Approach to Anaemia

Dr James Liang
Consultant Haematologist
Middlemore Hospital, Auckland

Date:

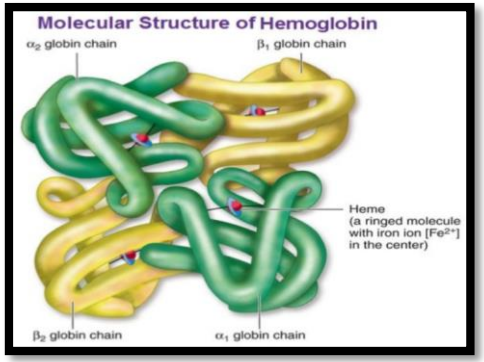
Outline

- Introduction
  - Definition
- Differentials
  - Red cell indices
  - Pathogenesis
  - Microscopy
- Approach
  - Clinical
  - Investigation
    - Level 1
- Cases

ANAEMIA 101

Red Blood Cell

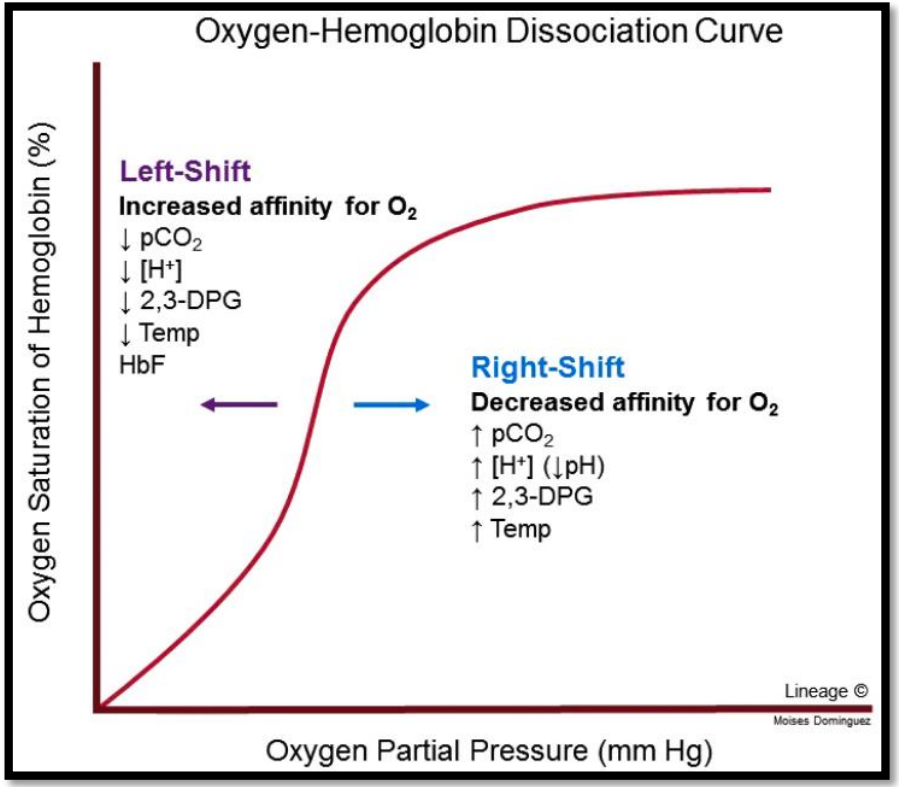
- Erythropoiesis
  - Bone marrow (factory)
    - Significant bone marrow reserve (8 fold)
  - Controlled via kidney/liver (order)
    - Erythropoietin production
  - Building blocks
    - Iron, B12 & folate
- Function
  - Haemoglobin
    - Oxygen delivery to tissue for metabolic processes
      - Brain
      - Cardiac
- Survival
  - 120 days



Definition

- When supply of oxygen to tissue do not meet physiological requirement
  - Supply
    - Oxygen carrying capacity
    - Mechanical delivery
    - Oxygen availability
    - Oxygen dissociation
  - Oxygen requirement
    - Activity

