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Managing Anaemia in Pregnancy

Claire L J Atterbury
CNS Transfusion Medicine

Is this important?

Is it just about reducing the amount of components used?

What am I going to talk about?

- Iron
- B_{12}
- Folate
- Increasing women's wellbeing
- Reducing midwives' workload
- A bit about the babies.

Iron

Increased requirements in pregnancy

Fetus	- 270mg
Placenta and cord	- 90mg
Delivery	- 150mg
Normal loss	- 280mg
(1mg per day)	
↑RCM	- 450mg
Total	-1240mg

Iron

- BUT + gain 240-480mg (no menses)
- Total loss 1240mg – 240/480 = 1000/760

Net requirement for all in 280 days 700 – 1400mg (2.5-5mg/d.)

Most women end their pregnancy low in iron but not necessarily anaemic

Therefore where are ….

- Primips?
- Multips?

Aim of Antepartum treatment - to get to 3 months post partum with normal iron stores. It is do-able.

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Patient blood management in obstetrics: management of anaemia and haematinic deficiencies in pregnancy and in the post-partum period: NATA consensus statement

M. Muñoz J. P. Peña-Rosas S. Robinson N. Milman W. Holzgreve C. Breymann F. Goffinet J. Nizard F. Christory C.-M. Samama J.-F. Hardy

UK guidelines on the management of iron deficiency in pregnancy

Sue Pavord Bethan Myers Susan Robinson Shubha Allard Jane Strong Christina Oppenheimer on behalf of the British Committee for Standards in Haematology

It starts at booking……

- A careful history
  - General health
  - Family history
  - Bleeding history – Obstetric and otherwise (menses, surgery)
  - Any previous history of anaemia?
- Beliefs and wishes and fears concerning blood transfusion
- Drug history (legal and other)
- Allergies

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[redacted]

Ante Natal Booking.

[redacted]

Request Reason : ANTENATAL

White Blood Cell Count	9.80	x10^9/L	(4 to 10)	Auth
Auto Neutrophil Count	7.00	x10^9/L	(1.8 to 7.7)	Auth
Auto Lymphocyte Count	2.10	x10^9/L	(1.5 to 3.5)	Auth
Auto Monocytes	0.32	x10^9/L	(0.2 to 1.0)	Auth
Automated Eosinophils	0.10	x10^9/L	(0.02 to 0.5)	Auth
Automated Basophils	0.19	x10^9/L	(0.02 to 0.1)	Auth
Red Blood Cells	3.62	X10^12/L	(3.8 to 4.8)	Auth
Haemoglobin	8.2	g/dL	(12.5 to 16.5)	Auth
Haematocrit	0.267	L/L	(0.36 to 0.46)	Auth
MCV	74.0	fL	(83 to 101)	Auth
MCH	22.6	pG	(27 to 32)	Auth
MCHC	30.6	g/dL	(31.5 to 34.5)	Auth
Platelet Count	340	x10^9/L	(150 to 400)	Auth

