-fatal MI	All-cause mortality, MI, hospitalization for CHF, or stroke	All-cause mortality, MI, myocardial ischemia, heart failure, and stroke
Hazard Ratio or Relative Risk (95% CI)	1.28 (1.06 - 1.56)	1.34 (1.03 - 1.74)	1.05 (0.94 - 1.17)
Adverse Outcome for Higher Target Group	All-cause mortality	All-cause mortality	Stroke
Hazard Ratio or Relative Risk (95% CI)	1.27 (1.04 - 1.54)	1.48 (0.97 - 2.27)	1.92 (1.38 - 2.68)

CHOIR study

(Correction of Haemoglobin and Outcomes In Renal Insufficiency)

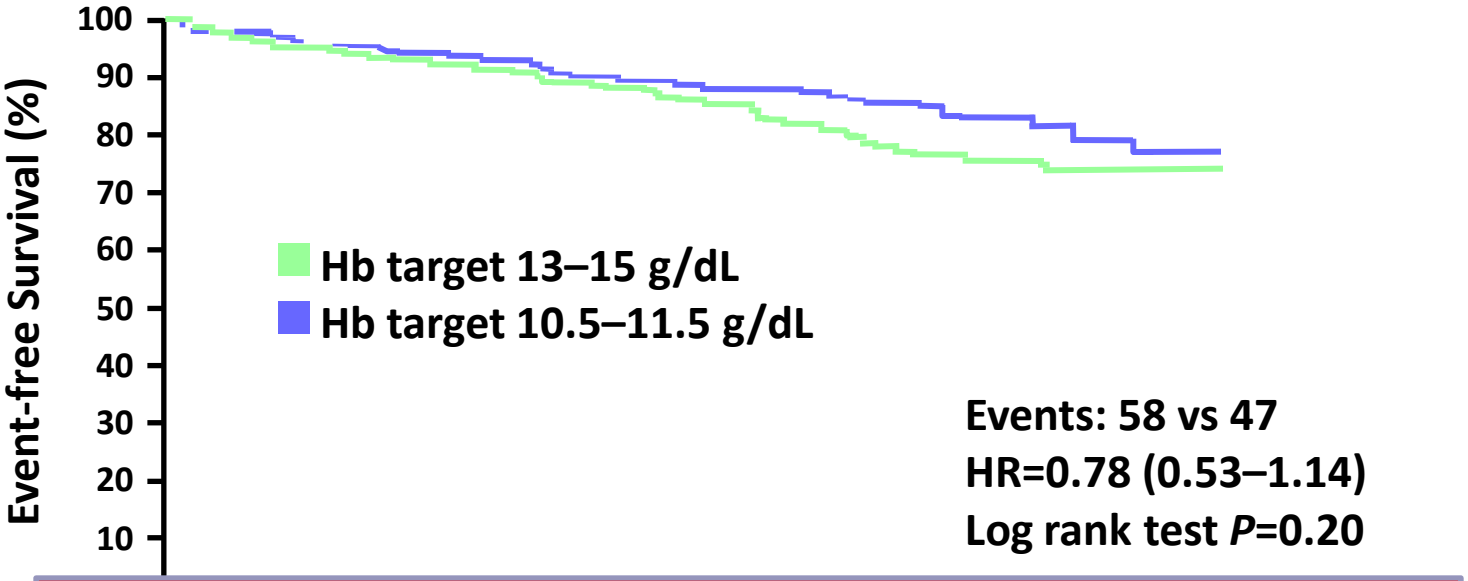
Time to the primary composite endpoint



Singh et al. *N Engl J Med*. 2006;355:2085-2098

CREATE study
(Cardiovascular risk Reduction by Early Anaemia Treatment with Epoetin beta)

Time to the primary endpoint of a first cardiovascular event†



No Significant Difference in Time to First CV Event

Patients at									
Group 1	301	279	268	249	207	158	97	56	2
Group 2	302	286	272	257	223	177	121	61	2

