Anaemia in Pregnancy

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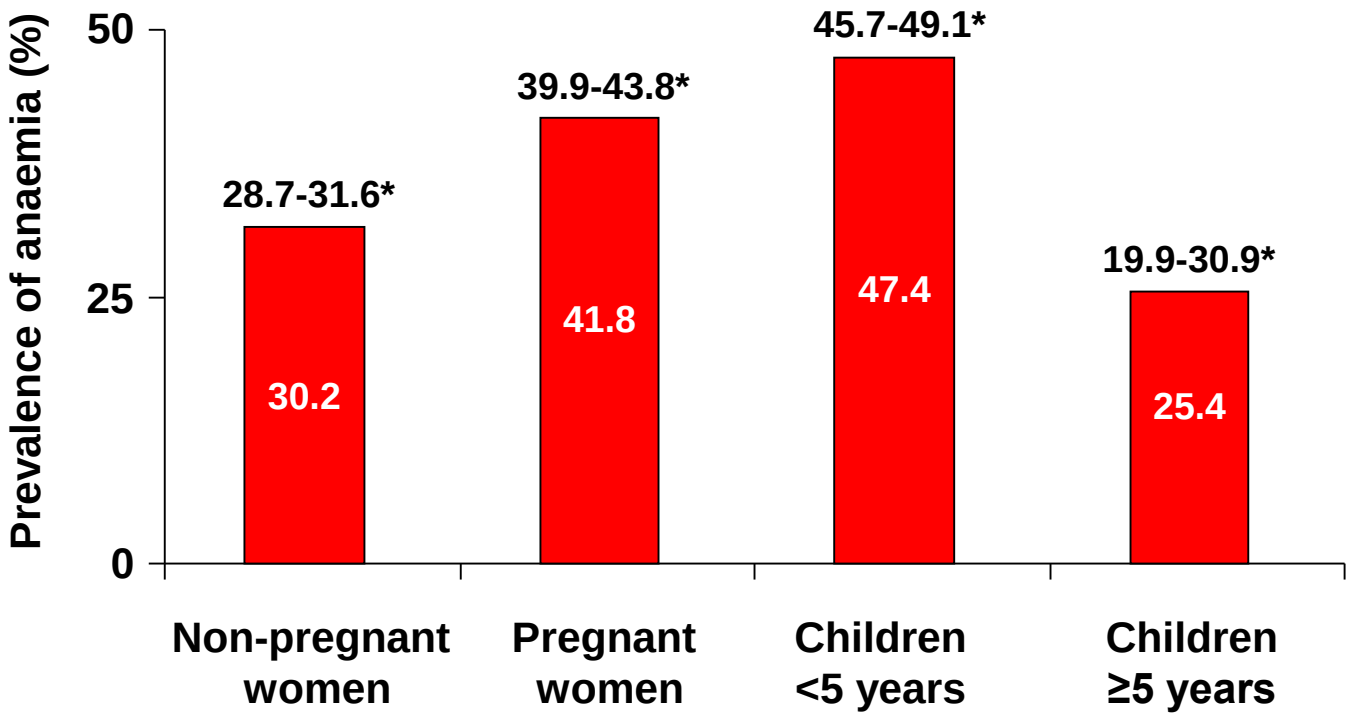
Leeds Teaching Hospitals NHS Trust

Prevalence of anaemia



*95% CI

World Health Organization. Worldwide prevalence of anaemia 1993–2005. Available at www.who.int

Anaemia during pregnancy is a global problem

WHO region	Prevalence of anaemia (%) in pregnant women [95% CI]	Number of pregnant women affected (millions) [95% CI]
Africa	57.1 [52.8-61.3]	17.2 [15.9-18.5]
Americas	24.1 [17.3-30.8]	3.9 [2.8-5.0]
Southeast Asia	48.2 [43.9-52.5]	18.1 [16.4-19.7]
Europe	25.1 [18.6-31.6]	2.6 [2.0-3.3]
Eastern Mediterranean	44.2 [38.2-50.3]	7.1 [6.1-8.0]
Western Pacific	30.7 [28.8-32.7]	7.6 [7.1-8.1]
Global	41.8 [39.9-43.8]	56.4 [53.8-59.1]

World Health Organization. Worldwide prevalence of anaemia 1993–2005.
Available at http://www.who.int/vmnis/publications/anaemia_prevalence/en/index.html.©WHO

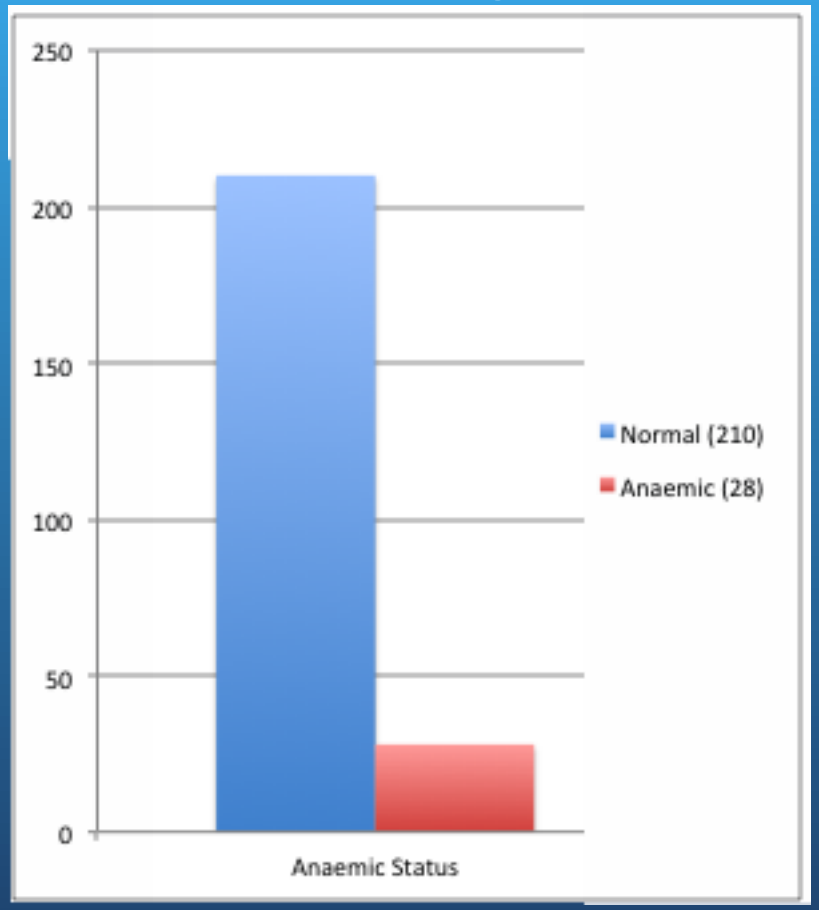
Anaemia in Pregnancy

- **Iron deficiency – 90% of all anaemias in pregnancy**
- B12 and Folate

- Affects 20% of the world's population
- It is poorly managed
- Significant cause of morbidity & mortality