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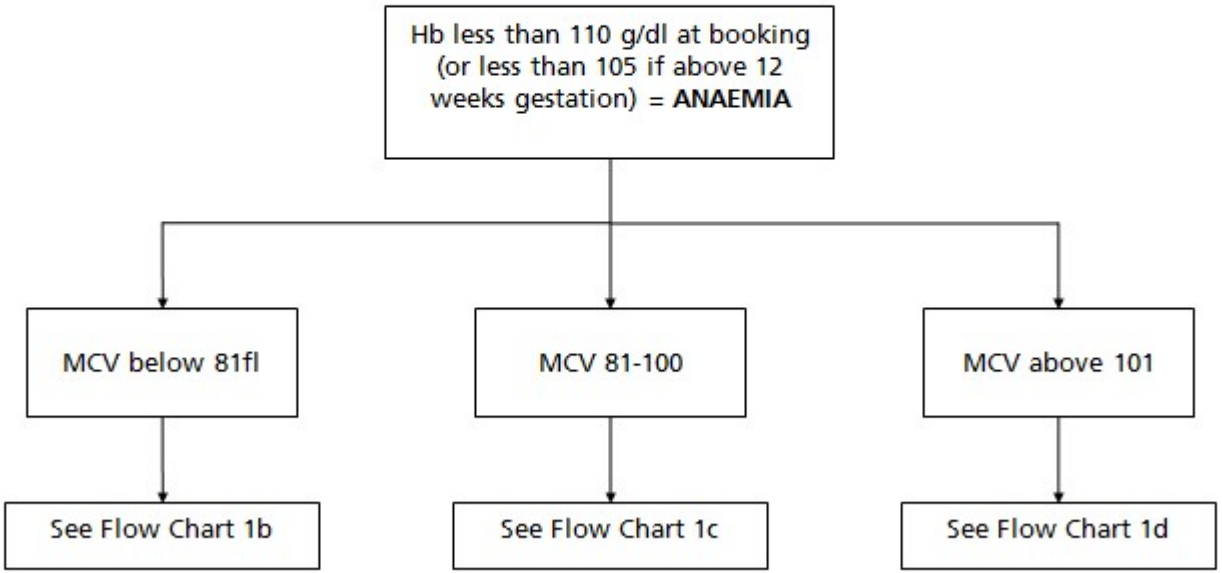
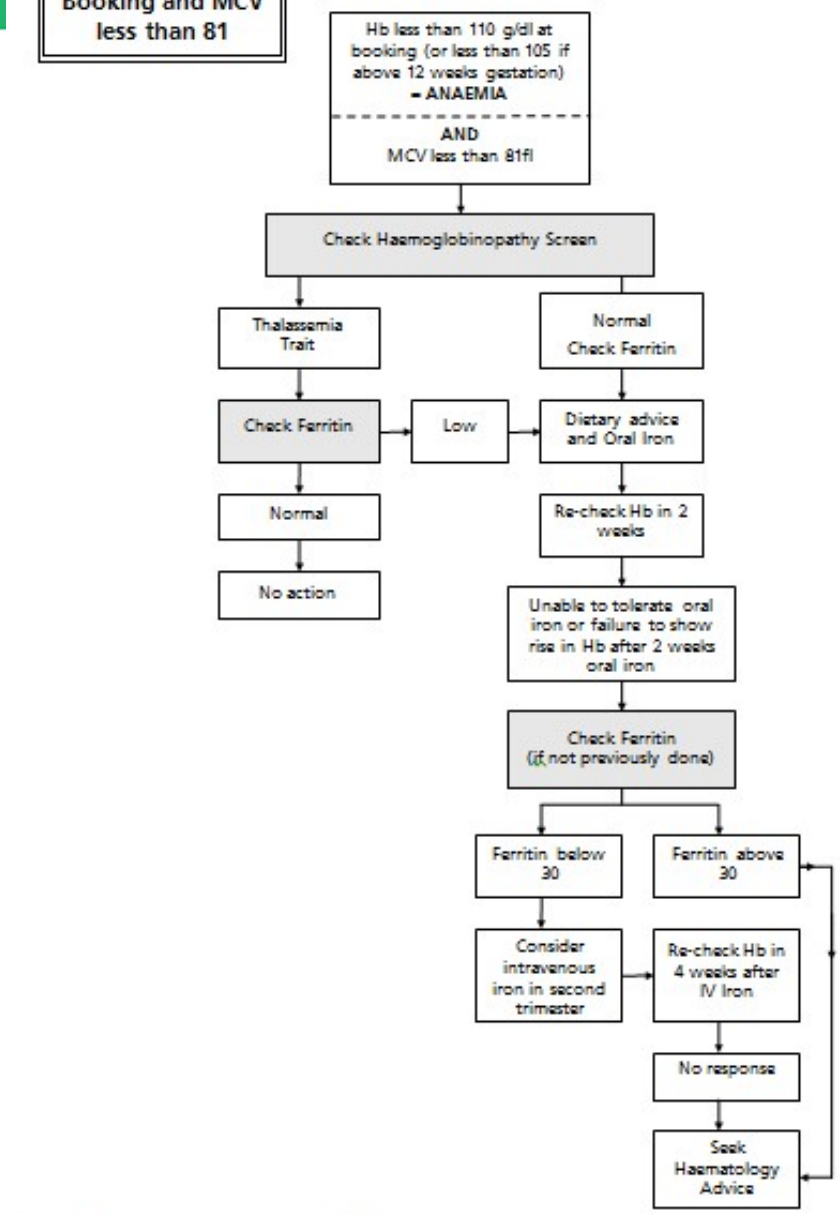
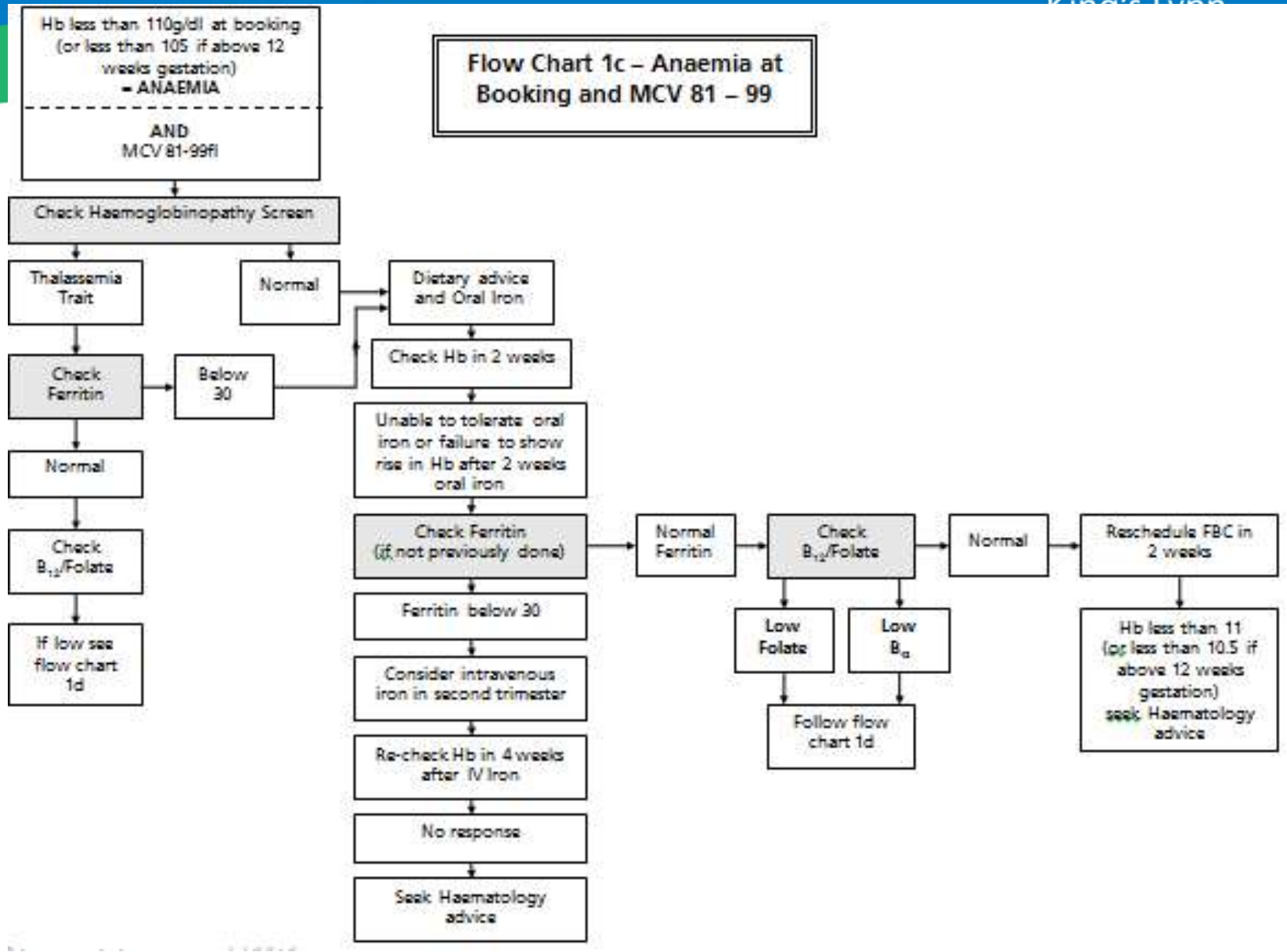
Flow Chart 1a – Anaemia at Booking