†Before censoring of data on patients at the time of initiation of dialysis

Drüeke et al. *N Engl J Med.* 2006;355:2071-2084

TREAT study

- Trial to Reduce Cardiovascular Endpoints with Aranesp
- 4000 patients
- CKD not requiring dialysis, DM
- Randomized assigned to Hb 13gm/dl vs 9gm/dl
- Result: No statistically difference in all-cause mortality and cardiovascular morbidity (heart failure, heart attack, stroke)

- Increasing evidence that it may be appropriate to treat each patient individually, and to tailor treatment according to a number of physiological and lifestyle variables, avoiding higher Hb in certain patient groups (such as those with cardiac problems).

FDA Warning

[24-6-2011] The U.S. Food and Drug Administration (FDA) is informing healthcare professionals of modified recommendations for **more conservative dosing** of Erythropoiesis-Stimulating Agents (ESAs) in patients with chronic kidney disease (CKD) to improve the safe use of these drugs

ESA labels now **recommend**:
For patients with CKD, consider starting ESA treatment when the hemoglobin level is less than 10 g/dL. This advice does not define how far below 10 g/dL is appropriate for an individual to initiate. This advice also does not recommend that the goal is to achieve a hemoglobin of 10 g/dL or a hemoglobin above 10 g/dL. Individualize dosing and use the lowest dose of ESA sufficient to reduce the need for red blood cell transfusions. Adjust dosing as appropriate

FDA Recommendations

1) Using ESAs to target a hemoglobin level of greater than 11 g/dL increases the risk of serious adverse cardiovascular events and has not been shown to provide additional patient benefit.

2) No clinical trial to date has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks.

3) The ESA Medication Guide (Epogen/Procrit or Aranesp) should be provided to each patient or their representative when an ESA is dispensed.

4) The lowest ESA dose sufficient to reduce the need for red blood cell transfusions should be used.

5) For patients with CKD not on dialysis:

-Consider initiating ESA treatment only when the hemoglobin level is less than 10 g/dL and the following considerations apply:

a) The rate of hemoglobin decline indicates the likelihood of requiring a red blood cell transfusion; and

b)Reducing the risk of alloimmunization and/or other red blood cell transfusion-related risks is a goal.

-If the hemoglobin level exceeds 10 g/dL, reduce or interrupt the dose of ESA and use the lowest dose of ESA sufficient to reduce the need for red blood cell transfusions.

6) For patients with CKD on dialysis:

Initiate ESA treatment when the hemoglobin level is less than 10 g/dL.
If the hemoglobin level approaches or exceeds 11 g/dL, reduce or interrupt the dose of ESA.

7) When initiating or adjusting therapy, monitor hemoglobin levels at least weekly until stable, then monitor at least monthly.

8) For patients who do not respond adequately over a 12-week escalation period, increasing the ESA dose further is unlikely to improve response and may increase risks.

Case Study 1

AB is a 77-year-old retired male office worker with a 6-year history of type 2 diabetes who has been treated with oral hypoglycemic agents and insulin. He had bilateral toe amputations 3 years ago, has had bilateral cataract surgery (3 and 4 years ago), and experienced a myocardial infarction 2 years ago.

He presents to his nephrologist complaining of dyspnea on minimal exertion and fatigue. The workup shows clinical evidence of chronic kidney disease (CKD) progression, including pulmonary congestion and hyperkalemia. His blood pressure is 146/72 mm Hg and his pulse rate is 64 beats per minute. Cardiovascular examination revealed a 1/6 systolic murmur and neurologic examination exhibited bilateral sensory neuropathy. The pulmonary examination reveals decreased breath sounds at the bases and scattered rales. The fecal occult blood test is negative. Both lower extremities exhibit 2+ pitting edema.