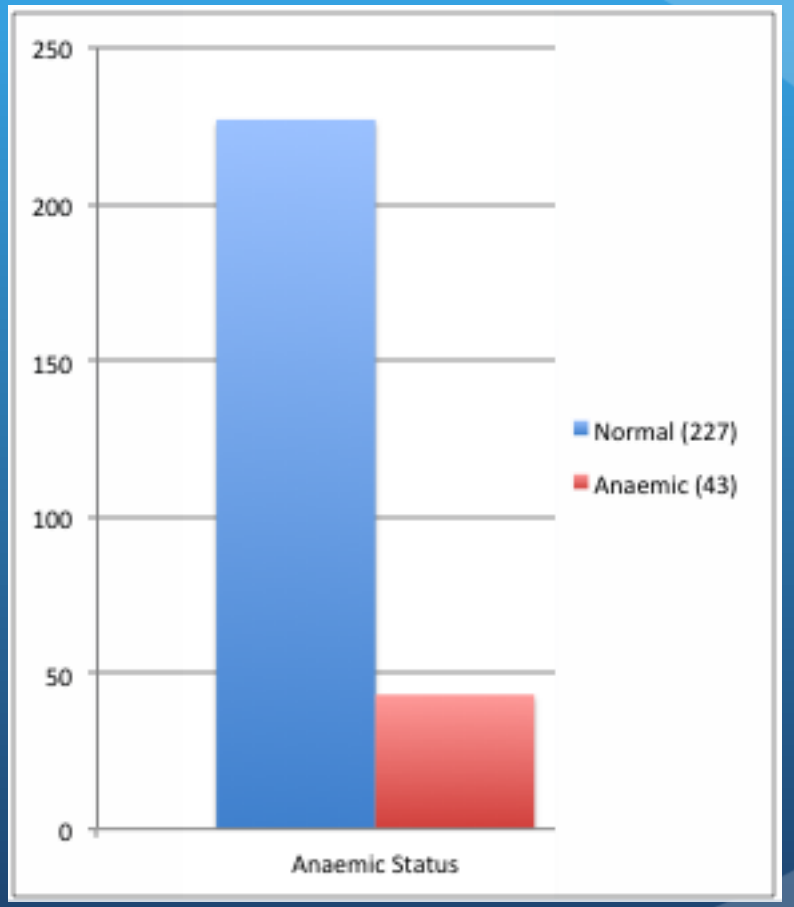
Anaemia Prevalence

Booking



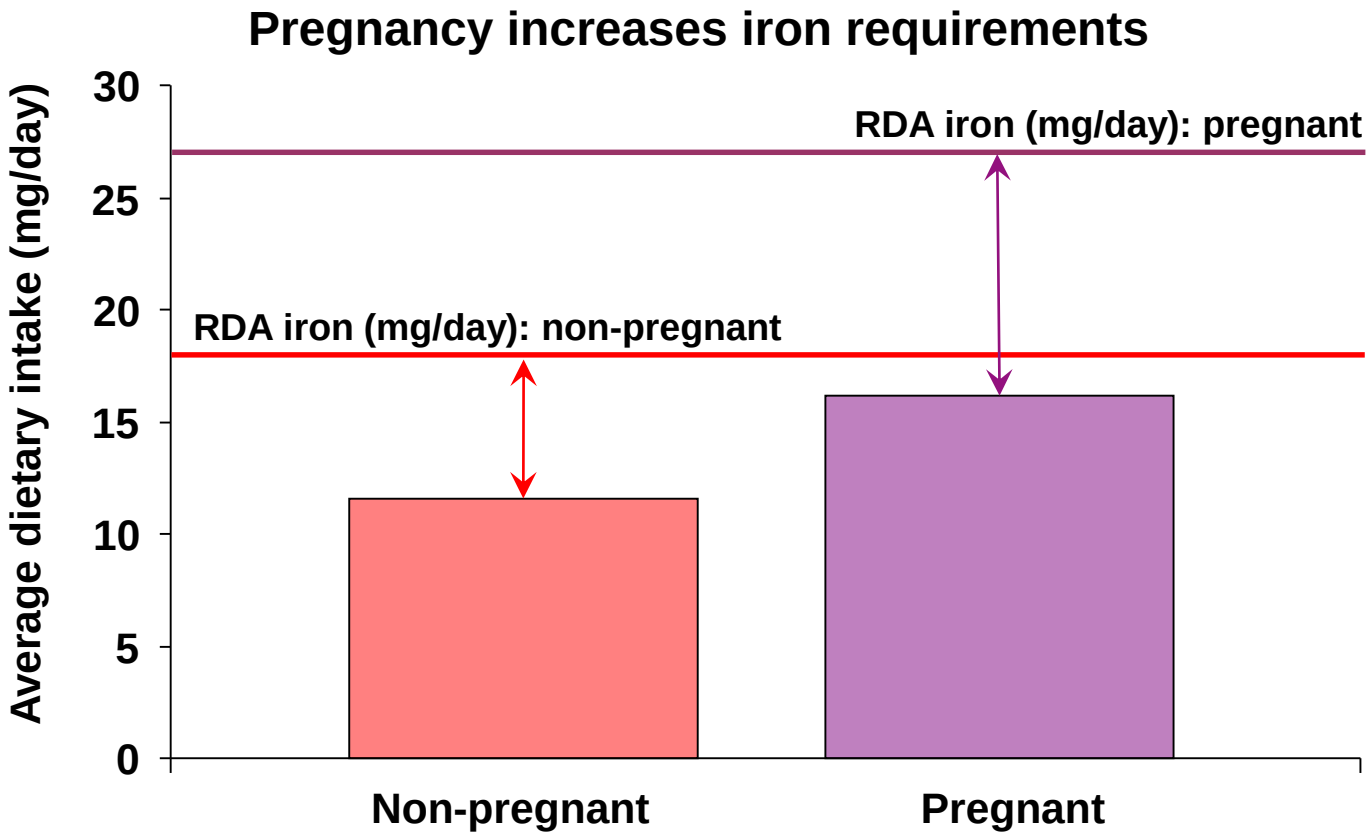
28/238 (11.8%)

28 Weeks



43/227 (18.9%)

Dietary iron intake compared to recommendations



RDA=Recommended daily allowance

1. Non-pregnant women www.hoptechno.com;
2. Institute of Medicine, Food and Nutrition Board 2001:1–28

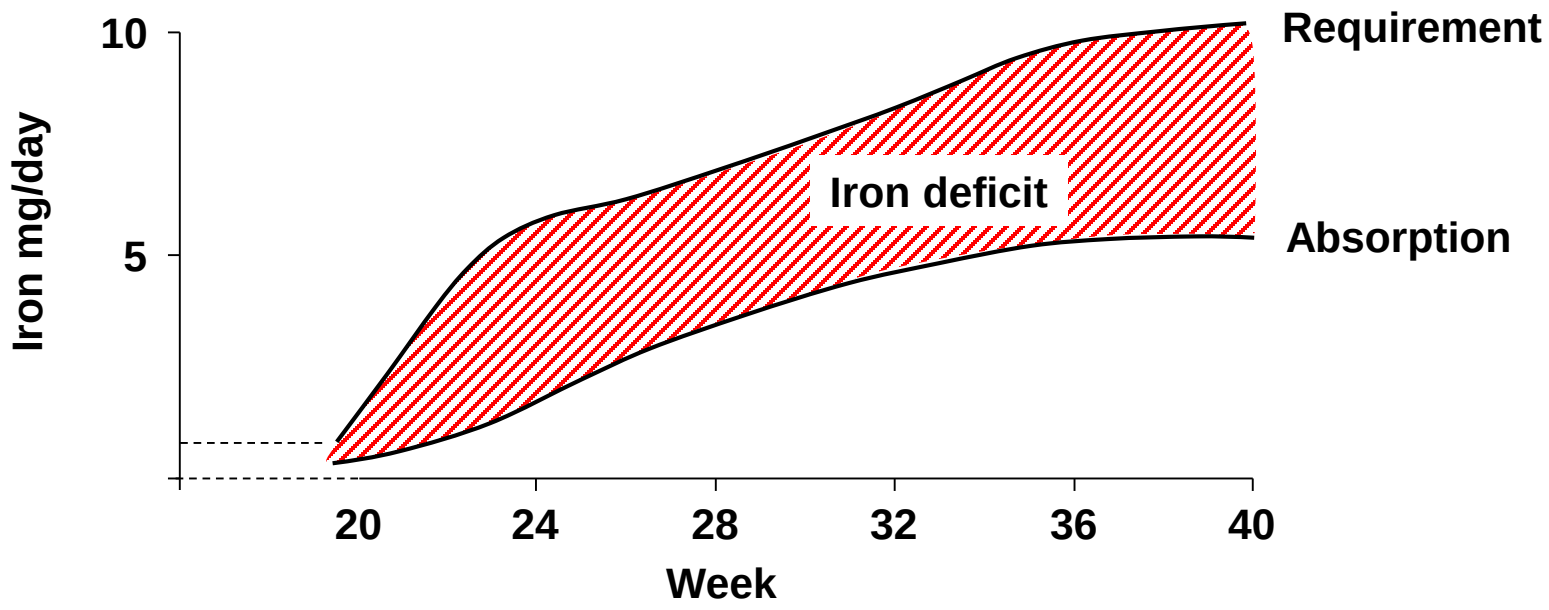
Iron Requirements

Source of increased iron requirement	Iron demand
Increase in red cell mass	450mg
Foetus & Placenta	300mg
Increase in basal maternal requirements	240mg
Blood loss at delivery (NVD)	250mg
Iron requirements for pregnancy, labour and delivery	**1240mg**