- Laboratory indices
  - Haemoglobin
  - Total RBC
  - Haematocrit



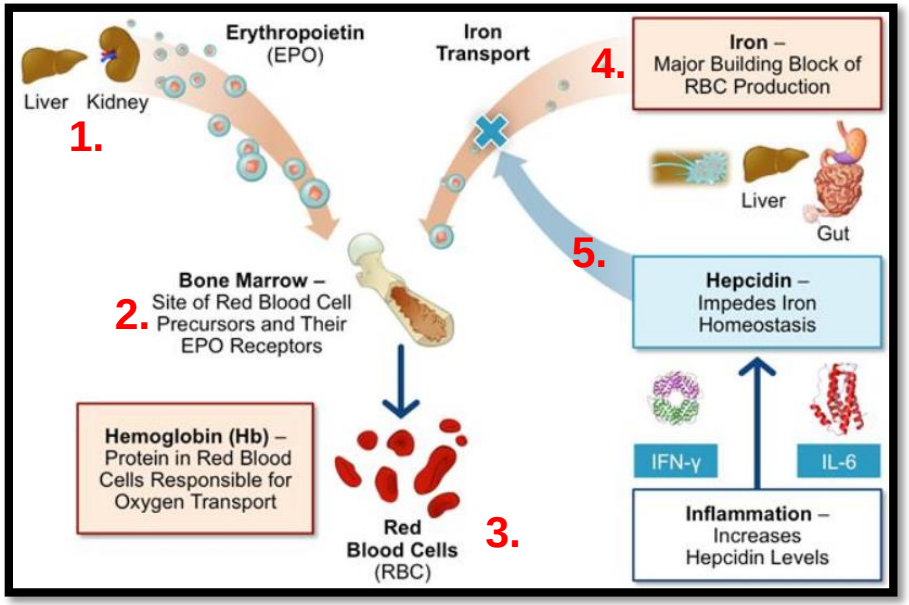
DIFFERENTIALS

Red Cell Parameter

- MCV
  - Microcytic
    - Iron deficiency
    - Thlassaemia/Haemoglobinopathy
    - Sideroblastic Anaemia
    - Anaemia of chronic disease (ACD)
  - Normocytic
    - Blood loss/Haemolysis
    - Anaemia of chronic disease
    - Anaemia of renal disease
    - Bone marrow infiltration/aplastic
  - Macrocytic
    - Blood loss/Haemolysis
    - Megaloblastic anaemia
    - Myelodysplasia

Pathogenesis

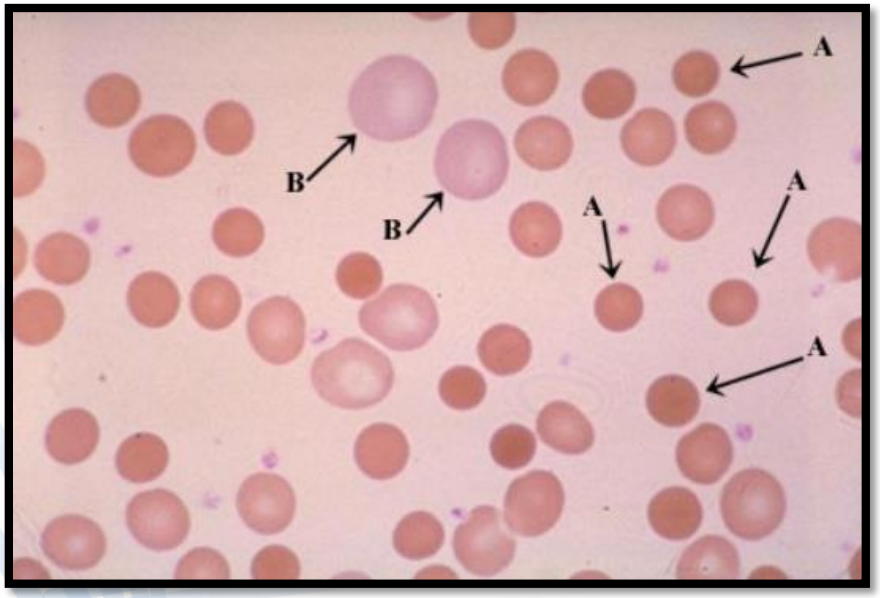
1. Reduced EPO
   - Anaemia of renal disease
2. Bone marrow disorder
   - Reduced production
     - Aplastic
     - Infiltration
     - Medication
   - Faulty production
     - Myelodysplastic
3. Reduced total RBC
   - Blood loss
   - Haemolysis
   - Sequestration
4. Nutritional Deficiency
   - Iron deficiency
   - B12/Folate deficiency
5. Impaired utilisation
   - Iron
   - Folate