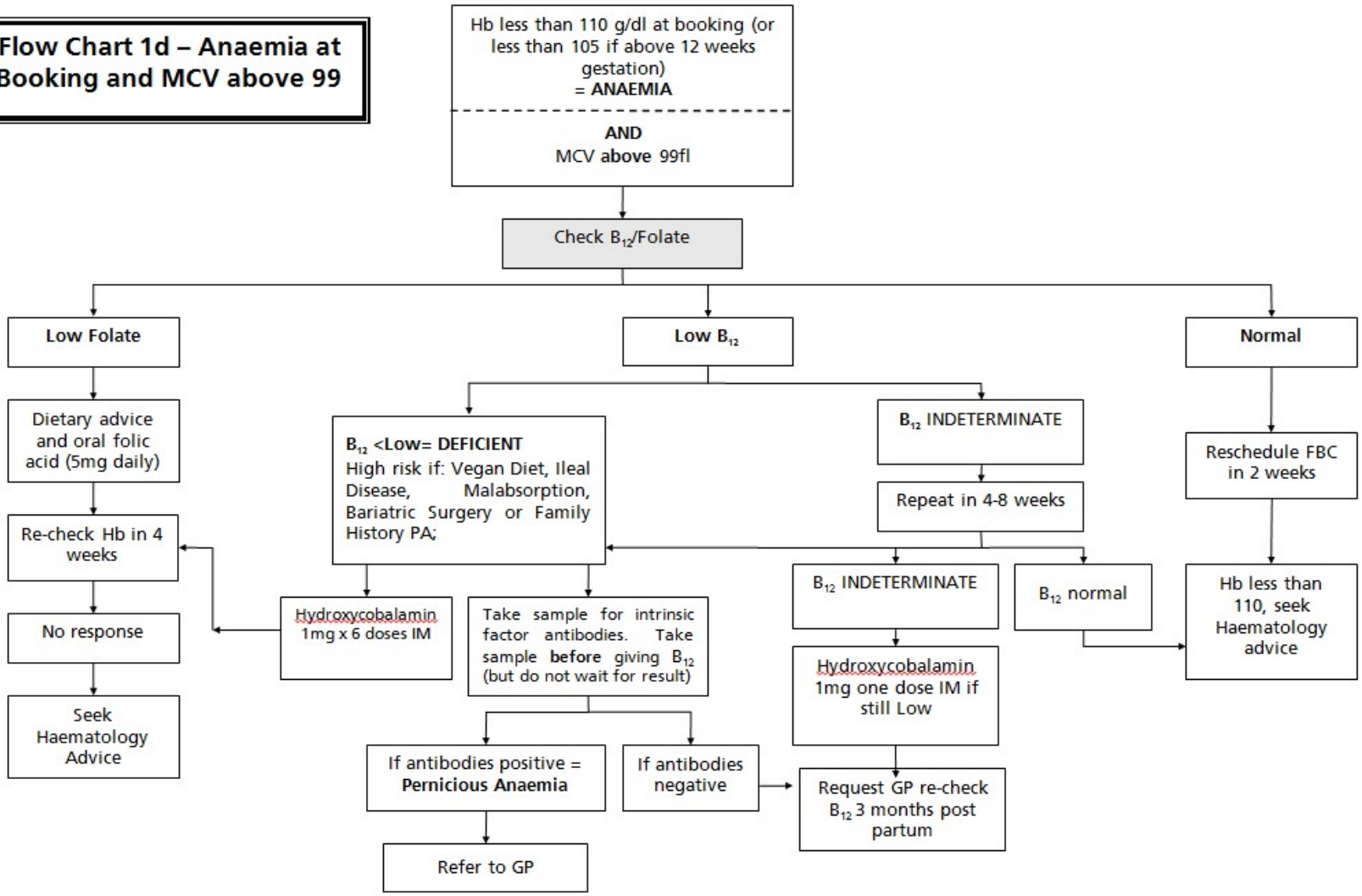
Flow Chart 1b – Anaemia at Booking and MCV less than 81



Flow Chart 1c – Anaemia at Booking and MCV 81 – 99



Flow Chart 1d – Anaemia at Booking and MCV above 99



Investigations based on your findings

- Anaemia screen as baseline if there are concerns
  - Repeat FBC
  - U&E and LFT
  - Clotting
  - B_{12} ,Folate and Ferritin
  - CRP
- Do a look back, if possible, to previous non pregnancy results – particularly the MCV, MCH
- Remember to ask them to tell you if they get any infections such as a UTI, chest infection, common cold, norovirus etc. More than one could mean they have become deficient.

Haemoglobin

- Anaemia = haemoglobin < 120g/l for all women (WHO)
- Haemoglobin concentration determined by:
  - Red cell mass (RCM)
  - Plasma volume (PV)
- True anaemia = fall in RCM
- During pregnancy:
  - PV rises by 1 litre (max. at 24 – 30/40)
  - RCM rises by 300ml (max. at 30/40)
  - Overall fall in Hb, max at 30/40 = dilutional anaemia
    (min. Hb =110g/l)

Into the 3rd Trimester

- **Look again at their blood**
- Has the MCV dropped?
- Think about Iron, B_{12} and Folate.
- If Iron is low use a treatment dose of oral iron
- But they are on Pregaday….?
- If time is marching on (32/40+) consider IV Iron for complete stores replacement

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[redacted]

Request Reason : Antenatal (28 weeks)

White Blood Cell Count	10.10	x10^9/L	(4 to 10)	Auth
Auto Neutrophil Count	6.54	x10^9/L	(1.8 to 7.7)	Auth
Auto Lymphocyte Count	2.50	x10^9/L	(1.5 to 3.5)	Auth
Auto Monocytes	0.74	x10^9/L	(0.2 to 1.0)	Auth
Automated Eosinophils	0.20	x10^9/L	(0.02 to 0.5)	Auth
Automated Basophils	0.13	x10^9/L	(0.02 to 0.1)	Auth
Red Blood Cells	3.76	X10^12/L	(3.9 to 4.8)	Auth
Haemoglobin	9.3	g/dL	(12.5 to 16.5)	Auth
Haematocrit	0.270	L/L	(0.36 to 0.46)	Auth
MCV	74.0	fL	(83 to 101)	Auth
MCH	24.8	pG	(27 to 32)	Auth
MCHC	33.5	g/dL	(31.5 to 34.5)	Auth
Platelet Count	342	x10^9/L	(150 to 400)	Auth

1 Date 2 Serial 3 Latest 4 rep seQ 5 Spec 6 DtT 7 Matches 8 Options 9 eXit X
Cursor Down for more

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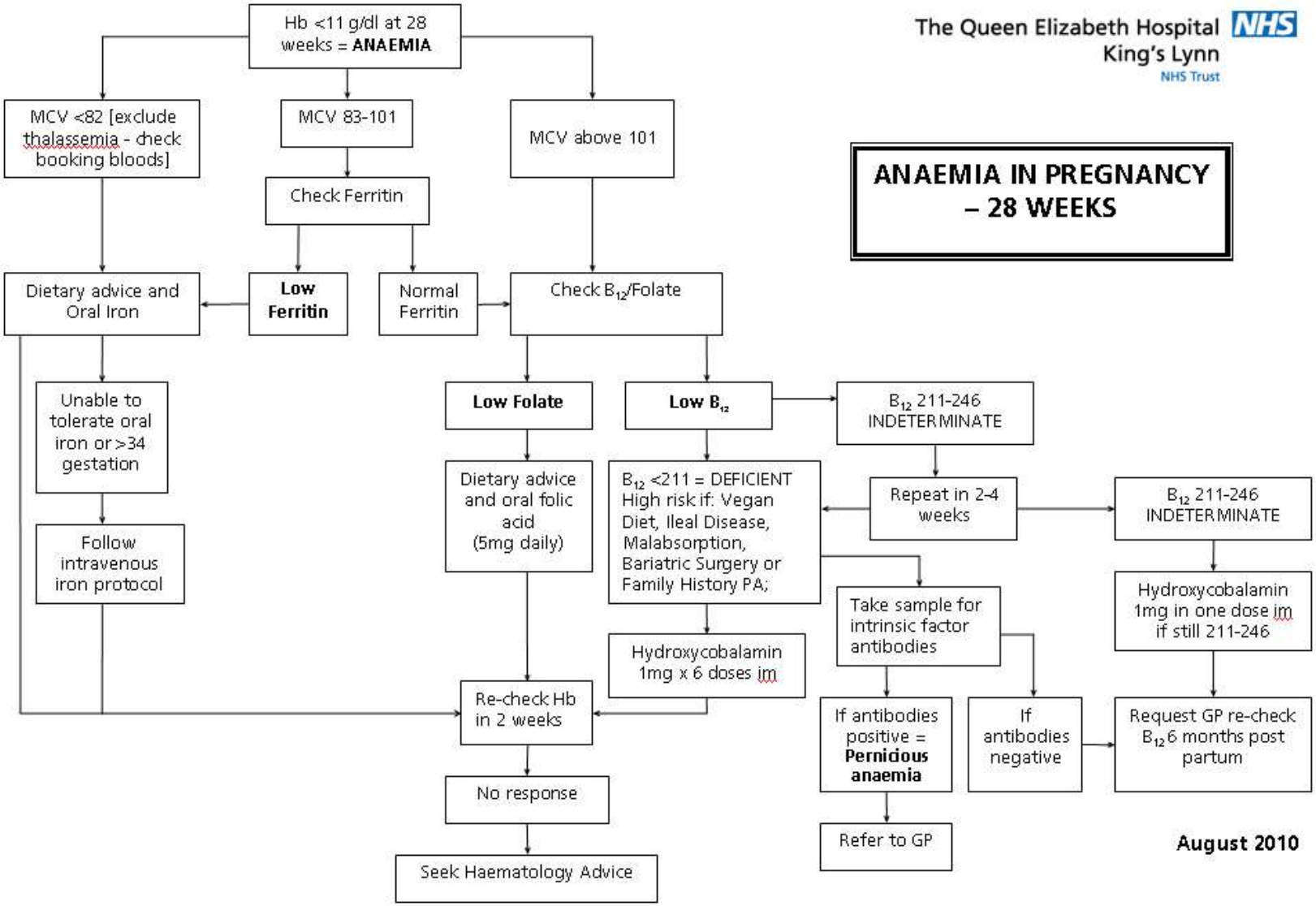
ANAEMIA IN PREGNANCY – 28 WEEKS