- Only 10% of dietary iron is absorbed
- Increased in pregnancy and triples from 1st to 3rd trimester, peaking at 30w

Iron deficit during pregnancy

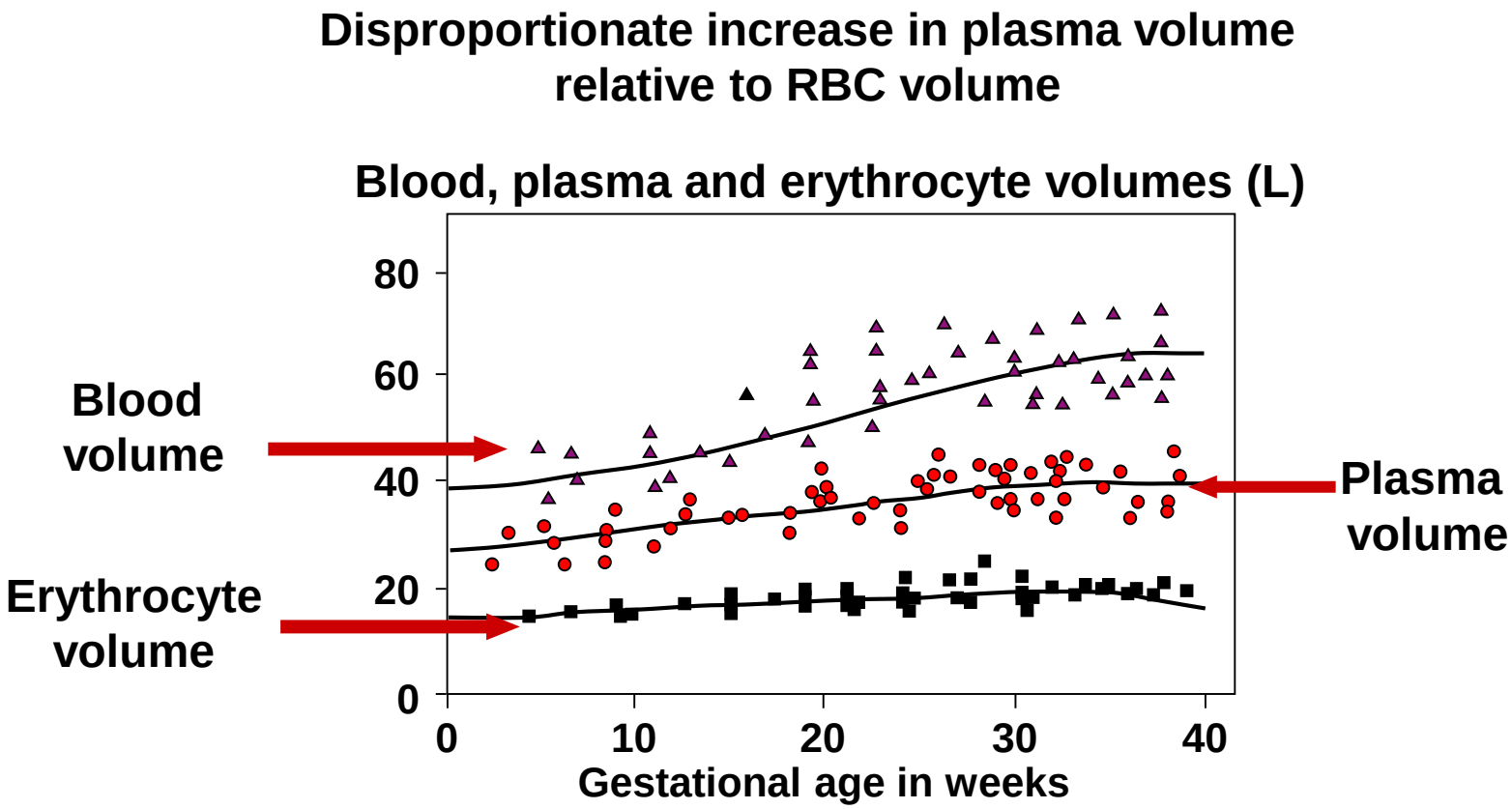
Difference between iron requirements and iron absorption has to be covered by iron mobilisation from stores or by iron supplementation



Hallberg L. In: Foman SJ, Zlotkin S, eds. Nutritional anemias. New York: Raven Press, 1992:13–28

Hallberg L. In: Foman SJ, Zlotkin S, eds. Nutritional anemias. New York: Raven Press, 1992:13–28. Reproduced with permission of Nestle.

Haemodilution affects Hb cut-off levels in pregnancy

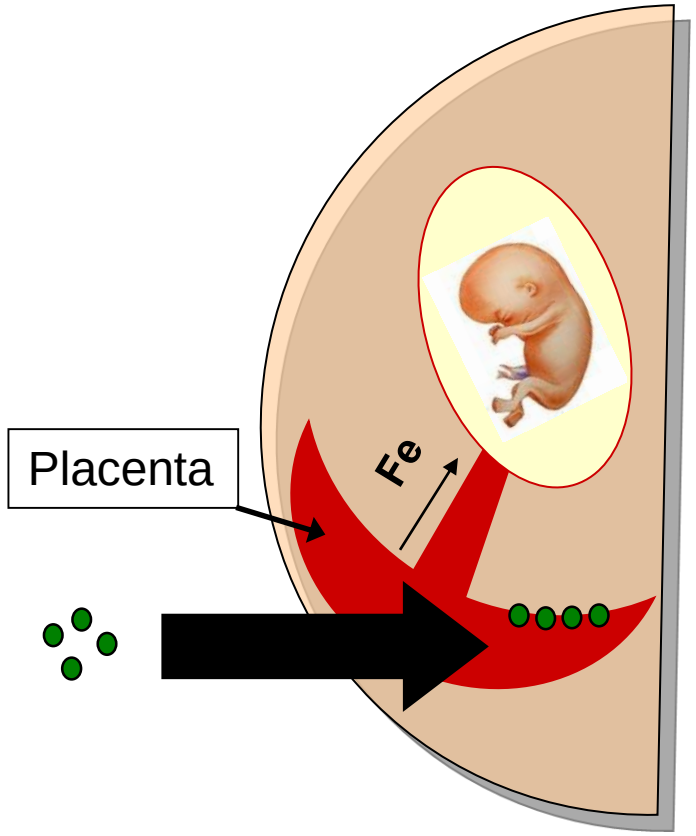


Longo LD, Hardesty JS. In: Scarpelli EM, Cosmi EV, eds. Reviews in Perinatal Medicine. New York: Alan R Liss Inc, 1984:35–59

With permission from UNI-Med science

Iron delivery to the foetus

- In pregnancy, iron is transferred from the mother to the developing foetus via the placenta
- When the maternal iron status is poor, the number of placental transferrin receptors increases to increase iron uptake
- If the mother is iron deficient, the capacity of this system may be inadequate to maintain iron transfer to foetus



Most iron transfer to the foetus occurs after week 30 of gestation

Allen LH. *Am J Clin Nutr* 2000;71:1280S–1284S
Breymann C & Huch R. Anaemia in pregnancy and the puerperium. 2008 UNI-MED

Iron in pregnancy

- Typical western diet contains 15mg/d of iron
- RDA of iron in pregnancy is 30mg/d

- Iron requirements in pregnancy rise from 1-2mg/d in 1st trimester to 4mg/d in 2nd trimester and peaking to 6mg/d in 3rd trimester
- Lactation requires 0.5-1.0mg/d of iron

- It takes 2 years of normal dietary iron to replace the iron lost with each pregnancy

- Only 50% of women have enough iron stored to fulfil the pregnancy requirements.