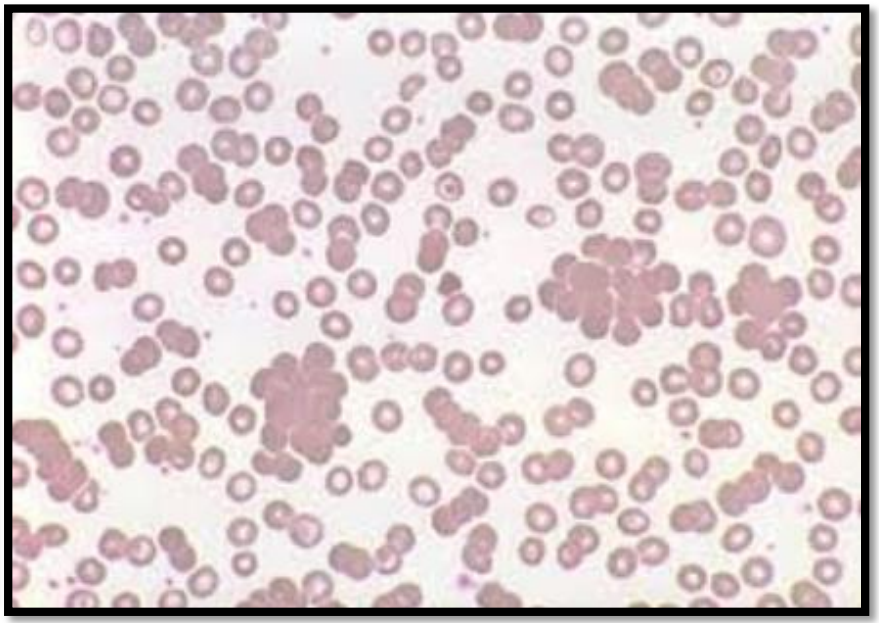
Morphology

COUNTIES MANUKAU HEALTH

Spherocyte



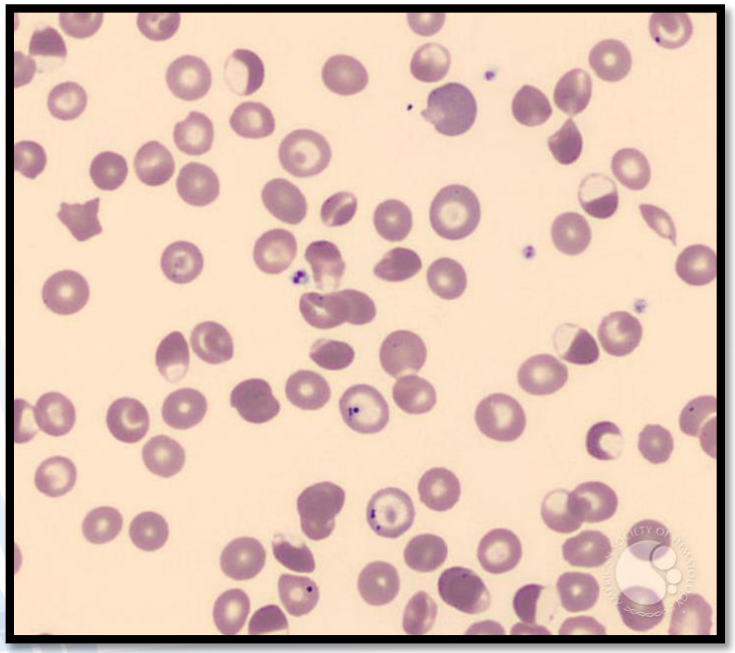
Red Cell Agglutination



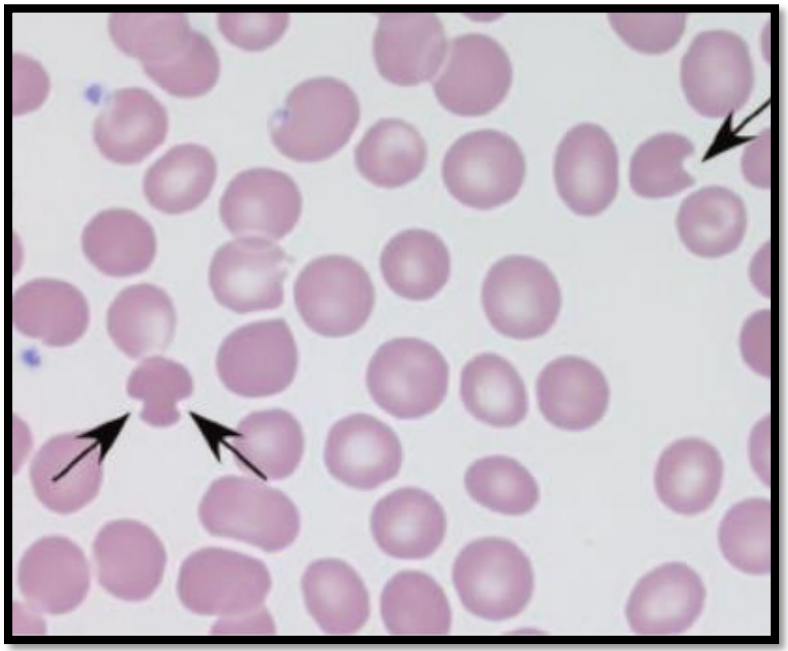
