Royal Hospital for Women (RHW)
BUSINESS RULE
COVER SHEET

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EXECUTIVE SPONSOR	Medical Co-directory of Maternity services
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SUMMARY	Assess and manage anaemia and haemoglobinopathies in pregnancy appropriately, including referral pathway to genetic counselling
KEY WORDS	Iron deficiency, Anaemia, Haemoglobinopathies, pregnancy

Royal Hospital for Women (RHW)
CLINICAL BUSINESS RULE

Iron Deficiency, Anaemia and Haemoglobinopathies in Pregnancy

RHW CLIN080

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Within this document we will use the term woman, this is not to exclude those who give birth and do not identify as female. It is crucial to use the preferred language and terminology as described and guided by each individual person when providing care.

1. BACKGROUND

Iron deficiency is the leading cause of anaemia during pregnancy affecting 38% of women worldwide. The correct management of anaemia and haemoglobinopathies is important to prevent fetal or maternal morbidity and mortality [6,12,13]

The aim of this CBR is to assess and manage anaemia and haemoglobinopathies appropriately, including referral pathway to genetic counselling

Anaemia in a pregnant woman is considered:

- <20 weeks gestation haemoglobin (Hb) ≤110g/L
- ≥20 weeks gestation Hb ≤105g/L

2. RESPONSIBILITIES

2.1 Medical staff – assessment, counselling, screening and referral to genetics and haematology if required

2.2 Midwifery staff – assessment and referral to obstetric or genetics if required

3. PROCEDURE

3.1 Clinical Practice

3.1.1 Screening

- Review woman, biological father and/or gamete donor's history and any prior investigations at first pregnancy contact (usually GP) for risk for anaemia and/or haemoglobinopathies
- Document risk factors for Iron deficiency or anaemia[21]:
    - Previous anaemia/iron deficiency
    - Inter-pregnancy interval < 1 year
    - Multiple pregnancy
    - Parity ≥ 3
    - Vegan/vegetarian

- Adolescent pregnancy
- Recent history of bleeding e.g. Postpartum Haemorrhage
- Aboriginal and Torres Strait Islander
- Woman who are unable to use blood products (e.g. Jehovah's Witness or red cell antibodies)

- Perform full blood count (FBC) and ferritin at booking visit and again at 26-28 weeks gestation
- Perform haemoglobinopathy screening (FBC, haemoglobinopathy screen and iron studies documenting ethnicity on request form) if not screened in past, or previous result is not available, with the following risk factors (appendix 2):
  - High risk ethnicity: Central and South East Asian, Indian, Sri Lankan, Pakistani, Bangladeshi, Middle Eastern, Mediterranean, African descent, Pacific Islander or New Zealand Maori, Central/South American, Brazilian
  - Mean corpuscular volume (MCV) <80fL or mean corpuscular haemoglobin (MCH) <27pg
  - Known haemoglobinopathy carrier, family history of haemoglobinopathy in woman, biological father or gamete donor's family
- Screen for and manage iron deficiency (ferritin < 30ug/L) (as per appendix 1)

3.1.2 Further Investigations

- Investigate anaemia as per appendix 2 if cause is unknown:
  - Review history and past investigations
  - Review blood film (microcytosis, fragmentation, sickle cells) and MCV, MCH
  - Iron Studies, vitamin B12 and active B12 (although note reference ranges for B12 are unknown in pregnancy and the levels normally fall), folate, haemoglobinopathy screen, Electrolytes Urea Creatinine (EUC), Liver Function Tests (LFTs), Lactate Dehydrogenase (LDH), reticulocytes, haptoglobin
- Screen biological father (FBC, haemoglobinopathy screen, iron studies) if any abnormalities identified on woman/gamete donor's haemoglobinopathy screen. Document woman's name and MRN on biological father's request form and state biological father's name and date of birth on woman request form. If gamete donor is a known carrier, document this on request form