Hepcidin

- Central regulatory molecule in iron metabolism in mammals
- Regulates **ferroportin** → enteroctyes, macrophages, hepatocytes and trophoblasts
- Low hepcidin = high ferroportin = iron absorption is promoted
- Hepcidin is lower in pregnancy compared to non-pregnant women
- Lowest levels in 3rd trimester
- Inflammation and infection increases hepcidin (including obesity and PET)

- Oral doses of supplemental iron acutely increase serum hepcidin
- Providing oral iron supplementation on alternate days and in single doses optimises iron absorption

Stoffel NU et al. Iron absorption from oral iron supplements given on consecutive versus alternate days and as single morning doses versus twice-daily split dosing in iron-depleted women: Two open label, randomised controlled trials. *Lancet Haematol* 2017; 4:524-33

Definition

- **A level of > 110g/L appears adequate in the first trimester and > 105g/L in the second and third trimesters.**

- **Postpartum anaemia is defined as a haemoglobin of < 100g/L**

Management if iron deficiency in pregnancy: UK Guideline
British Society for Haematology, Obstetric Haematology Group &
British Committee for Standards in Haematology

Consequences of IDA

- Impact of IDA on pregnant women
- Impact of IDA on the foetus
- Implications of prepartum iron deficiency in infancy
- Impact of postpartum IDA on the mother
- Health economic aspects

Consequences of IDA in pregnant women

- Preconception IDA can lead to chronic placental insufficiency[1]
- Impaired physical performance[2]
- Increased cardiac failure and maternal death from heart failure in severe anaemia[2–4]
- Poor maternal thyroid status and wound healing[5,6]

1. Pavlova TV et al. *Arkh Patol* 2007;69:31–32; 2. Viteri FE. *SCN News* 1994;11:14–28; 3. Villar et al. *J Nutr* 2003;133:1606S–1625S; 4. Reveiz L et al. Cochrane Database of Systematic Reviews 2007, Issue 2. Art No: CD003094. DOI: 10.1002/14651858.CD003094.pub2; 5. Zimmermann MB et al. *J Clin Endocrinol Metab* 2007;92:3436–3440; 6. Hercberg S et al. *Clin Drug Invest* 2000;19(suppl 1):1–7

Consequences of maternal IDA for the fetus

Hb levels <90 g/L increase risk of:[1–5]

- Spontaneous miscarriage
- Low birth weight/small for gestational age
- Pre-term delivery if anaemia present in early pregnancy

Hb levels <60 g/L associated with:[6]

- Chronic placental insufficiency

Low Hct (<29%) associated with:[7]

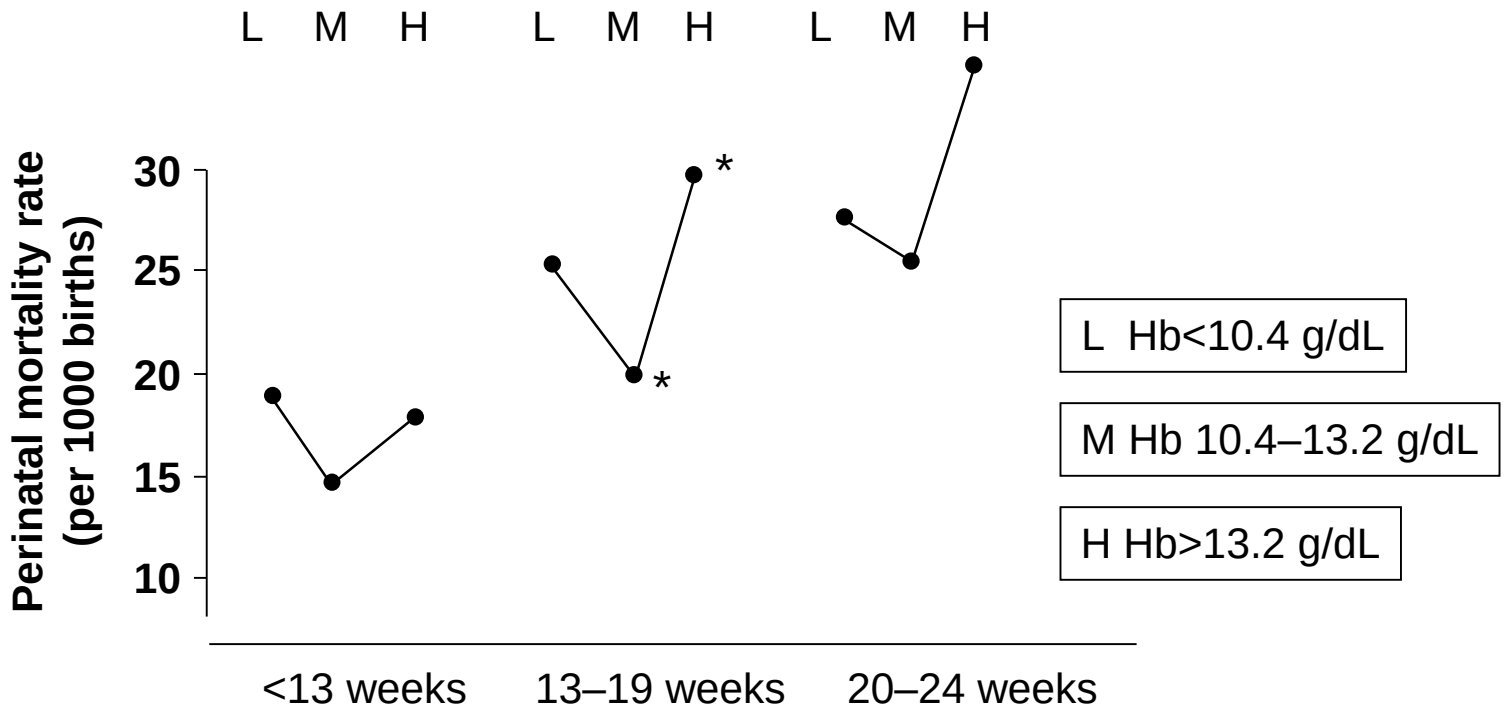
- Medical abnormalities
- Growth restriction
- Foetal death

Hct, haematocrit

1. Breymann C. *Fetal Matern Med Review* 2002;13:1–29; 2. Allen L. *Nutr Rev* 1997;55:91–101; 3. Murphy JF et al. *Lancet* 1986;1:992–995; 4. Ren A et al. *Int J Gynaecol Obstet* 2007;98:124–128; 5. Allen LH. *Am J Clin Nutr* 2000;71:1280S–1284S; 6. Pavlova TV et al. *Arkh Patol* 2007;69:31–32; 7. Garn SM et al. *Sem Perinatol* 1981;5:155–162

Prepartum Hb can affect newborn mortality

Defining the optimum Hb level in pregnancy:
very high and low Hb levels are associated with perinatal mortality