His medications include enalapril 10 mg a day, amlodipine 10 mg a day, rosuvastatin 10 mg a day, furosemide 40 mg daily, and aspirin 150mg a day.

His blood urea nitrogen (BUN) and creatinine have increased from 18 and 316umol, respectively, 6 months ago to 25umol/dL and 572umol/dL, respectively, at this most recent visit. Other laboratory values are sodium 133 mmol/L, potassium 6.2 mmol/L, chloride 94 mmol/L, CO_2 18.0 mmol/L, phosphate 4.2 mg/dL, glucose 216 mg/dL, white blood cell (WBC) count 8600/uL, hemoglobin (Hb) 8.9 g/dL, hematocrit (Hct) 26.9%, platelets 170,000/µL, estimated glomerular filtration rate (eGFR) 8 mL/min, serum ferritin 259 ng/mL, serum iron 30 µg/dL, transferrin saturation (TSAT) 18.5%, total iron binding capacity 181 µg/dL, folic acid 7.6 µg/L, and vitamin B_{12} 846 pg/mL.

From the information given, what potential source of anemia is most likely in this patient?

1) Absolute iron deficiency
2) Dietary deficiencies
3) Erythropoietin (EPO) deficiency or hyporesponsiveness
4) Medications

Iron Deficiency Anemia

Iron Status	Description	Indicators	Contributing Factors
Absolute iron deficiency	Depletion of iron stores and absence of stainable iron in bone marrow; occurs when iron is insufficient for Hb synthesis	Ferritin <100 ng/mL, TSAT <20%	HD patients at increased risk owing to blood loss; dietary deficiencies
Relative (functional) iron deficiency	Stored iron is sufficient, circulating iron is deficient (iron stored in RES is not released to transferrin)	•Ferritin normal or elevated, TSAT <20% •IV iron results in increased Hb or decreased ESA requirement •No Hb response to ESA therapy in patients with adequate iron stores	•ESA therapy stimulates RBC production beyond available iron supply for Hb synthesis •Chronic inflammation, infection, malignancies, autoimmune disease •Hepcidin release occurring as iron stores ↑
Iron overload	Accumulation of excessive iron in tissues and organs	Ferritin >800 ng/mL and TSAT chronically >50%	•Transfusions •IV iron overshoots

Type of Iron

Agent (Trade Name)	Indications	Presentation	Dosage & Administration	Half-life	Safety Profile[a]
Approved Parenteral Iron Formulations					
HMW iron dextran (Dexferrum)	Treatment of iron deficiency when oral administration is unsatisfactory or impossible	Single-dose 2-mL vial containing 100 mg elemental iron (50 mg/mL)	Test dose of 0.5 mL, then single IV dosage based on BW and Hb target	60 hr	SAE risk: high Risk of dextran-induced anaphylaxis: yes
LMW iron dextran (INFeD)	Treatment of iron efficiency when oral administration is unsatisfactory or impossible	Single-dose 2-mL vial containing 100 mg of elemental iron per mL (50 mg/mL)	Test dose of 0.5 mL, then single IM or IV dosage based on BW and Hb target	5-20 hr	SAE risk: moderate Risk of dextran-induced anaphylaxis: yes
Iron sucrose (Venofer)	Treatment of iron deficiency anemia in adult patients with CKD	Single-dose 2.5-, 5-, or 10-mL vials containing 50 mg, 100 mg, or 200 mg elemental iron (20 mg/mL)	Test dose, then IV injection HD patients: IV infusion or slow injection (100 mg) over 15 min Cumulative dose of 1000 mg over 10 HD sessions	6 hr	SAE risk: low
Ferric gluconate (Ferrlecit)	Treatment of iron deficiency anemia in patients ≥6 y with CKD receiving HD with supplemental EPO	Single-dose 5-mL vial containing 62.5 mg of elemental iron (12.5 mg/mL)	IV infusion or slow injection of 10 mL (125 mg of elemental iron) per dialysis session Cumulative dose of 1000 mg over 8 HD sessions	1 hr	SAE risk: low