3.1.3 Management

- Discuss appropriate diet, high in iron and vitamin C rich foods to optimise iron stores (see Iron (dietary) in pregnancy factsheet) and inform woman of symptoms of anaemia
- Do not commence iron replacement without confirming iron deficiency, as low MCV or Hb may be due to haemoglobinopathy
- Treat other specific causes of anaemia (e.g. folate or B12 deficiency)[6]
- Refer to obstetrician or haematologist if thrombocytopenia, pancytopenia, unexplained anaemia, moderate to severe anaemia (Hb < 90g/L), significant symptoms, late gestation >34 weeks or failure to respond to a trial of oral iron
- Refer haemoglobinopathy carriers to an obstetrician/haematologist for maternal management
- Refer to genetics if both gamete donor/biological parents known or suspected

haemoglobinopathy carriers for further counselling on fetal implications

3.1.4 Oral Iron Treatment

- Treat iron deficiency (ferritin <30, regardless of Hb) with oral iron supplementation (see information sheet Oral Iron Treatment in Pregnancy)
- Give woman information handout on Oral Iron Treatment in Pregnancy
- Ensure woman with gastrointestinal (GIT) conditions (e.g. inflammatory bowel disease, coeliac disease and/or GIT surgery) tolerate treatment, as absorption of iron may be impaired. Treatment can be trialed but should be closely monitored
- Recommend oral iron preparations that contain ferrous iron as these offer superior results over ferric iron preparations[16]. Ferrous fumarate preparations provide best absorption and tolerance[17]:
    - Administer low dose ferrous oral iron, 65mg to 100mg daily[15,16,18,19]
    - Commence ferrous oral iron on alternate days to improve tolerance and absorption if there is adequate time until birth[15,16]. Increase to daily if there is no improvement seen in Hb or ferritin
    - Avoid split-dosing (morning and evening) or doubling the dose as this has a limited additional effect compared with daily administration[15,16]
    - Take ferrous oral iron on an empty stomach (1 hour before or 3 hours after food and other medications including multivitamins) for optimal absorption
- Recommend ferric iron preparations such as iron polymaltose complex(Maltofer) for a woman with GIT conditions/nausea and vomiting, or when ferrous iron preparations are not tolerated
    - Iron polymaltose complex must be taken with food or soon after food for best absorption, and the dose can be doubled to improve a response
    - See Table 1 for different types of and elemental iron levels of oral preparations available

Table 1 **Oral Preparations**

Brand name	Elemental iron	Iron salt	Additional content	Form
Ferro-F-tab***	100mg	ferrous fumurate 310mg	folic acid 350mcg	tablet
Ferropods iron & vitamin C	100mg	ferrous fumurate 304mg	vitamin C (ascorbic acid) 20mg	capsule
Ferro-Tab	65.7mg	ferrous fumurate 200mg		tablet
Ferro-Gradumet***, Ferrogen	105mg	ferrous sulfate 325mg		MR tablet*
Ferrograd C, Ferro Plus C, Ferro-Max C, Ferrogen Iron + vitamin C	105mg	ferrous sulfate 325mg	vitamin C (ascorbic acid) 500mg	MR tablet*
FGF	80mg	ferrous sulfate 250mg	folic acid 300mcg	MR tablet*
Fefol	87.4mg	ferrous sulfate 270mg	folic acid 300mcg	capsule

Ferro-Liquid	6mg/ml	ferrous sulfate 30mg/ml		oral liquid
Maltofer**	100mg	ferric iron polymaltose 370mg		tablet
Maltofer Syrup**	50mg/5ml	ferric iron polymaltose 50mg/5ml		oral syrup

*MR = Modified release. These have a reduced rate of release of active substance and allows release of the iron over several hours. Release of iron distal to the site of maximal intestinal absorption may theoretically limit response in some patients.
** Response to oral iron polymaltose may be slower than with ferrous iron. Maltofer is licensed in Australia for the treatment of iron deficiency in adults and adolescents where the use of ferrous iron sulphate is not tolerated or otherwise inappropriate. ***Iron formulations available on formulary for inpatients