Morphology

COUNTIES MANUKAU HEALTH

Blister/Ghost Cell



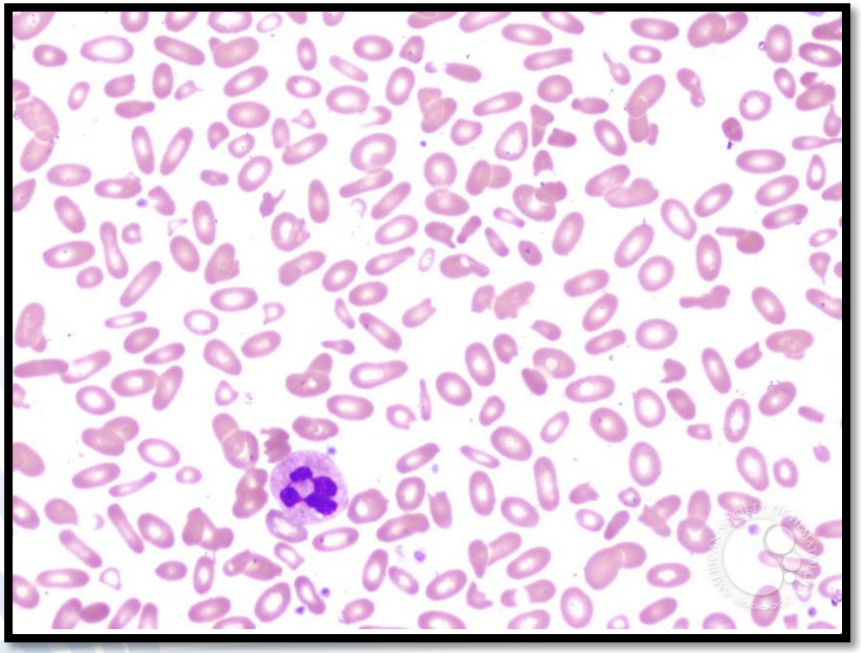
Bite Cell



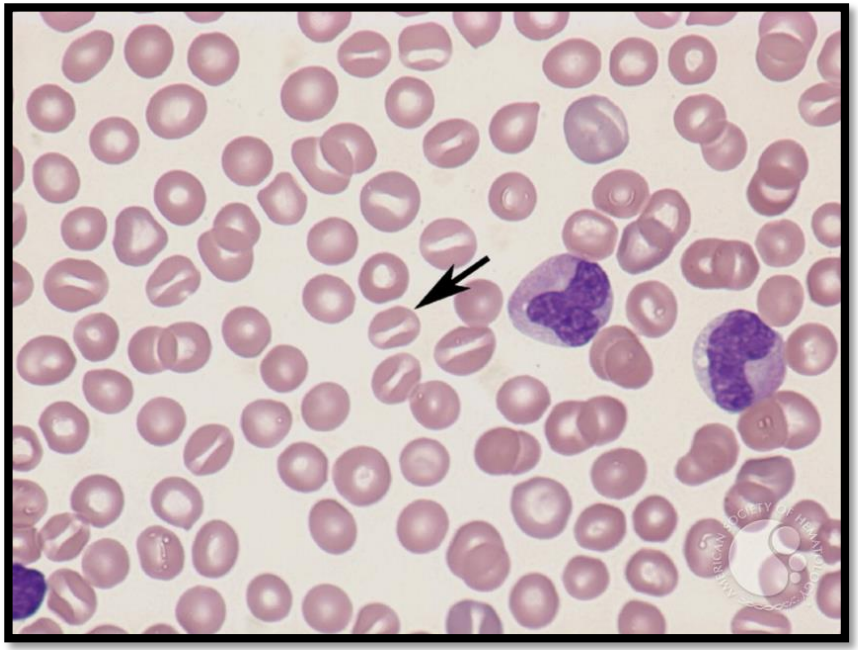
Morphology

COUNTIES MANUKAU HEALTH