INRAVENOUS IRON PROTOCOL

To administer if Serum ferritin ≤ 200ng/ml and TSAT ≤ 30%
(If serum ferritin 200-500 ng/ml or TSAT = 30%, IV iron maybe given

To administer test dose in patient receiving IV iron for the first time
(IV iron 25mg STAT)

If develop allergic reaction, STOP IV iron and inform Dr-in-charge

If no complication, to proceed with treatment

Optimal target:
Serum ferritin: 200-500 ng/ml
TSAT ≥ 30%

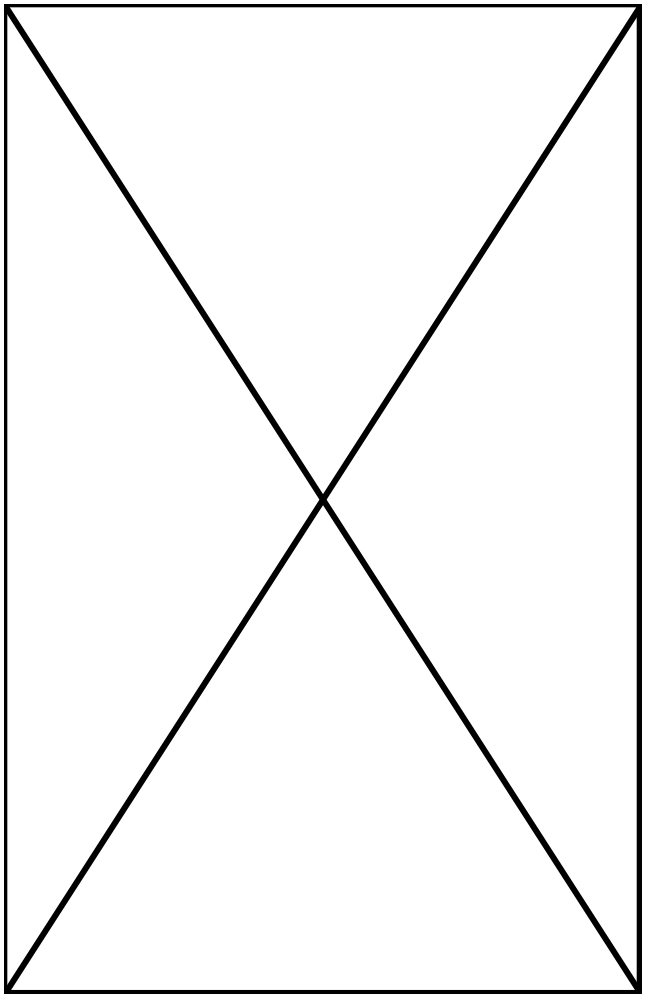
To administer IV iron 100 mg in 100 ml normal saline, given at 3rd hour of every HD session (total of 10 sessions)

Repeat Hb, iron studies and TSAT after 2 weeks completion of IV Iron

- If serum ferritin ≥ 800ng/ml and TSAT ≥ 50%, STOP IV iron
- If serum ferritin is 500-800 ng/ml, to give IV iron 100 mg every month
- If serum ferritin is 200-500ng/ml, to give IV Venofer 100mg every 2 weeks
- If serum ferritin ≤ 200ng/ml, to repeat protocol of 10 doses