- Discuss gastrointestinal side effects of iron supplementation and options to prevent/mitigate. If the woman is troubled by these side effects:
  - change to alternate day dosing[15]
  - change the dose
  - increase fluid intake
  - take mild laxative e.g. Metamucil, Movicol, docusate sodium (Coloxyl®)
  - take with food
  - Change to another oral iron preparation
- Monitor response to oral supplementation:
  - retest Hb and ferritin in four weeks from commencement of supplementation
  - evaluate compliance/adherence to treatment at each visit and further options if Hb not increasing[6]
  - continue replacement for three months, and until at least six weeks post-partum[6] once the Hb is in the normal range

3.1.5 Intravenous Iron preparation

- Consider intravenous iron in the following circumstances (see for more details and administration Intravenous Iron Infusion)
  - Iron deficiency anaemia in a woman with:
    - Hb <80
    - birth expected within four weeks
    - inadequate response to oral iron (e.g poor compliance)
    - impaired absorption of oral iron e.g. inflammatory bowel disease, bariatric surgery
    - risk of significant blood loss
  - Symptomatic blood loss
  - Woman is unwilling/unable to accept blood products[2] (see CBR Blood products – Management of pregnant woman unable to use blood products)

3.2 Documentation

- Antenatal Card
- Medical record

3.3 Educational Notes

- Iron deficiency is the leading cause of anaemia during pregnancy. It is associated with increased risk of perinatal morbidity and mortality, low birth weight, preterm birth, blood transfusion, and maternal morbidity [6,12,13]
- Over-the-counter oral iron preparations contain two different types of iron salts: ferrous and ferric iron. Instruct women about appropriate administration depending on the type of ferrous salts to enable an adequate response to treatment (see information sheet Oral Iron Treatment in Pregnancy)
- Studies have found that fractional iron absorption (FIA) is higher from lower iron doses compared to higher doses, leaving less unabsorbed iron in the intestinal lumen to irritate the gut[15.16.18.19]
- There exists evidence to support the important role of the liver hormone, hepcidin, in the regulation of iron absorption
- High ferritin levels may be associated with inflammation and infection, functioning as an immune response and not as a marker of iron status. This needs to be considered when assessing women with chronic disease such as HIV, renal, cardiac and rheumatological conditions or any recent acute infection. Measuring transferrin saturation may helpful.
- Available evidence on oral iron in pregnancy is limited. Study samples are often small, involve non-pregnant participants, or occur in settings that are not similar to Australia.
- Australian Red Cross Lifeblood has many resources available at Iron optimisation in maternity guide

3.4 Implementation, communication and education plan

This revised CBR will be distributed to all medical, nursing and midwifery staff via @health email. The CBR will be discussed at ward meetings, education and patient quality and safety meetings. Education will occur through in-services, open forum and local ward implementation strategies to address changes to practice. The CBR will be uploaded to the CBR tab on the intranet and staff are informed how to access

3.5 RELATED POLICIES / PROCEDURES / CLINICAL PRACTICE

- Australian College of Midwives (AM) Guidelines for consultation and referral
- Iron Infusion - Intravenous
- Postpartum Haemorrhage – Prevention and Management
- Blood products – Management of pregnant woman unable to use blood products

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4. ABORIGINAL HEALTH IMPACT STATEMENT DOCUMENTATION

- Considerations for culturally safe and appropriate care provision have been made in the development of this Business Rule and will be accounted for in its implementation.
- When clinical risks are identified for an Aboriginal and/or Torres Strait Islander woman or family, they may require additional supports. This may include Aboriginal health professionals such as Aboriginal liaison officers, health workers or other culturally specific services