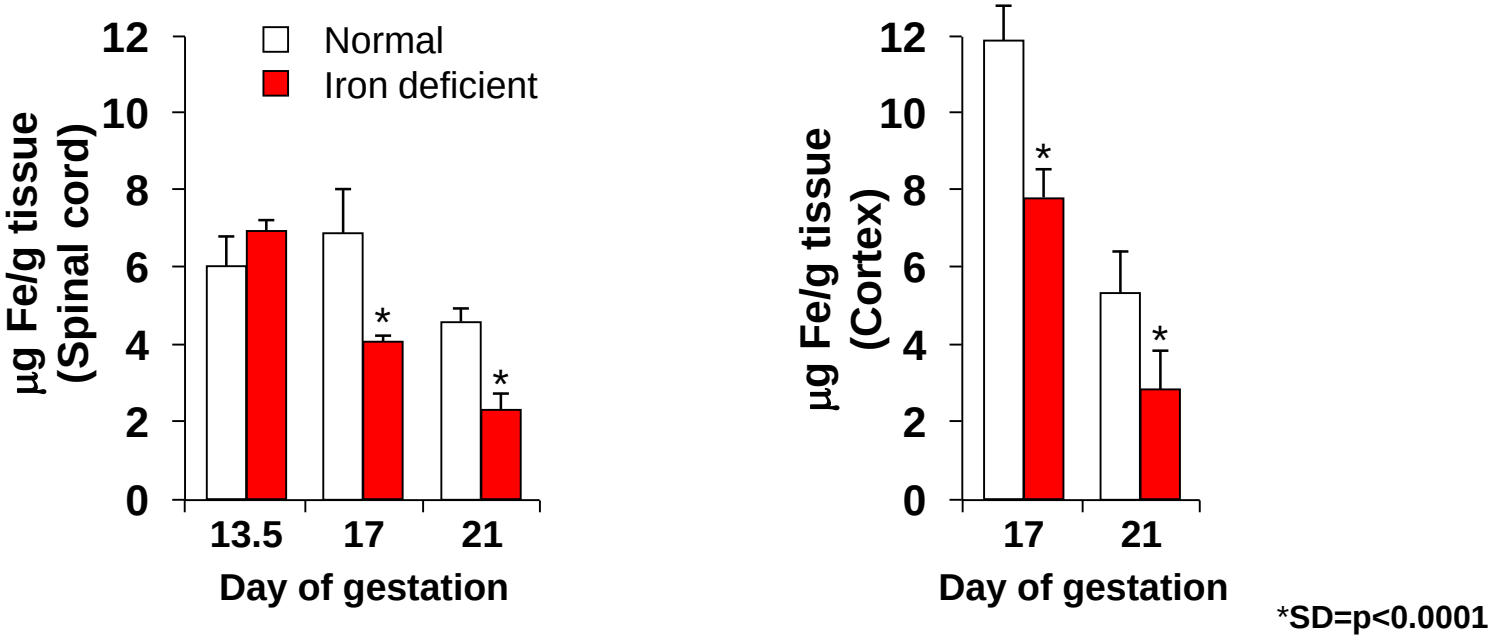
* Significant difference in perinatal mortality between those with high and median Hb at 13-19 weeks‘ gestation (p<0.01)

Murphy JF et al. *Lancet* 1986;1:992–995

Reprinted from The Lancet, Murphy JF et al. Relation of haemoglobin levels in first and second trimesters to outcome of pregnancy. Lancet 1986;327(8488):992–995, Copyright (1986), with permission from Elsevier

Prepartum ID affects neurological development of the foetus

Iron-deficient diet during pregnancy associated with iron depletion in embryonic CNS tissue (nonclinical study in rats)



*SD=p<0.0001

Morath DJ & Mayer-Proschel M. *Dev Neurosci* 2002;24:197–207

Morath DJ & Mayer-Proschel M. *Dev Neurosci* 2002;24:197–207. With permission from S. Karger AG

Implications of iron deficiency anaemia in infancy

Significant changes in brain biochemistry including dopamine metabolism and myelin fatty acid composition[1]

Poor locomotive development[2]

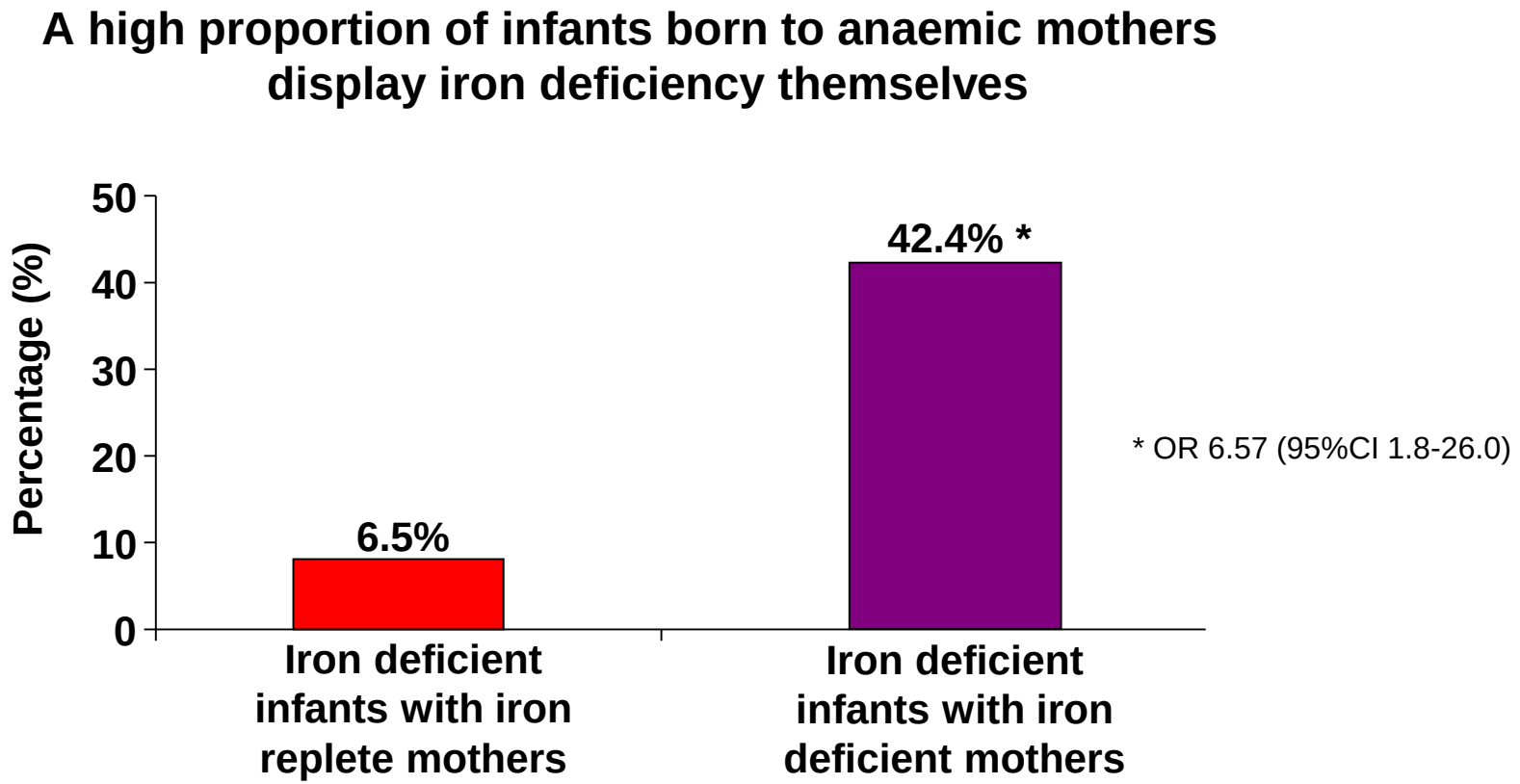
Poor performance on behavioural tests[2]

Impaired socio-emotional behaviour[2]

Poor cognitive performance[2]