August 2010

Adverse effects/risks of Iron deficiency in Pregnancy, Delivery and Post partum to Mum

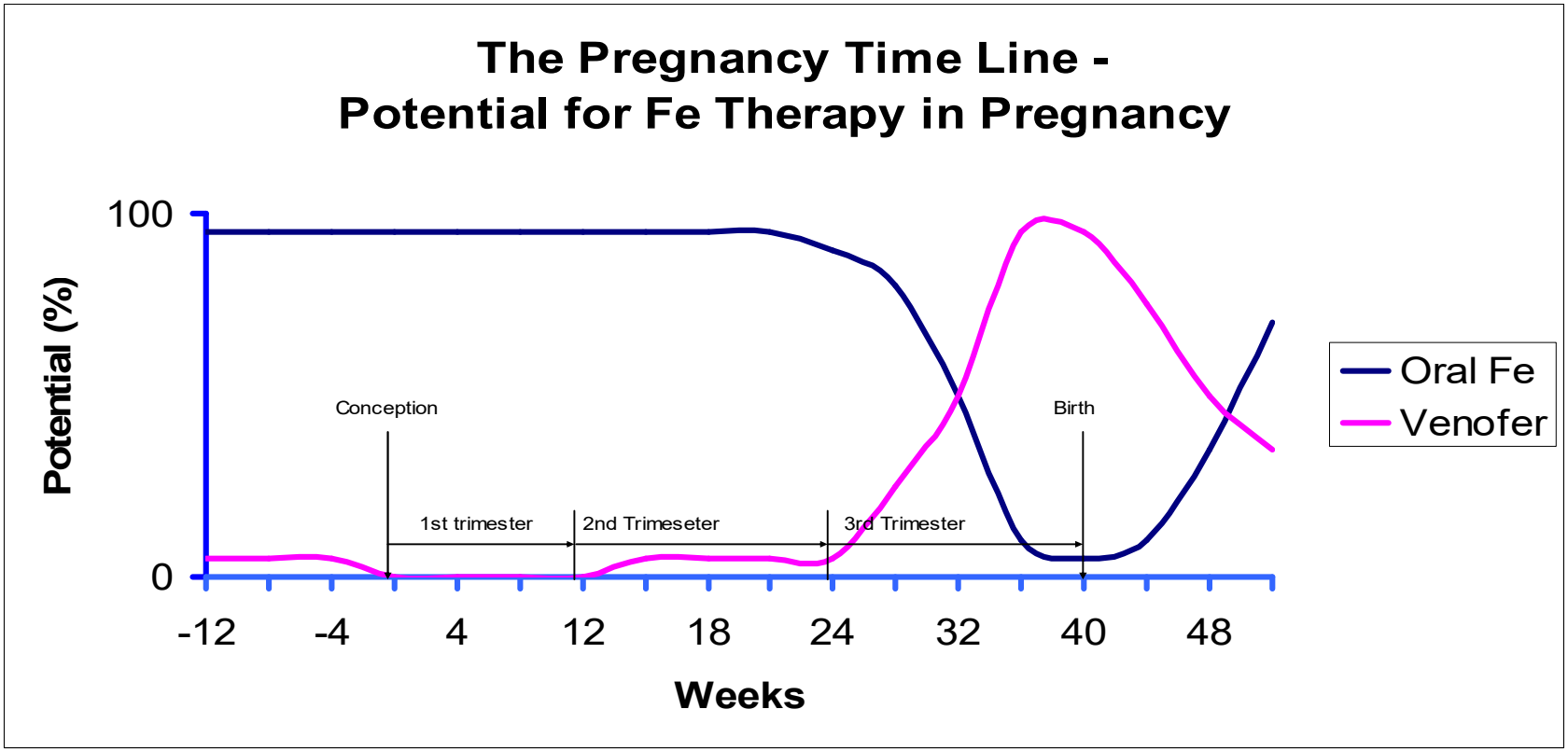
- Unpleasant symptoms
  - Lethargy, dyspnoea, fatigue, **insomnia**, light headedness, dizziness and disorientation
- Increased susceptibility to **infection**
- Decrease in thermoregulation
- Ante partum **haemorrhage** ++
- Post partum **haemorrhage** ++
- Delayed wound healing
- Reduced quality and quantity of **Lactation** or even halted
- **Excessive fatigue and failure to cope**

And for the wee ones……

- Poor uterine growth
- Decreased liquor
- Asymmetrical growth patterns
- Small for dates
- Premature delivery
- Low birth weight
- Failure to thrive (poor lactation)
- And if it continues - poor concentration and reduced scholarly achievements

- And for the Midwife……..??!!