5. CULTURAL SUPPORT

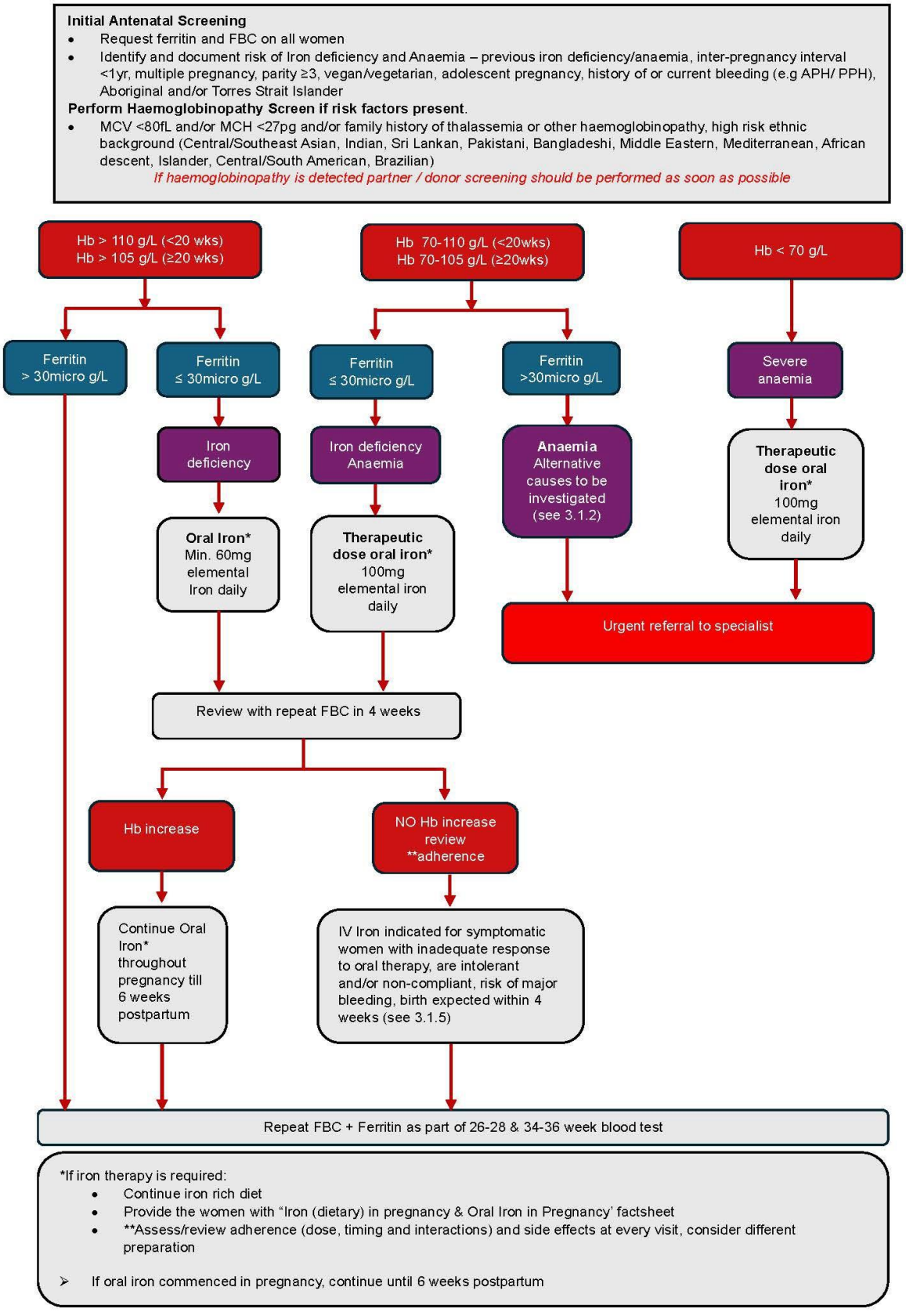
- For a Culturally and Linguistically Diverse CALD woman, notify the nominated cross-cultural health worker during Monday to Friday business hours
- If the woman is from a non-English speaking background, call the interpreter service: NSW Ministry of Health Policy Directive PD2017_044-Interpreters Standard Procedures for Working with Health Care Interpreters.