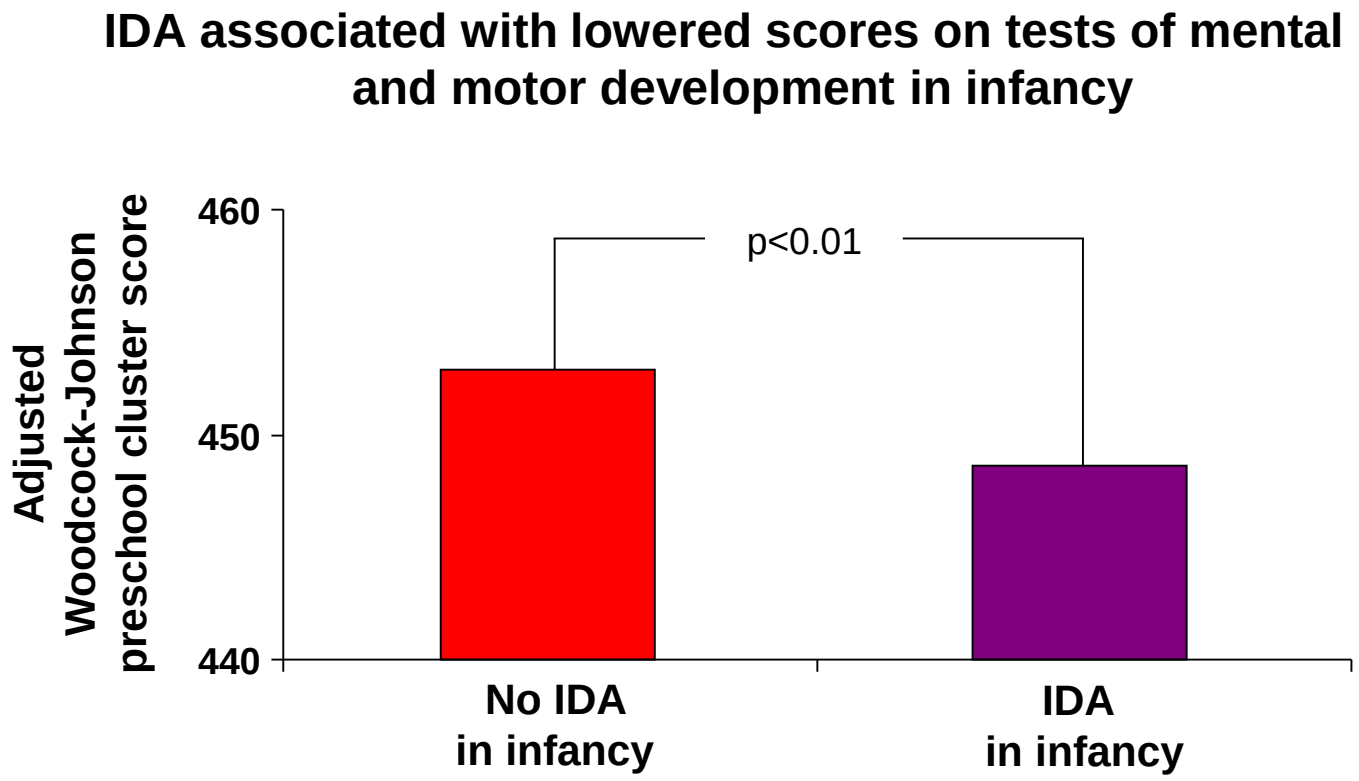
1. Kwik-Uribe CL et al. *J Nutr* 2000;130:2821–2828
2. Lozoff B et al. *Nutr Rev* 2006;64:S34–S43

Long-term consequences of prepartum IDA: implications for child



Colomer J et al. *Paediatr Perinat Epidemiol* 1990;4:196–204

Long-term consequences of prepartum IDA: implications for child



Lozoff B et al. *N Engl J Med* 1991;325:687–694

Consequences of postpartum IDA

Cognitive function[1]

- Lower cognitive performance

Cardiac function[2]

- Increased risk of cardiac failure in severe anaemia

Immune function[3]

- Lowered resistance to infection
- Impaired wound healing

Blood transfusions[4]

- Increased risk

Milk production[4]

- Reduced milk production (insufficient milk syndrome)
- Shorter lactation periods
- Increased supplementary feeding

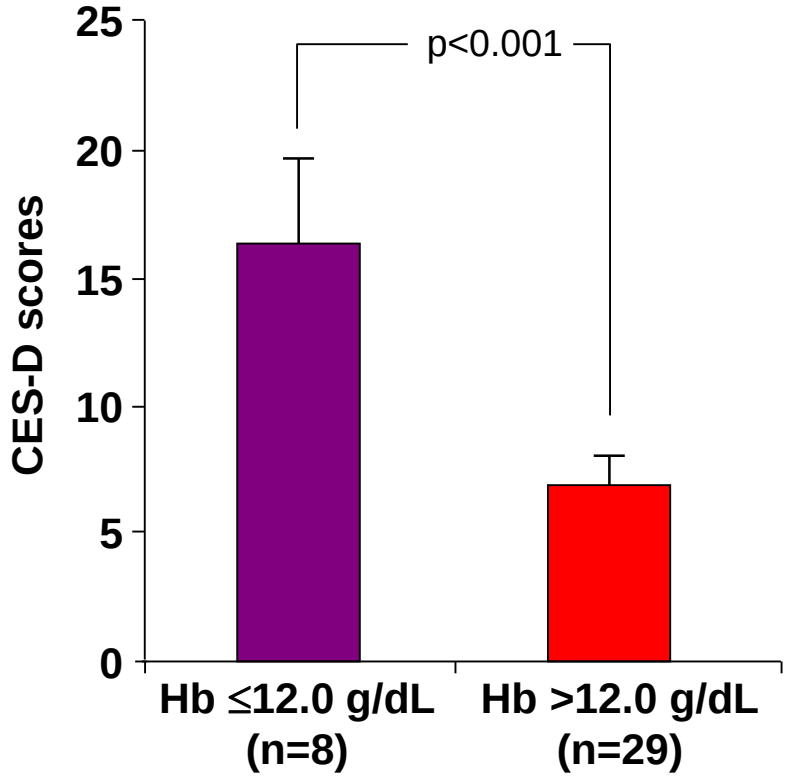
Psychological[5]

- Feeling of not enjoying motherhood
- Apathy
- Emotional instability
- Stress
- Irritability
- Altered thyroid hormone metabolism

1. Beard JL et al. *J Nutr* 2005;135:267–272; 2. Reveiz L et al. Cochrane Database of Systematic Reviews 2007, Issue 2. Art No: CD003094. DOI: 10.1002/14651858.CD003094.pub2; 3. Harrison KA. *Clin Obstet Gynaecol* 1982;9:445–777; 4. Breymann C & Huch R. Anaemia in pregnancy and the puerperium. 2008 UNI-MED; 5. Corwin EJ et al. *J Nutr* 2003;133:4139–4142

Postpartum IDA and depression

Postpartum Hb predicts postpartum depression, with a higher rate of self-reported depressive symptoms



CES-D, Center for Epidemiological Studies-Depressive Symptomatology Scale

Corwin EJ et al. *J Nutr* 2003;133:4139–4142

JOURNAL OF NUTRITION. ONLINE by Corwin EJ. Copyright 2003 by American Society for Nutrition. Reproduced with permission of American Society for Nutrition in the format Presentation via Copyright Clearance Center

Iron deficiency during pregnancy: economic burden

Iron deficiency in pregnant women can result in economic burden on society

- Complications during pregnancy and postpartum, including blood loss and need for transfusion, have cost implications on healthcare systems[1]
- Iron deficient pregnant women have impaired cell-mediated immunity,[2] making them more susceptible to infection[1] (cost to society)
- Reduction in capacity to work caused by anaemia well established; may be extrapolated to pregnancy[2]

1. Harrison KA. *Clin Obstet Gynecol* 1982;9:445-477
2. Viteri FE. *SCN News* 1994;11:14–18

Iron deficiency during pregnancy: economic burden

Ongoing impact on child can result in economic burden on society

- Negative effects on infant as a result of foetal abnormalities[1] and preterm delivery[2] requiring additional neonatal care
- Impact of IDA on future mental development of child[3] requiring increased care and education, and potentially affecting future work capacity[4]
- Possible effect on coronary function of child in later life[5] could have far-reaching impact on future societal burden