Iron Therapy Timeline in Pregnancy



Oral Iron

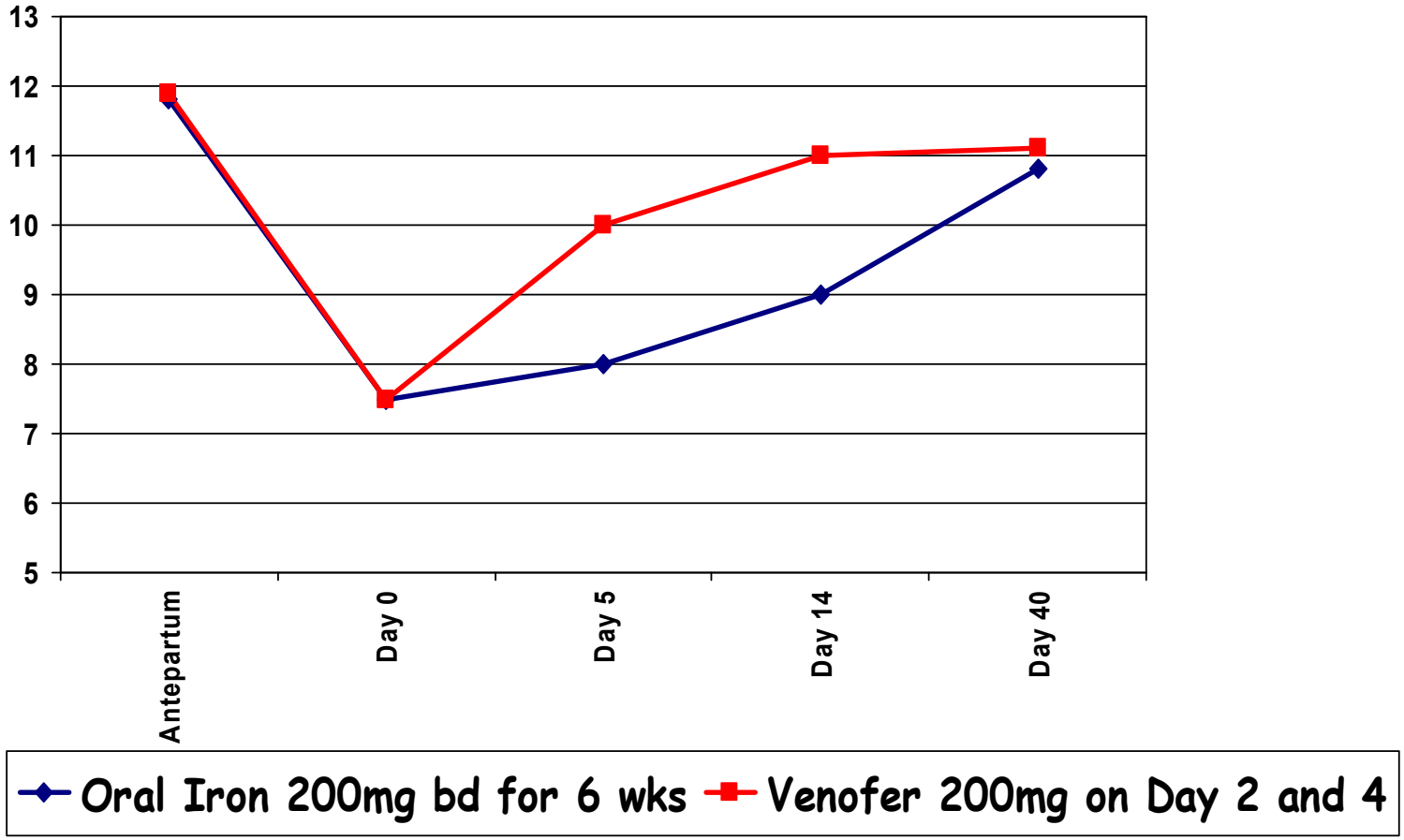
- Very cheap
- Get the right dose and length of treatment.
- Slow to work but will raise Iron stores within 1/52.
- Side effects!
- Patient and practitioner confidence.
- Every day or every other day?

Intravenous

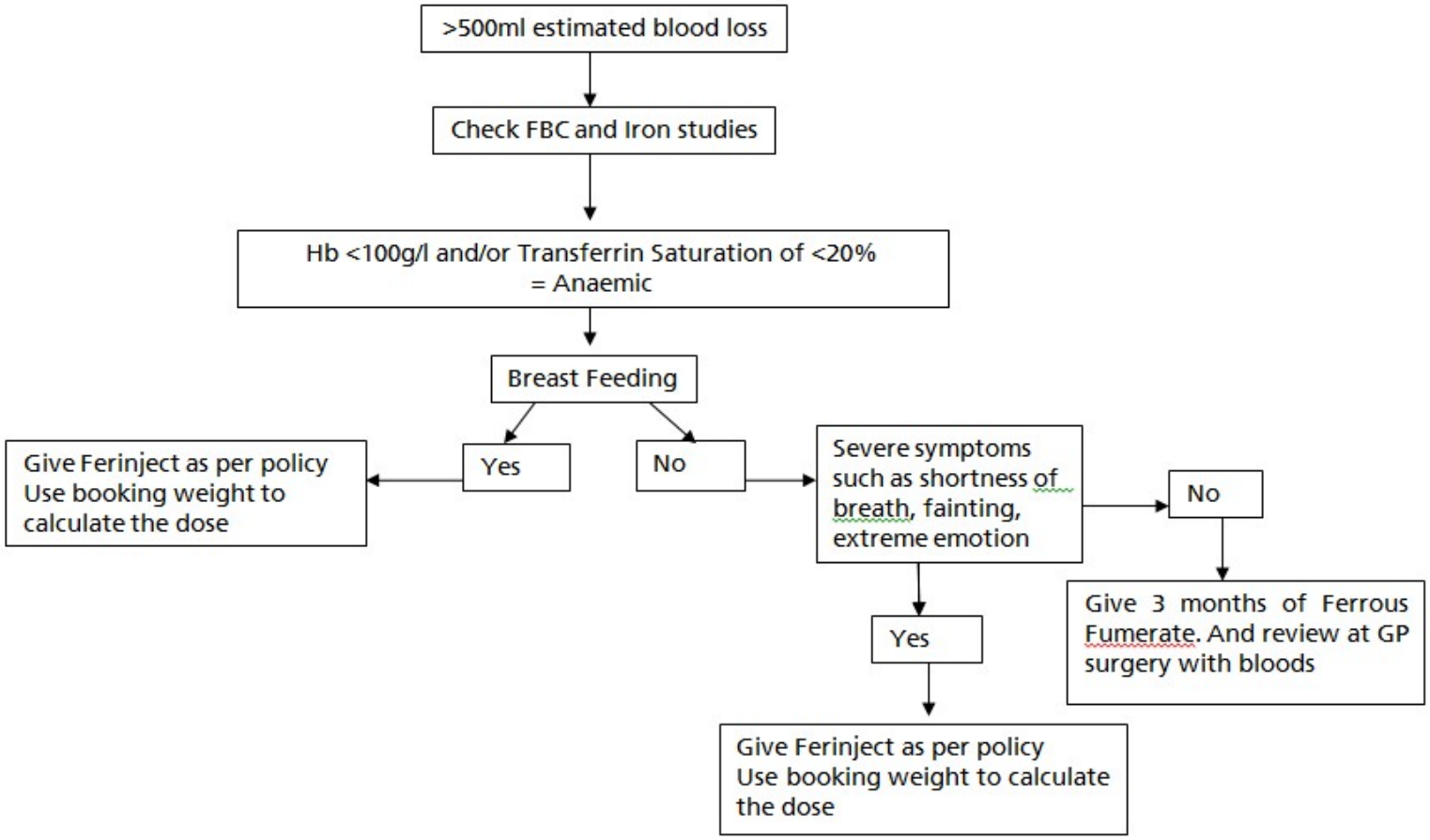
- Rapid (almost as fast as a transfusion, ~ 4-5 days).
- Can target an exact level of Iron and Hb.
- Licensed in 2nd and 3rd Trimester.
- Side effects?
  - Minor and rare but can be frightening. Most gone within 30 minutes.
  - Nausea (may last 24 hours)
  - Facial and limb flushing
  - Hypertension
  - Anaphylaxis is extremely rare in the product we use (1: 800 000 doses here)
  - All p[atients must be observed for 30 minutes
- Which product is available to you? Venofer, Cosmofer, Ferinject, Monofer

Oral Iron vs Venofer in the Postpartum

(Dr Nav Bhandal, John Radcliffe, Oxford, personal communication)



Post-Partum Anaemia or Iron Deficiency following >500ml bleed.