Other Causes of Anemia in CKD

Haemodialysis adequacy



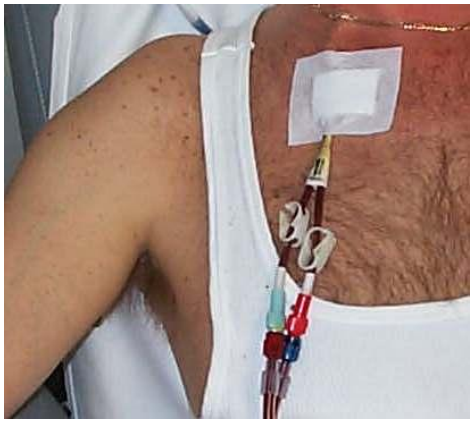
- Increase in epoetin dosage up to 54% in underdialysed patients
- HD should be performed 3x/week
- Duration of HD should not be < 4 h per session if HD 3x/week
- HD dose quantified every 3/12 using Kt/V

  (Kt/V ≥1.2, URR > 65 %)

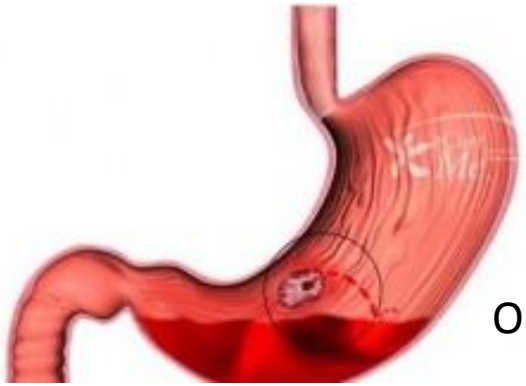
continuous monitoring & routine blood tests

residual blood in extracorporeal circuits (dialysers & tubing)

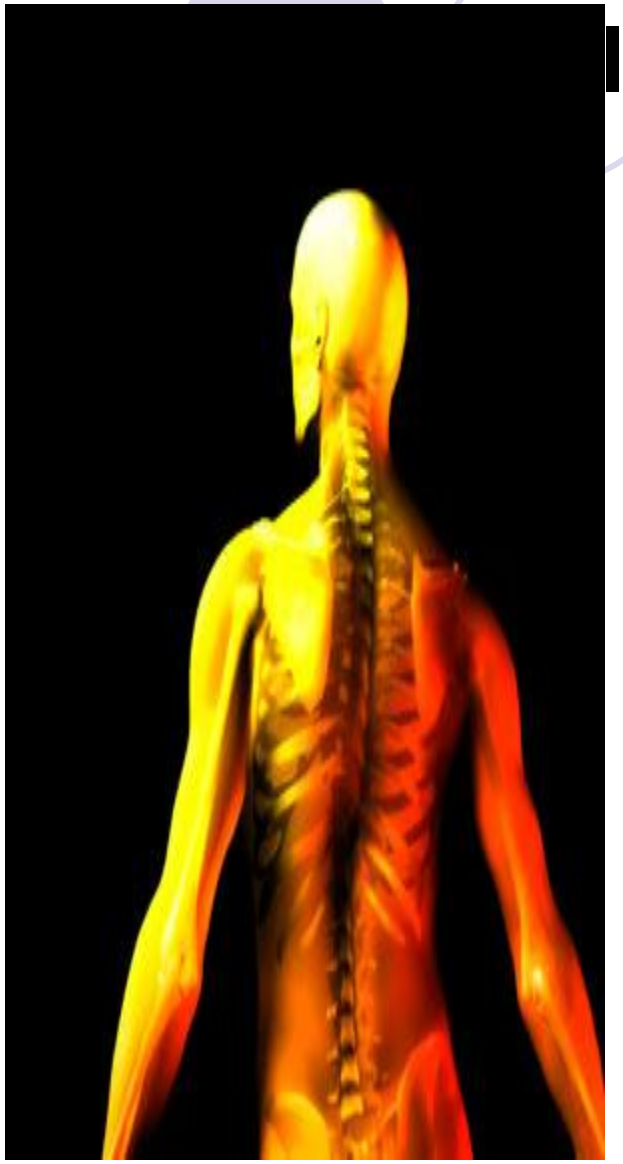
BLOOD LOSS in HD patient



the use of catheters



Occult gastrointestinal loss



lammation

- CRP routinely every 3 months
- If CRP elevated (>5mg/l), biocompatibility of dialyser membrane and haemodialysis fluid quality should be checked
- Patient with i.v catheters
- Failed renal transplant