1. Viteri FE. *SCN News* 1994;11:14–8; 2. Hercberg S et al. *Clin Drug Invest* 2000;19:1–7;
3. Lozoff B et al. *Nutr Rev* 2006;64:S34–S43; 4. World Health Organization (2001). WHO/NHD/01.3;
5. Davis L et al. *J Physiol* 2005;565:35–41

Management of anaemia

Haemoglobin

- Accuracy of Hb measurement in pregnant women still debated:[1]
  - Physiological alterations in blood volume and red blood cell mass during pregnancy reduce the reliability of Hb or Hct assays

- Hb value and erythrocyte indices, such as MCV and MCH, have low specificity and sensitivity for detection of iron deficiency[2,3]
  - Significant changes manifest only in late phases of iron deficiency[2]

MCV, mean corpuscular volume
MCH, mean corpuscular Hb

1. Carriaga MT et al. *Am J Clin Nutr* 1991;54:1077–1081;
2. Breymann C. *Fetal Matern Med Review* 2002;13:1–29;
3. Cook J et al. *Blood* 1976;48:449–455

Serum ferritin

- Serum ferritin is commonly used to determine adequate iron stores[1–3]

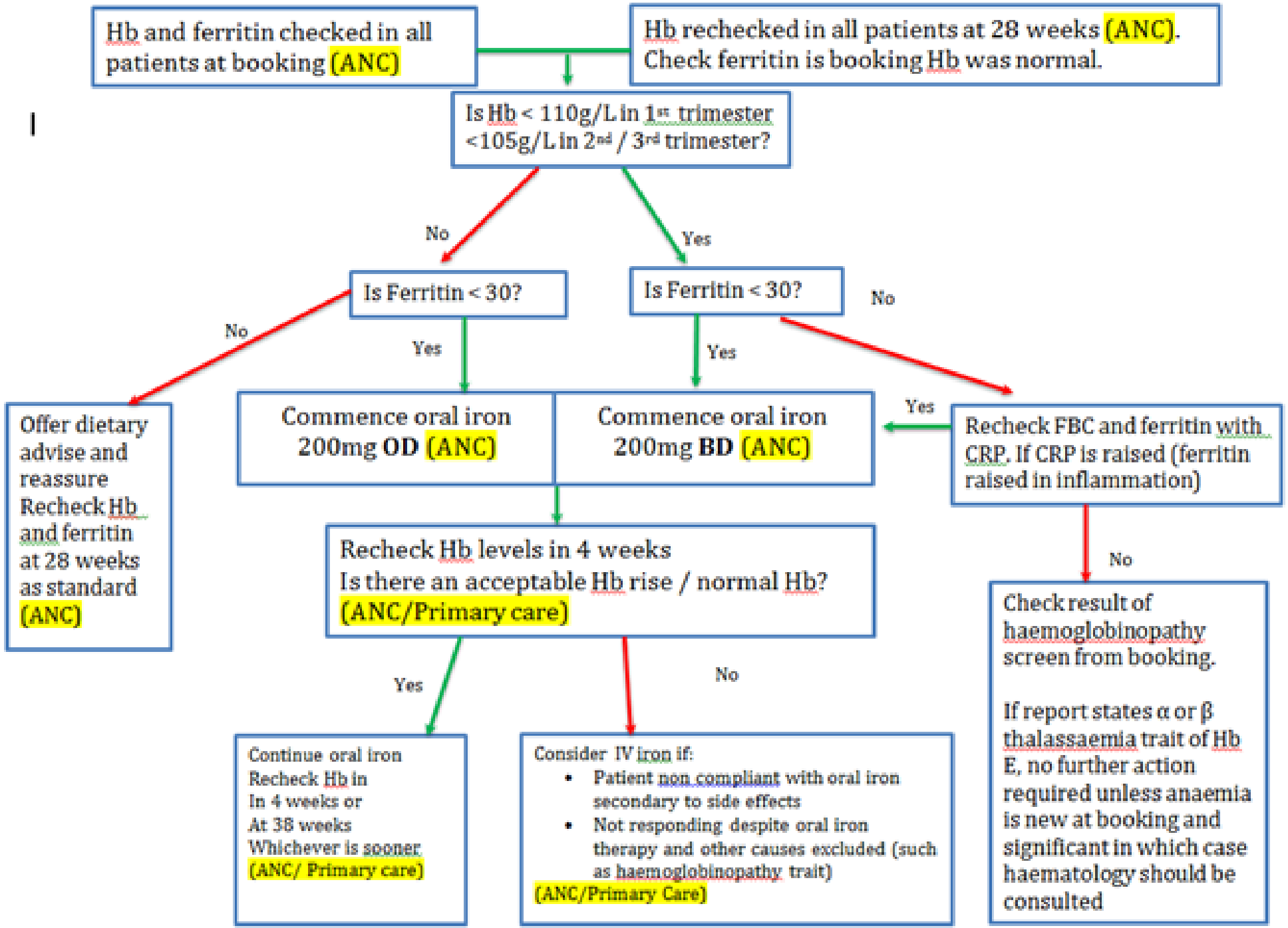
Ferritin levels <30 µg/L suggest low iron status[4,5]

Ferritin levels <15 µg/L indicate iron deficiency[1,4–7]

Ferritin levels <12 µg/L are often associated with anaemia[4,6,8]

- Serum ferritin may be elevated in women with infections or inflammatory disorders[1,3,4]
  - If suspected, plasma C-reactive protein should be measured to assess inflammation[4]

1. Breymann C. *Fetal Matern Med Review* 2002;13:1–29; 2. Cook J et al. *Blood* 1976;48:449–455; 3. Müngen E. *J Perinat Med* 2003;31:420–426; 4. Milman N. *Ann Hematol* 2008;87:949–959; 5. van den Broek NR et al. *Brit J Haematol* 1998;103:817–824; 6. Milman N et al. *Dan Med Bull* 1983;30:115–120; 7. Centers for Disease Control and Prevention. *MMWR* 1998;47:(No RR-3); 8. Blot I et al. *Curr Opin Hematol* 1999;6:65–70


Hb and ferritin checked in all patients at booking (ANC)
Hb rechecked in all patients at 28 weeks (ANC). Check ferritin is booking Hb was normal.
Is Hb < 110g/L in 1st trimester <105g/L in 2nd / 3rd trimester?
No
Yes
Is Ferritin < 30?
Is Ferritin < 30?
No
No
Yes
Yes
Yes
Offer dietary advise and reassure Recheck Hb and ferritin at 28 weeks as standard (ANC)
Commence oral iron 200mg OD (ANC)
Commence oral iron 200mg BD (ANC)
Recheck FBC and ferritin with CRP. If CRP is raised (ferritin raised in inflammation)
Recheck Hb levels in 4 weeks
Is there an acceptable Hb rise / normal Hb?
(ANC/Primary care)
No
Yes
Check result of haemoglobinopathy screen from booking.
If report states α or β thalassaemia trait of Hb E, no further action required unless anaemia is new at booking and significant in which case haematology should be consulted
Yes
No
Continue oral iron
Recheck Hb in
In 4 weeks or
At 38 weeks
Whichever is sooner
(ANC/ Primary care)
Consider IV iron if:
• Patient non compliant with oral iron secondary to side effects
• Not responding despite oral iron therapy and other causes excluded (such as haemoglobinopathy trait)
(ANC/Primary Care)

Anaemia in Pregnancy

An e-learning package

Click here to start…

Main Menu

1. Why anaemia in pregnancy is important?
2. How can I detect it?
3. What I can do to prevent it?
4. Extra resources & mini test

Click on the boxes above to go to the different sections

How can I detect it?

Consider these ‘at risk groups’

- younger mothers
- short pregnancy intervals
- diets low in iron

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Next

What can I do to prevent it?

In general follow this sequence…

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Next

What can I do to prevent it?