Don't forget Folate deficiency (or B_{12})

- Pregnancy requires extra 200 micro grams per day

- **Increased risk of deficiency**:
  - Poor nutrition
  - Twins
  - Haemolysis (autoimmune, viral)
  - Malaria
  - Infection
  - Drugs

- Diagnosis:

1. Haemoglobin↓
2. MCV↑
3. Serum folate
4. Red cell folate

- Treatment
  - Folic acid 5mg OD throughout pregnancy
  - Hydroxycobalamin as per ante natal policy
  - Patients should be checked

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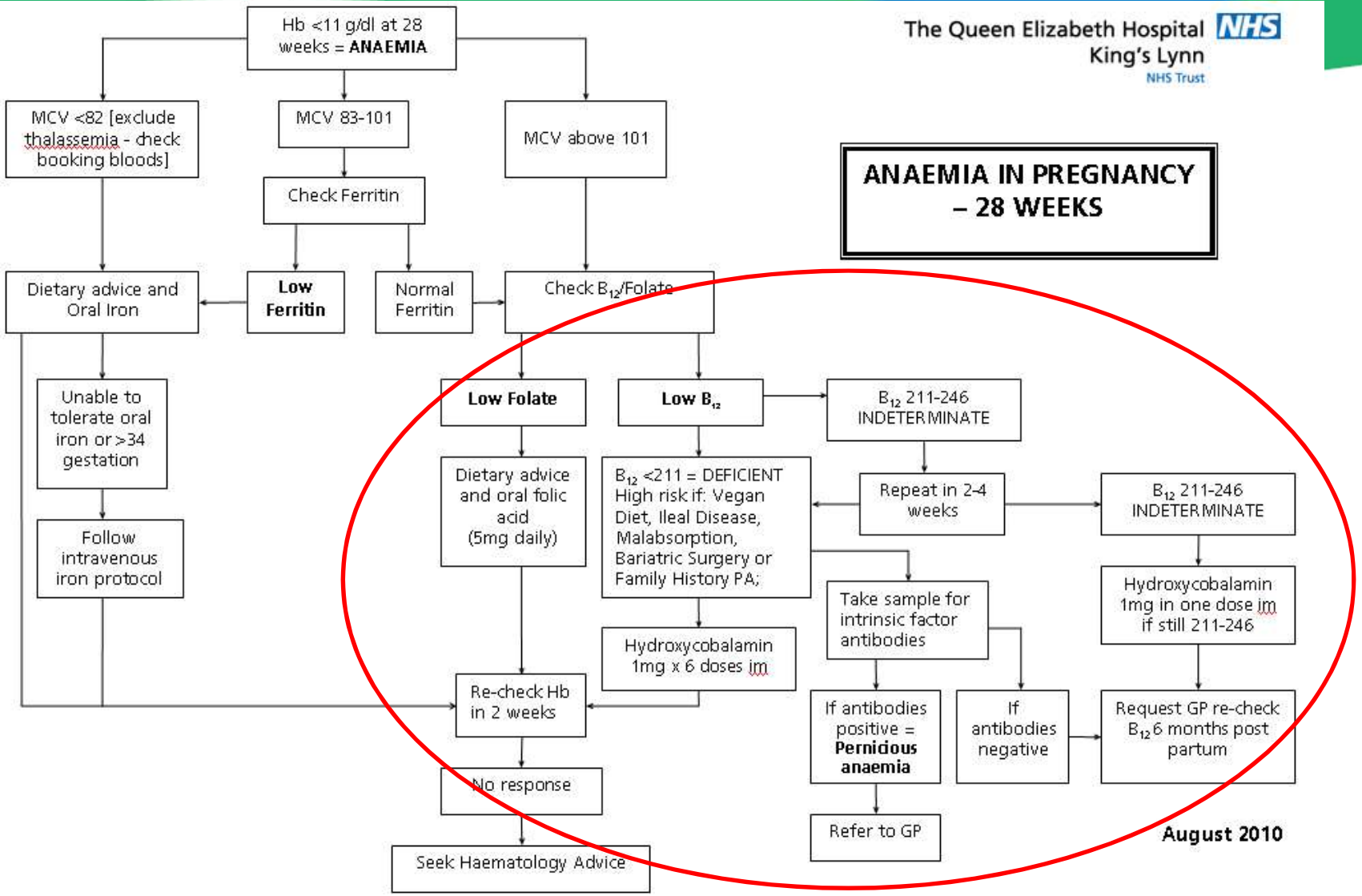
ANAEMIA IN PREGNANCY – 28 WEEKS



August 2010

Blood is more dangerous than you might think……

Mini transplant of live cells from the donor to the recipient including some antibodies in plasma.

What consequences may happen now?

In the future?

THE TIMES Thursday February 15 2007

Anita Roddick: I've had hepatitis C for more than 30 years

Helen Nugent

Anita Roddick, the founder of the Body Shop famous for her ethical business stance and clean living, announced yesterday that she is suffering from hepatitis C.

Dame Anita, 64, said that she contracted the disease through an infected blood transfusion in 1971 during the birth of her youngest daughter, Sam. The condition went undiagnosed for more than 30 years until a blood test in 2005.

She wrote in a posting on her website that she also has cirrhosis of the liver, one of the effects of hepatitis C. None of her family has the virus.

Dame Anita, who founded the Body Shop from a single store in Brighton in 1976, told *The Times*: "If I was 20 years old and just found out that I had passed this on to one of my kids, I would have been furious. But you can't be angry with things you didn't know existed. I just think it's a bummer, you groan and you move on." She said that with no discernible symptoms for so long, she had not taken her condition seriously until recently.

"The one symptom I had last year was itching skin on my ankles and wrists," she said. "I had a little bit of trouble concentrating as well but I thought, I'm 64, there's nothing unusual in that. I just wasn't educated about it."

She now has tests every three months to monitor the disease. "The next tests are to check for tumours. I'm taking it more seriously now.

"I could still have a good few years — even decades — of life left, but it's hard to say. I could be facing liver cancer tomorrow. What I can say is that having hep C means that I live with a sharp sense of my own mortality, which in many ways makes life more vivid and immediate."

Dame Anita made £130 million when she sold the Body Shop to L'Oréal, the French beauty group, for £652 million last year. She vowed to give the money away. Today the high street chain numbers more than 2,000 stores serving nearly 80 million customers.

Dame Anita's daughter Sam, who owns the erotic boutique Coco de Mer in London, said that she was proud of her mother for making her condition public.