Drugs- ACEi or ARB

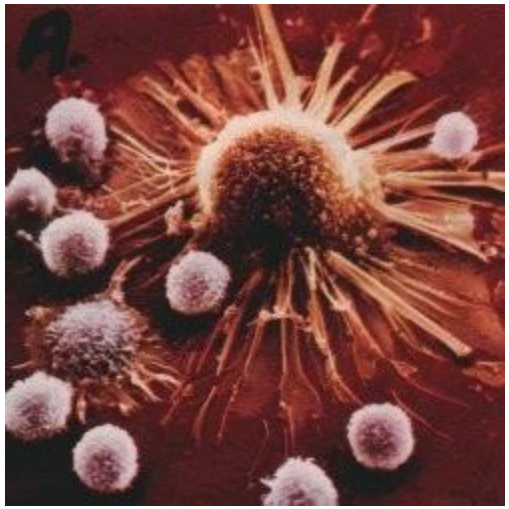
Renal bone disease

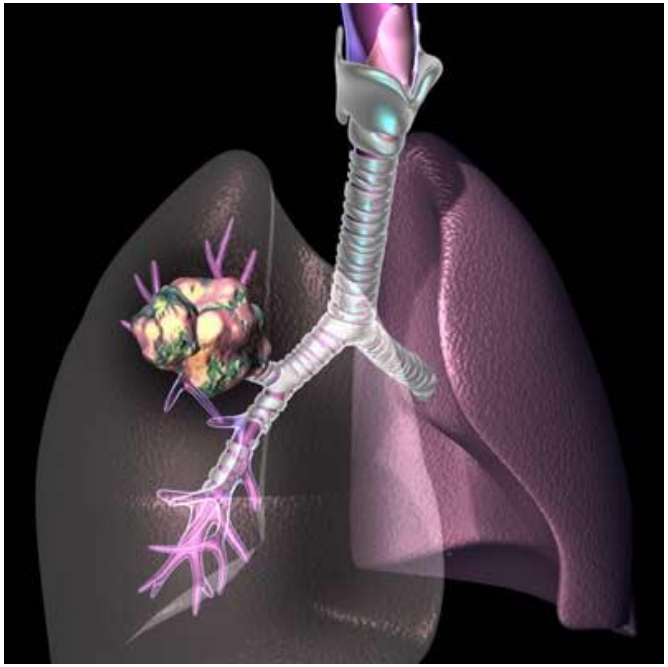
- Hyperparathyroidism- bone marrow fibrosis
- Aluminium toxicity