Elliptocytes



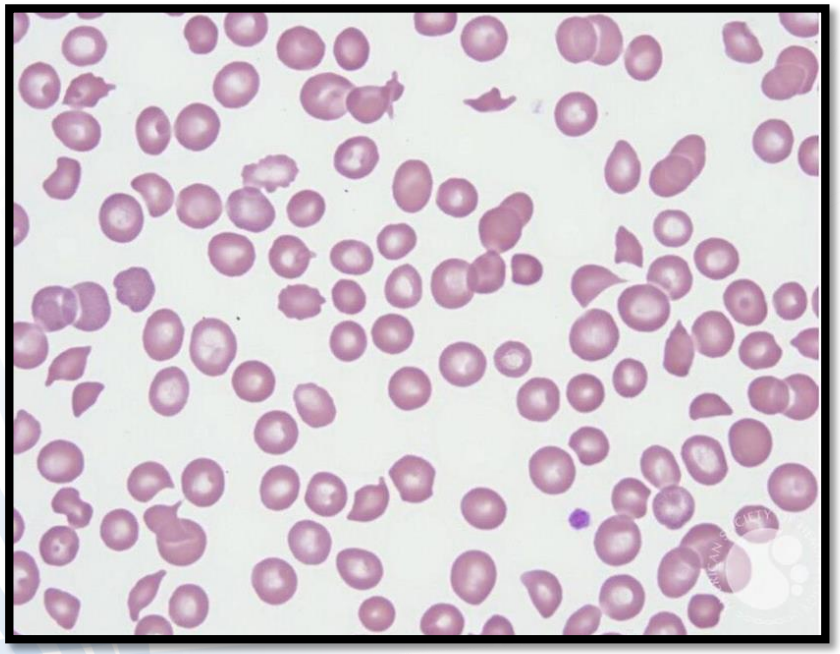
Stomatocytes



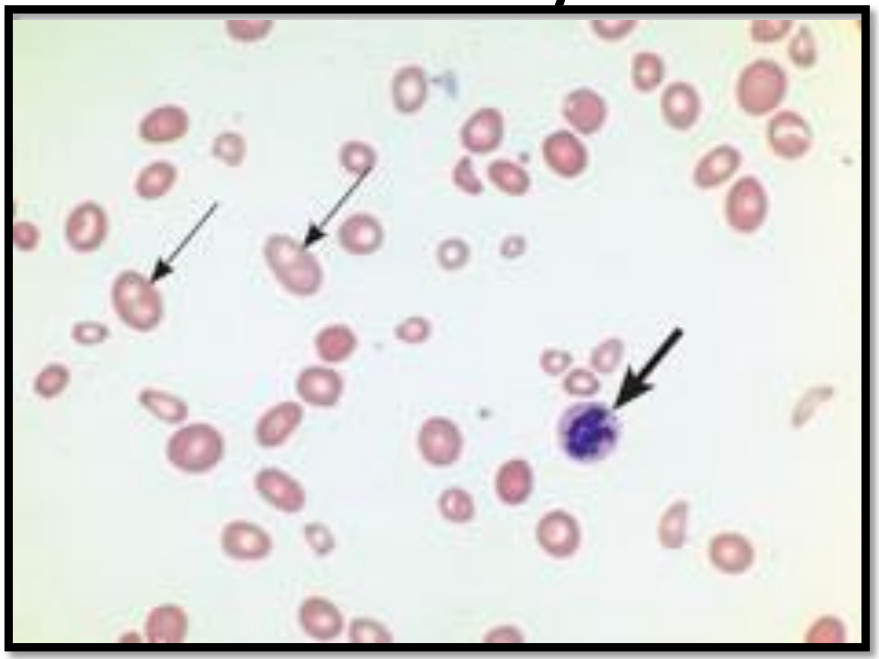
Morphology

COUNTIES MANUKAU HEALTH

Fragment (schistocyte)