Below are foods rich in iron – click on them to see how much iron they contain

Nuts & Dried Fruits	Wholegrain & Cereals	Green vegetables	Protein
2 Tbsp Pumpkin seeds = 2.5mg Iron	1 bowl of fortified cereal = 3.0mg Iron	30g spinach = 3.0mg Iron	1 medium sized steak = 4.3mg Iron
6 prunes = 0.5mg Iron 5 figs = 2.0mg Iron	1 slice of Wholemeal Bread = 0.9mg Iron	175g cooked broccoli = 1.1mg Iron	Small can of Baked Beans = 3.25mg Iron

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NHS
Blood and Transplant

Iron in your diet

IMPORTANT PATIENT INFORMATION

Recommendation

- All women should be counselled regarding diet including
- details of iron-rich sources
- factors that may inhibit or promote iron absorption

- Written information for patients, which is appropriate for dietary type and language

What can I do to prevent it?

Oral Iron

- safe, effective, cheap
- **1st** – try tablets
- **2nd** try liquid

  (if tablets are not tolerated)
- re-check Hb after 4 weeks

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What can I do to prevent it?*

Oral iron – tablet options:

Ferrous Sulphate	
Dosage	200mg - BD
Elemental iron	65mg
Cost per tablet	Hospital – 1p Community – 5p

Ferrous Fumarate	
Dosage	210mg - BD
Elemental iron	68mg
Cost per tablet	Hospital – 2p Community – 2p

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If printed, this document is valid only on 02/10/2017

Appendix 2

The Protocol and Procedure Guide for Administering Intravenous Iron Ferinject® for the Treatment of Iron Deficiency Anaemia in Pregnancy and Puerperium

Ferric Carboxymaltose (Ferinject®) is a parenteral iron treatment which can give up to 1000mg over 20 minutes as an infusion and has a low side effect profile. Ferinject® enables women to be treated quickly, potentially with one infusion therefore increasing patient compliance and decreasing both time in the antenatal day unit and postnatal stay.

Ferinject® is not licensed for use within the first trimester; however it is licensed for use in the second and third trimester and the postpartum period. (1)

DIAGNOSIS AND INVESTIGATION

Prior to treatment with Ferinject® a haemoglobin and ferritin levels should be taken and a target hemoglobin level decided. Vitamin B12 and folate deficiency should be treated.

Each woman who is going to receive Ferinject® needs to have their weight taken and documented on the drug chart so that the dosage of Ferinject® can be double checked by both the midwife and the pharmacist.

Indications for Parenteral Iron therapy

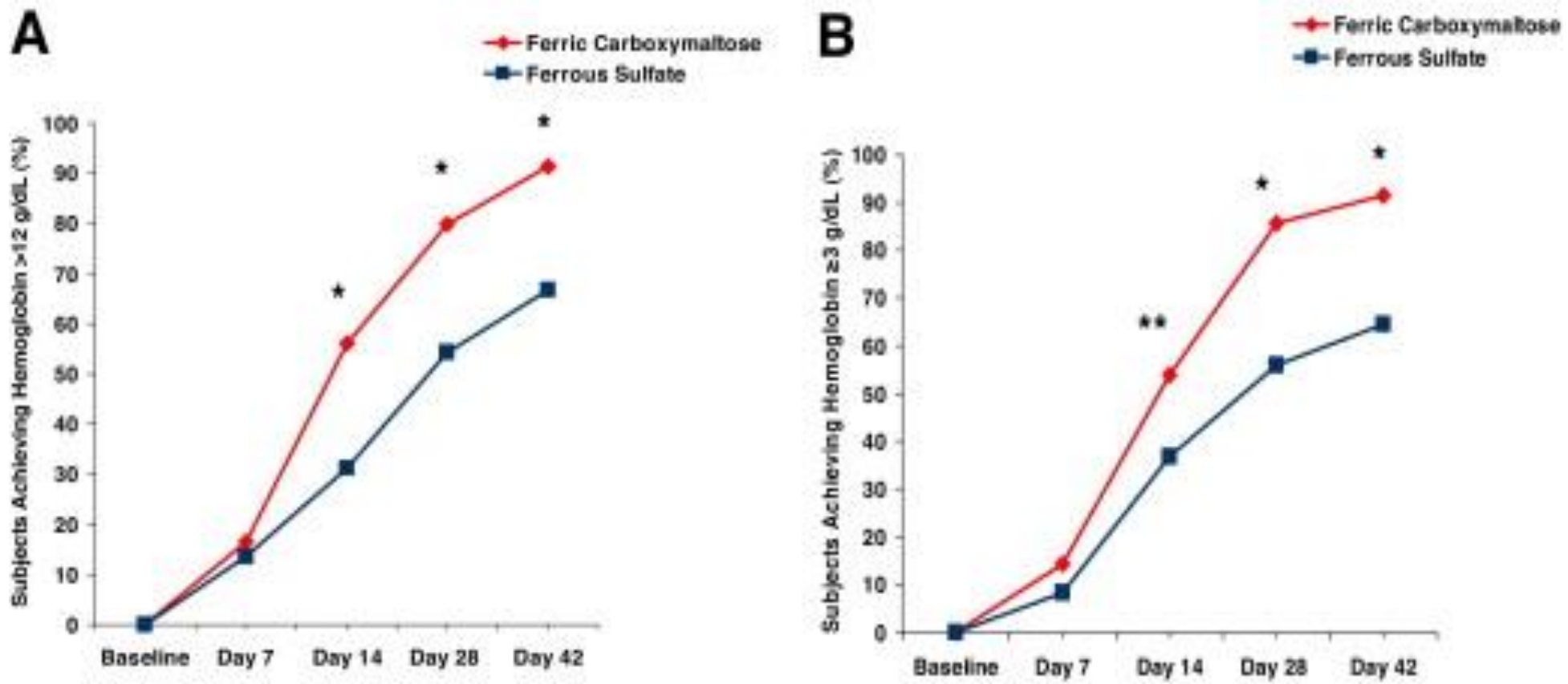
1. Second, third trimester of pregnancy, or the immediate postpartum period
2. Demonstrable intolerance to oral iron therapy
3. Clinical need to deliver iron quickly to iron stores
4. Non-compliance or resistance to oral iron therapy
5. Contraindication to oral iron therapy such as inflammatory bowel disease
6. Refusal of blood products on religious or principle basis

Contraindications to parenteral iron therapy (1)

1. First trimester

IV Iron Therapy during pregnancy

- 291 women <10d after delivery with Hb 100g/l or less: ferric carboxymaltose vs ferrous sulphate



IRON SUCROSE VS FERRIC CARBOXYMALTOSE

- Christoph et al – journal of perinatal medicine 2012
- Retrospective analysis of 206 women treated with either ferric carboxymaltose or iron sucrose for iron-deficiency anaemia

	Ferric Carboxymaltose	Iron Sucrose
Mean rise in Haemoglobin (g/l)	15.4	11.7
Adverse effects (mild) - %	7.8	10.7

Use of Ferric Carboxymaltose in Leeds

- 30 women over 11 months (2014)
- 23 – antenatally
- 7 – postnatally
- Antenatal rise in Hb – 30g/L
- Postnatal Hb pre treatment – 65-97g/L
- No adverse effects

Not only IDA

Mrs SW

- 27 year old
- Previous h/o (L) common femoral and iliac vein DVT extending to IVC – thrombolysed
- Conceived three months later
- On prophylactic LMWH
- Significant haemorrhoids
- Presented with Hb of 57g/l and platelets of 90 (dropped to 56)
- LDH >6.000
- High MCV and MCH
- Blood film in keeping with megaloblastic anaemia
- Folate 0.7
- B12 100
- Treated with FA and B12 supplements
- **Hb 117g/L; Platelets 264 pre-delivery**

Conclusion

- **Anaemia in Pregnancy**

- prevalent
- can lead to significant consequences to mum and baby
- treatable
- we are trying hard but still not enough
- partnership between primary and hospital care can improve management