Haemoglobinopathy

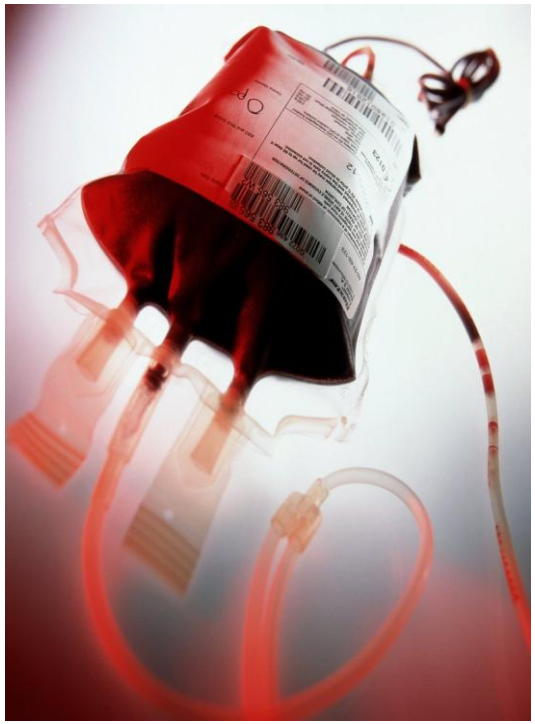
- Thalassaemia
- Sickle cell anaemia

Malignancy/cancer





Anaemia and Blood Transfusions



- Please try to **avoid**!
- Hb < 80 g/L and symptomatic
- Blood transfusions expose patients to white blood cells in the transfusion which have human leucocyte antigens (HLA) on their surface. The patients then produce HLA antibodies - “sensitization” - making it more difficult to find a good donor match for a future kidney transplant.

Conclusion

- Although anaemia management has improved in patients with CKD over the last 5 years, many patients still have Hb below the current recommendations
- ESA usage and correction of iron deficiency is still not optimum in HD units
- Significant improvement in anaemia management can be made by good medical practice

- Malaysian National Renal Registry data……..

Table 6.3.3: Distribution of Haemoglobin Concentration on Erythropoietin, HD patients 2000-2009

Year	No. of subject	Mean	SD	Median	LQ	UQ	% Patients ≤10g/dL	% Patients >10g/dL	% Patients ≤11g/dL	% Patients >11g/dL
2000	2332	9.4	1.7	9.4	8.3	10.5	65	35	85	15
2001	3049	9.4	1.6	9.4	8.3	10.5	65	35	85	15
2002	3859	9.5	1.7	9.5	8.4	10.7	62	38	81	19
2003	4783	9.6	1.6	9.6	8.5	10.7	61	39	81	19
2004	5806	9.8	1.6	9.9	8.8	10.9	54	46	77	23
2005	7218	10	1.6	10	8.9	11.1	50	50	73	27
2006	9415	10.1	1.6	10	9	11.1	50	50	72	28
2007	10696	10.2	1.5	10.3	9.1	11.3	44	56	69	31
2008	12985	10.2	1.5	10.3	9.1	11.3	44	56	69	31
2009	15169	10.3	1.5	10.4	9.2	11.4	42	58	67	33

Table 6.1.1: Treatment for Anaemia, HD patients 2000 to 2009

Year	No. of subjects	% on Erythropoietin	% received blood transfusion	% on oral iron	% received parenteral iron
2000	4392	56	15	88	5
2001	5194	62	13	88	5
2002	6108	67	10	85	7
2003	7017	72	12	83	8
2004	8064	74	11	80	10
2005	9344	81	14	74	11
2006	11679	83	18	76	16
2007	12907	85	15	74	17
2008	15348	88	16	63	23
2009	17540	89	15	60	26

Table 6.2.3: Distribution of Serum Ferritin on Erythropoietin, HD patients 2000-2009

Year	No. of subjects	Mean	SD	Median	LQ	UQ	% Patients ≥100 ng/ml
2000	1174	588.3	456.6	475.5	219	860	91
2001	1637	597.5	444.2	491	236	894.2	91
2002	2224	593.1	459.3	464.8	231.3	878.2	91
2003	3134	640.8	428.1	563.3	298	931	94
2004	3904	669.7	460.4	571	306	976.5	94
2005	5116	682.7	471	599.5	315.3	971.5	93
2006	6765	640.3	459	543	291.2	881	93
2007	8032	658.8	452.2	564.4	315.5	914	94
2008	9910	703.5	469.2	611.1	337.5	979.2	95
2009	11961	679.8	458.5	597.7	320.5	942	94

Table 6.2.7: Distribution of Transferrin saturation on Erythropoietin, HD patients, 2000-2009