Macroovalocyte



Blood Film Cheat Code

- Polychromasia
  - Suggests increased reticulocytes
- Spherocytes
  - Suggests either
    - Immune mediated haemolysis
    - Red cell membrane disorder (inherited)
- Red Cell Agglutination
  - Cold agglutination (may be laboratory artifact)
  - Could trigger haemolysis
- Blister/Ghost/Bite Cell
  - Oxidative Haemolysis
- Elliptocytes/Stomatocytes
  - Potential red cell membrane disorder
- Red Cell Fragments
  - Can be seen in valvular disease, renal and liver disease.
  - Important to exclude
    - DIC, HUS/TTP
- Macro-ovalocytes
  - Suggests B12/folate deficiency
- Rouleaux
  - Raised inflammatory marker or globulin
- Teardrop
  - Possible myelofibrosis

CLINICAL

History

- Presenting compliant
  - Bleeding
  - Bowel changes
  - Travel
  - Recent surgery
- PMHx
  - Renal disease
  - Chronic illness
  - Transfusion history
  - Bowel surgery
- Family history
  - Thalassaemia/Haemoglobinopathy
  - Membranopathy
- Diet
  - Vegan
  - Fava bean
- Medication
  - Anticoagulant/antiplatelet
  - Methotrexate
  - Dapsone

Examination

- Signs of anaemia/nutritional deficiency
  - Pallor
  - Angular stomatitis
  - Koilonychia
  - Jaundice
- Cardiovascular
  - Hyperdynamic circulation
  - Compromise
- Bleeding manifestation (guided by history)
  - PR exam for melaena
- Significant diseases to rule out
  - Hepatosplenomegaly
  - Lymphadenopathy
  - Everything else guided by history

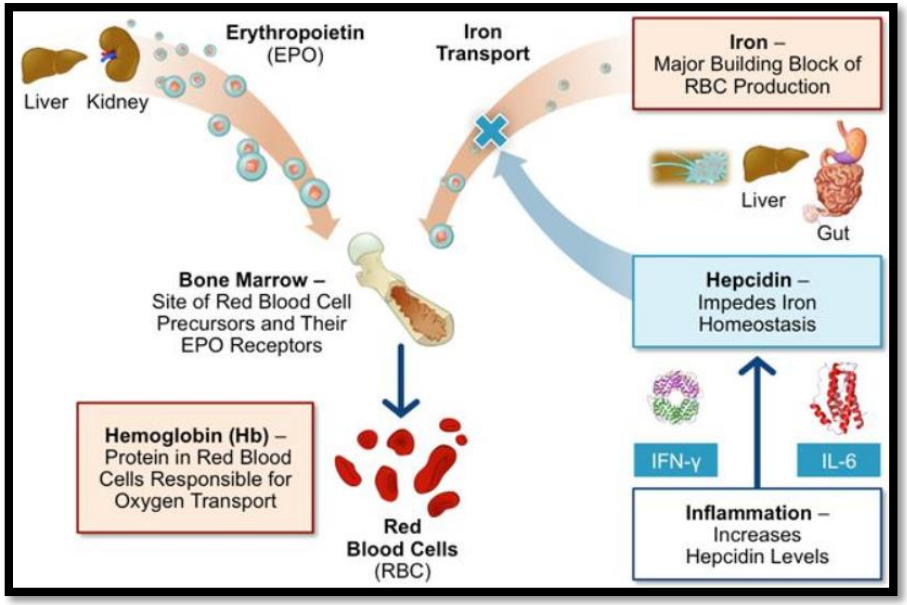
INVESTIGATIONS

Level 1

- Must
  - CBC
  - Reticulocyte
- Dependent
  - Renal function
  - Inflammatory Marker
  - LFT
  - Haematinics
    - Full iron study
      - Not just ferritin
    - B12/folate
    - TSH

Full/Complete Blood Count

1. Patient Detail
   - Appropriate reference range
2. Look at all 3 lineages
   - Pancytopenia
     - Think global
       - BM related
       - B12/folate deficiency
       - Splenic sequestration
     - May be more than just one process
3. MCV
   - Refer to earlier lists
4. Reticulocyte
   - Bone marrow response
5. Blood film comment
   - Spherocytes
   - Red cell fragments
   - Malaria parasite
   - Abnormal lymphocytes