"I think she is brave for coming out and saying this," she said. "There are certain stigmas attached to hepatitis C like there are to other liver diseases. She has put herself in a vulnerable position to talk about something that directly affects her life. She is dedicated to blowing apart the myth about the condition."

No vaccine exists to prevent hepatitis C, but drugs are available that are effective in more than half of cases.

Dame Anita also announced that she has become a patron of the Hepatitis C Trust and will campaign for better awareness of the condition.

Dame Anita contracted the disease from a blood transfusion

Transfusion

- What component?
- Any special requirements?
  - Irradiation /CMV negative?
  - Antibodies?
  - Childbearing age females - Kell negative (can be a precursor to HDN – rarely)

What if they tell you they REALLY don't want blood?

- Find out why.
- What do they mean by blood?
- Are there fears or questions you can explain and answer?
- Get advice from the hospital transfusion team.
- Get an anaemia management and bleeding plan into the notes.
- Inform the Consultant Obstetrician, Anaesthetist and Haematologist (I always tell the lab too).
- Ask that they complete an Advanced Directive.
- If they are Jehovah's Witnesses suggest they discuss what to include in the AD with their Hospital Liaison Elder.

Case study1

- 37 yr Jehovah's Witness – G5 P4
- Delivered at 39/40
- Hb at delivery 10.1g/dl
- Previous PPH x3

  (no one though uh-oh or told anyone)
- Massive bleed
- Hb dropped to 4.5

Plan

- Take her to Theatre – ASAP (ligation not TAH).
- Ventilate on ITU.
- Check and recheck Advance Directive.
- Give 200mg Venofer TIW
- Give 3x doses 40K Eprex
- Hb dropped to 1.9 (eek!)
- Haematologists dash off to Athens to conference
- Hold nerve (mostly by phone)
- Hb 5.6 @1 week post delivery
- Hold debriefing meeting post discharge

What did we learn?

- Alert Consultant, Hospital Transfusion Team (HTT) and Anaesthetist at booking if refusing blood.
- Refer to CNS Transfusion (HTT) to make a plan and communicate clearly and widely to cover several eventualities.
- If PPH occurs out of hours call in the consultants (Obs, Haem and Anaesthetics) even if minor to start with.
- ITU were fantastic – ask for review early if bleeding.
- Advance directives are VERY useful especially in an emotionally charged situation.

Bleeding plan

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CARE PLAN FOR WOMEN IN LABOUR REFUSING A BLOOD TRANSFUSION

(As referred to in the *RCOG News* of the Royal College of Obstetricians & Gynaecologists)

This document is an aid for medical staff and midwives managing a Jehovah's Witness or other patient who declines blood. Autologous procedures such as **blood salvage** and the use of **plasma-derived products** such as clotting agents are a **matter of personal choice for each Witness.** Most will carry an advance decision document expressing their wishes. Please check with the patient.

Risk management

- All Jehovah's Witnesses or those declining a blood transfusion should be seen in a consultant clinic.
- Clinicians should **plan in advance for blood loss.** If the Hb is ≤ 10.5g/dl use **ferrous sulphate 200mg tds and folic acid**–with acidic fruit juice or 100mg ascorbic acid to aid absorption. If unresponsive to oral iron, use **IV iron** which replenishes iron stores faster and more effectively than oral iron[1,2]. A single total-dose IV iron preparation may be more acceptable to the patient than repeat infusions. Addition of **recombinant human erythropoietin (EPO)**, which does not cross the placenta and is reportedly safely used in pregnancy, enhances Hb response[3,4].
- High-risk patients should be booked into a unit with **facilities such as interventional radiology, blood salvage and surgical expertise.** All elective surgery must be planned as far ahead as possible.
- For **high-risk caesarean section**, e.g. abnormal placentation, consider with the interventional radiologist elective insertion of catheters for **uterine artery embolisation** immediately pre-operatively and arrange **blood salvage**.
- At the time of labour ensure the **consultant obstetrician and anaesthetist are aware a Jehovah's Witness has been admitted.**
- The **third stage of labour should be actively managed with oxytocics** with consideration of **prophylactic syntocinon** infusion.
- Consider **delayed cord clamping 1-2 min for pre-term infants** to maximise Hb, with controlled cord traction after placental separation[5].
- Check patient's **vital signs and evidence of uterine contraction** every 15 min for 1 to 2 hours after delivery.
- Contact the **Hospital Liaison Committee for Jehovah's Witnesses in an emergency** (contact details over page).

Management of active haemorrhage

First steps: AVOID DELAY. Involve obstetric, anaesthetic and haematology consultants. Establish IV infusion, along with **uterine massage** (every 10 min for 1 hour can reduce blood loss[6]). **Give oxytocic drugs first, then exclude retained products of conception or trauma** (this could save time). Proceed with **bimanual uterine compression**. Give oxygen. Catheterise and monitor urine output. Consider CVP line. **Slow, but persistent blood loss requires action.** Anticipate coagulation problems. Keep patient fully informed. Proceed with following strategies if bleeding continues:

Oxytocic agents: Ergometrine with oxytocin (Syntometrine): Marginally more effective than oxytocin alone. If patient is hypertensive, use **oxytocin** 10U (not 5U) by slow IV injection (in serious PPH the benefits of higher dose outweigh the risks)[7,8]. **Carboprost (Hemabate)** 250µg/ml IM, can be repeated after 15 min. Direct intra-myometrial injection is faster (less hazardous at open operation).

Misoprostol (Cytotec): Useful option in atonic PPH where first-line treatment has failed. Can be given either by **sub-lingual** (600-800µg), **rectal** (800-1000µg) or **intrauterine route** (800µg)[9,10,11]. Control of haemorrhage reported for rectal and intrauterine routes when unresponsive to oxytocin, ergometrine and carboprost[10,11].

Intrauterine balloon tamponade: Have available purpose-designed 500 ml **Bakri tamponade balloon** (Cookmedical). Drainage of blood and cessation of bleeding can be observed via the catheter drainage shaft. Continue oxytocin. Expulsion of balloon can be prevented by vaginal packing. To minimise bleeding risk during removal, use graduated deflation or slowly deflate to half volume and observe; if no bleeding, continue deflation; if bleeding starts, reinflate[12,13]. Alternatively, stomach balloon of **Sengstaken-Blakemore oesophageal catheter** has controlled haemorrhage in 84% of 43 cases (in 2 studies), in the majority of successful cases bleeding was due to uterine atony[12,14]. Distal end of tube beyond balloon should be cut off to reduce risk of occlusion or perforation. Indwell time of balloon averaged 24 hours[14]. **Bakri balloon also used to control PPH due to vaginal lacerations**[15].

Non-inflatable anti-shock garment: Recently developed neoprene Velcro-fastened garment (zoexniasg.com) can be applied in 2 minutes and allows perineal access for obstetric procedures. Can reduce blood loss and reverse hypovolaemic shock within minutes by the transfer of 0.5 to 1.5 litres of blood from the lower body and abdomen to the vital organs. This can stabilise the patient and gain time while awaiting senior staff input. Successful trials have been conducted with >400 women experiencing PPH in developing countries[16].