6. REVISION AND APPROVAL HISTORY

Date	Revision No.	Approval
03/07/2024		Maternity CBR committee
Reviewed and endorsed Maternity LOPs July 2020 Approved Quality & patient Safety Committee 21/11/13 Endorsed Obstetrics LOPs 5/11/13 Reviewed and renamed November 2013 (previously – Anaemia In Pregnancy Guideline) Approved Patient Care Committee 5/2/09 Endorsed Obstetric Clinical Guidelines Group December 2009		

Appendix 1

Iron Deficiency and Anaemia Flowchart



Royal Hospital for Women (RHW)
CLINICAL BUSINESS RULE

Iron Deficiency, Anaemia and Haemoglobinopathies in Pregnancy

RHW CLIN080

Action following Antenatal Haemoglobinopathy Screen: A Guide for the Antenatal Clinic **June 2024**

Request Haemoglobinopathy Screen if any of:

- High risk ethnicity in patient & partner: Central/South east Asian, Indian, Sri Lankan, Pakistani, Bangladeshi, Middle Eastern, Mediterranean, Black African, Pacific Islander, Maori, Central/South American, Brazilian
- MCV <80fL or MCH <27pg
- Known haemoglobinopathy carrier, family history of haemoglobinopathy in mother or partner's family

Request
- Full Blood Count
- Haemoglobinopathy screen
- Iron studies

Haemoglobinopathy Screen Result

Beta thalassaemia trait, δβ thalassaemia
or
Abnormal variant detected, such as HbS, HbE, HbC, HbD-Punjab, HbO-Arab, Hb Lepore
or
Hb Constant Spring
or
HbH disease, alpha thalassaemia detected

yes → *Further action required*

HbA_2: 2.0 - 3.2% → yes → MCV <80fl or MCH < 27pg * → yes → Reflex alpha thalassaemia molecular testing by laboratory (Medicare) → α thalassaemia variant present → yes → *Further action required*

no

HbA_2: 3.3 - 3.7% * → yes → Atypical heterozygous beta thalassaemia cannot be excluded → *Further action required*

HbH bodies detected
or
ICT strip positive → yes → *Further action required*

Additional Comments

Molecular studies would be required
Alpha thalassaemia cannot be excluded
Atypical beta thalassaemia cannot be excluded
Partner should be screened

→ *Further action required*

Alpha thalassaemia molecular testing may automatically be performed by laboratory. Read the report carefully.

Further Action

If only mother's results available → then **partner** must be **screened** with urgent haemoglobinopathy screen

If 'further action required' from **BOTH** mother AND father's results → **refer urgently** to Genetics or Haematology

Contacts: **RHW** Prenatal Genetic Service Phone: 9382 6098; 9382 6099; 9382 6042 Fax: 9382 6038
StG Department of Clinical Genetics Phone: 9113 3635 Fax: 9113 3694

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Action that occurs through Genetics or Haematology following Antenatal Haemoglobinopathy Screen, when *both* parents involved.

Beta globin problem in both parents (Box A or B)

Box A
HbA_2: 3.3 – 3.7%
Atypical heterozygous beta thalassaemia cannot be excluded
Molecular studies required

→ *Beta gene molecular testing*

Variant present ↓

Box B
Beta thalassaemia trait
HbS, HbE, HbC, HbD-Punjab, HbO-Arab
δβ thalassaemia, Hb Lepore

→ *Urgent genetic referral*

Alpha globin problem in both parents (Box C or D)

Box C
MCV <75fl or MCH < 25pg
HbH bodies detected
ICT strip positive
Alpha thalassaemia cannot be excluded
Molecular studies required
Beta thalassaemia trait
HbE with % HbE <27%
HbS with MCV < 80 or HbS % <35%

→ *Alpha gene molecular testing*

2 gene deletion present ↓

Box D
Hb Constant Spring
HbH disease

→ *Urgent genetic referral*