Year	No. of subjects	Mean	SD	Median	LQ	UQ	% Patients ≥20 %
2000	1247	34.9	16.7	30.4	23	44	84
2001	1634	36.2	17.9	32.3	23.6	45	84
2002	1995	34.6	17.6	30.6	22.2	43.6	81
2003	2641	39.6	18.4	35.9	26.6	48.8	90
2004	3269	39.6	17	36.1	27.8	48.1	93
2005	4808	36.6	17.2	32.8	24.6	45	87
2006	6384	35.1	16.4	31.6	24.1	42.1	87
2007	7604	34.7	15.4	31.6	24.4	41.6	88
2008	9528	34.7	15.4	31.5	24	41.6	87
2009	11647	34	15.4	30.9	23.8	40.5	86

d) Proportion of patients on erythropoietin with transferring saturation ≥20%, HD centres

Year	No. of centres	Min	5th centile	LQ	Median	UQ	95th centile	Max
2000	43	20	60	78	86	94	100	100
2001	54	57	60	77	88.5	96	100	100
2002	60	32	54.5	70	83	92	100	100
2003	90	45	69	86	92.5	100	100	100
2004	113	53	73	90	94	100	100	100
2005	149	30	70	84	91	95	100	100
2006	187	20	61	80	90	95	100	100
2007	216	27	61	83	90	96	100	100
2008	264	12	65	81	89	95	100	100
2009	305	32	59	80	88	94	100	100

	Normal Hematocrit Study (NHS) (N = 1265)	CHOIR (N = 1432)	TREAT (N = 4038)
Time Period of Trial	1993 to 1996	2003 to 2006	2004 to 2009
Population	CKD patients on hemodialysis with coexisting CHF or CAD, hematocrit 30 ± 3% on epoetin alfa	CKD patients not on dialysis with hemoglobin < 11 g/dL not previously administered epoetin alfa	CKD patients not on dialysis with type II diabetes, hemoglobin ≤ 11 g/dL
Hemoglobin Target; Higher vs. Lower (g/dL)	14.0 vs. 10.0	13.5 vs. 11.3	13.0 vs. ≥ 9.0
Median (Q1, Q3) Achieved Hemoglobin Level (g/dL)	12.6 (11.6, 13.3) vs. 10.3 (10.0, 10.7)	13.0 (12.2, 13.4) vs. 11.4 (11.1, 11.6)	12.5 (12.0, 12.8) vs. 10.6 (9.9, 11.3)
Primary Endpoint	All-cause mortality or non-fatal MI	All-cause mortality, MI, hospitalization for CHF, or stroke	All-cause mortality, MI, myocardial ischemia, heart failure, and stroke
Hazard Ratio or Relative Risk (95% CI)	1.28 (1.06 - 1.56)	1.34 (1.03 - 1.74)	1.05 (0.94 - 1.17)
Adverse Outcome for Higher Target Group	All-cause mortality	All-cause mortality	Stroke
Hazard Ratio or Relative Risk (95% CI)	1.27 (1.04 - 1.54)	1.48 (0.97 - 2.27)	1.92 (1.38 - 2.68)

New Drugs in The Horizon

- Peginesatide (Hematide) is a pegylated, peptidic ESA (also called an erythropoietin mimetic [EPO mimetic]) that currently remains in phase 3 trials for the treatment of anemia of chronic kidney disease.
- Hypoxia inducible factor (HIF) is a key regulator of erythropoietic gene expression, iron absorption, energy metabolism, pH, and angiogenesis; as its name implies, HIF is induced by hypoxia.

Summary

- Anaemia is very common in CKD/ESRD patients
- Correcting anaemia improve quality life and also survival
- Multiple factors contribute to anaemia
- Erythropoetin deficiency is one of the commonest cause

Key factors in anaemia management:

- 1. **Exclude blood loss**
- 2. **Ensure dialysis adequacy**
- 3. **Correct deficiency of any RBC percursor**

  - Adequate dose of Erythropoiesis stimulating agent (ESA)
  - correct iron deficiency to improve effectiveness of ESA
  - correct folate and B12 deficiency

- 4. **Exclude other haematological cause**

  eg Thalasaemia trait, apalstic anaemia

Thank you