Recombinant factor VIIa (NovoSeven): Increasing evidence of effectiveness for control of PPH unresponsive to standard therapies. This product and the following haemostatic agents should be used under consultant guidance. 90 µg/kg provide site-specific thrombin generation, repeat if unresponsive. Successfully used to stop or reduce bleeding in 88% of 118 massive PPH cases[17]. Also to control bleeding in 17 anecdotal PPH cases complicated by DIC[18]. (Novo Nordisk have 24-hour emergency distribution for UK-wide delivery [01889 566652] or a small stock can be held to avoid delivery delay.) Occasional failure of FVIIa has been attributed to a low fibrinogen level[19]. The **fibrinogen concentrate Haemocomplettan** (a plasma-derived **alternative to cryoprecipitate**; available on a named-patient basis within 24 hours from CSL Behring; 01444 447400) can enhance clot strength and normalise clotting in the presence of FVIIa[20,21].

Other haemostatic agents: Prothrombin complex concentrates (PCCs) such as **Beriplex** and **Octaplex** (plasma-derived), are proposed as substitutes for fresh frozen plasma and are widely prescribed as such in Europe. Beriplex reported to achieve control of bleeding in cardiac and other surgery[22]. **Tranexamic acid (Cyklokapron)**: anti-fibrinolytic agent well established for controlling haemorrhage, use 1gm IV x tds, slowly[23]. **Fibrin sealants**: **Flowseal** used to arrest massive bleeding in surgical bed following hysterectomy[24]; **Tisseel** has controlled bleeding of complicated vulval and vaginal lacerations when suture haemostasis failed due to tissue friability[25]. Also consider IV **vitamin K**.

B-Lynch uterine compression suture: The B-Lynch brace suture can also be **combined with intrauterine balloon catheter** if bleeding persists[26]. **Prophylactic insertion of this suture** has been used in high-risk caesarean section[4]. The **Hayman suture technique** may be a simpler procedure and quicker to apply as the lower uterine segment is not opened[27].

Embolisation/ligation of internal iliac arteries or embolisation/bilateral mass ligation of uterine vessels: Angioplasty balloon catheters can be used for emergency temporary occlusion in theatre, with transfer to the angiography suite for definitive embolisation[28].

Hysterectomy and care in theatre: Subtotal hysterectomy can be just as effective, also quicker and safer. Use Flowtrons Excell to decrease risk of DVTs. Avoid hypothermia (impairs coagulation), use fluid warmer, bair hugger, hats etc. Avoid unnecessary over-dilution. Have blood salvage and experienced operator on hand (see below).

Intraoperative blood salvage: Endorsed by NICE (2005) and RCOG (2008) guidelines. Should be set up whenever possible (check if acceptable to the patient). Either single or double suction methods can be used for collection. However, to maximise blood recovery, there is good evidence that single suction is a safe procedure[29]. Swab washing also increases RBC recovery. A 'collect only' set-up of the anticoagulation/suction tubing will enable blood salvage to begin within minutes[30]. Conventionally, a leukocyte filter has been used when reinfusing, though in an emergency situation the filter may be removed completely to maximise the flow rate, as prior to availability of filters no adverse events were reported. These are clinical decisions based on the balance of benefit/risk.

Management of postpartum anaemia—continued over page

VI. **APPENDIX II**

Bleeding Plan for Patient's Refusing Blood (to include Jehovah's Witnesses)

Patient Details:

K no: **Tel no:**
GP: **Surgery tel no:**
NHS no: **Consultant:**

Sister in charge: Sister Claire Atterbury, Transfusion CNS

Date: **Weight (booking weight if pregnant):**

Patient will NOT accept:

Patient WILL accept:

Clinical Details:
(CLJA)

a. **Minor Oozing**
Watch and wait.

b. **Significant Oozing (<1000 ml)**
1. Check haemoglobin and clotting.
2. If haemoglobin > **90 g/L** consider 2 x 200 mg of **Ferinject** IV in 100 ml of normal saline as per protocol.
3. If haemoglobin < **90 g/L** give 200 mg of **Ferinject** IV in 100 ml of NACL as per protocol and discuss with either transfusion specialist on bleep 2795 or consultant haematologist on-call.

c. **Significant and ongoing blood loss > 1000 mls and continuing**
1. Check FBC and clotting.
2. If haemoglobin < **80 g/L** give 1000 mg of **Ferinject** IV in 100 ml of normal saline over 15 minutes (unless <35 Kg then give 500 mg).
3. Contact Consultant Haematologist to discuss the use of **EPREX** 300 iu/kg/day
Pt Dose = ----------
NB: ROUND DOSE UP TO AVAILABLE PREP SIZE NOT DOWN (maximum of 3 doses).
4. Contact Critical Care Outreach Team and Consultant to discuss patient assessment or possible ventilation.

Copies to: Critical Care Outreach Team, Medical Notes, Haem Server, Consultant in charge of patient.

Claire L J Atterbury, Clinical Nurse Specialist Haematology and Transfusion Medicine (bleep 2795)

Document Number:	B01f.1	Version:	1.03
Document Name:	Patients Refusing Blood	Review date:	JUNE 2018
Review Interval:	Biennially	Reviewed by:	Owner

Case Study 2

- 22 year old – G3 P2
- 37/40
- Admitted to Castleacre with Norovirus
- Christmas.
- Septic
- Distressed baby → crash section
- Hb 31g/l, Platelets 41 $x10^9$/l , Neutrophils 0.3 $x10^9$/l
- B_{12} 99, Folate 1.6, CRP 280

Then…

- 14 days as inpatient
- Septic shock – removal to ITU
- 8 units of Red cells
- 1 unit of Platelets
- IV antibiotics
- Lots of stress and anxiety for everyone…….she didn't sue us

Back up a bit.....

- 30.9.08 - 28 week bloods showed MCV **109** and film comment "macrocytic anaemia. Probable B_{12} deficiency"
- 6.11.08 MCV 116. Hb 90 Film comment "Macrocytic picture ?Liver ?B_{12} /Folate deficiency."
- 13.11.09 B_{12} 117, Folate 0.9 (3-20) Red Cell Folate 48 (93-641)
- Patient given oral iron. Usual Midwife on AL. Patient moved house.
- 10.12.09 UTI – E-Coli
- 27.12.09 Admitted with diarrhoea. Norovirus. Baby distressed.

Case study 3

- 36 year old Journalist
- Best friend a Transfusion Nurse Specialist (woohoo)
- Not keen on blood transfusion
- On Pregaday
- Hb 90 at 28weeks
- MCV lower than pre-pregnancy (91→85)
- Asked for advice by midwife

Plan

- Increase oral Iron to $FeSO_4$ 200mg BD from week 28
- Continue folic acid to delivery

- Delivered at 42/40
- 1400 ml bleed
- Hb at 2 days PP 100g/l

Remember - No blood needs planning (and nerve!)

- Assessment of anaemia for all patients at booking.
- Get advice and a plan from the HTT (it's all in the planning and preparation).
- Find out if your patient really is immovable if refusing blood.
- Blood should only be used in Obstetrics to save a life
- Advance Directives help.
- Use an appropriate product that is safe and cost effective.

THANK YOU!