Microcytic Anaemia

	IDA	Thal/Haem	ACD	SA
Ferritin	↓	↑↓	↔	↔
Blood Film	Pencil cells Dimorphic*	Target cells Basophilic stippling	Rouleaux	Dimorphic Dysplasia
Thrombocytosis	↑	↔	↑	↔
RDW	↑	↔	↔	↑
Reticulocyte	↓	↑	↓	↑
CRP/ESR	↔	↔	↑	↔
sTFR	↑	↑	↔	↑
RBC	↓	↑	↓	↓

IDA = Iron Deficiency Anaemia SA = Sideroblastic Anaemia REt-He = Reticulocyte Haem sTFR = Soluble Transferrin Receptor

Normocytic Anaemia

	Blood Loss	Haemolysis	ACD	Renal Disease	Bone marrow	Drug
Retic	↑	↑	↑↓	↑↓	↑↓	↑↓
Haptoglobin	↔	↓	↑↓	↔	↔	↔
Urea	↑↓	↔	↔	↑	↔	↔
Cr	↔	↔	↔	↑	↔	↔
Film	Polychromasia Leucoerythroblastic	Polychromasia Various	Normal	Echinocytes	Normal Malignant cells Leucoerythroblastic	Normal

- Consider myeloma screen

Macrocytic Anaemia

	MA	MDS	Liver	Hypothyroidism	Drug	Blood Loss or Haemolysis
B12/folate	↓	↑	↑	↑	↑	↑
Thyroid Fx	↔	↔	↔	↓	↔	↔
LFT	↔	↔	↑	↔	↔	↔
Retic	↑	↑	↑	↑	↑	↑
Film	Macroovalocyte	Dysplasia	Acanthocytes	Normal	Normal	See before

MA = Megaloblastic Anaemia

MDS = Myelodysplastic syndrome

CASE

Case 1

- FBC/CBC

		Ref. Range
Haemoglobin	62	(115 – 155)
RBC	1.93	(3.60 – 5.60)
HCT	0.21	(0.35 – 0.46)
MCV	107	(80 – 99)
MCH	32.1	(27.0 – 33.0)
Platelets	223	(150 – 400)
WBC	3.6	(4.0 – 11.0)
Neutrophils	1.9	(1.90 – 7.50)
Lymphocytes	1.2	(1.00 – 4.00)
Monocytes	0.3	(0.20 – 1.00)
Eosinophils	0.0	(<0.51)
Basophils	0.0	(0.00 – 0.20)

- Additional Test

		Ref. Range
Reticulocytes	247	(10 – 100)

- Blood Film
  - Increased number of macrocytes, polychromasia and oval cells. Reported by XXXX scientist.
- What are the differential?

Macrocytic Anaemia

	MA	MDS	Liver	Hypothyroidism	Drug	Blood Loss or Haemolysis
B12/folate	↓	↑↑	↑↑	↑↑	↑↑	↑↑
Thyroid Fx	↔	↔	↔	↓	↔	↔
LFT	↔	↔	↑	↔	↔	↔
Retic	↑↑	↑↑	↑↑	↑↑	↑↑	↑
Film	Macroovalocyte	Dysplasia	Acanthocytes	Normal	Normal	See before

Blood loss or anaemia?

Case 1

- No history of blood loss

		Ref. Range
Haemoglobin	62	(115 – 155)
RBC	1.93	(3.60 – 5.60)
HCT	0.21	(0.35 – 0.46)
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MCH	32.1	(27.0 – 33.0)
Reticulocytes	247	(10 – 100)
Blood film	Increased number of macrocytes, polychromasia and oval cells. Reported by XXXX scientist. Spherocyte and polychromasia are not prominent. Reported by XXXX haematologist.	

- Haemolysis Screen

		Ref. Range
Haptoglobin	<0.3	(0.3 – 2.0)
Bilirubin (conj)	15	(0 - 5)
Total Bilirubin	63	(<25)
LDH	677	(120 - 250)
DAT (Coomb's Test)	4+	

- Diagnosis?
  - Immune mediated haemolysis
    - Auto or allo-immune

Question?

Case 2

- FBC/CBC

		Ref. Range
Haemoglobin	92	(115 – 155)
RBC	5.41	(3.60 – 5.60)
HCT	0.30	(0.35 – 0.46)
MCV	56	(80 – 99)
MCH	17.0	(27.0 – 33.0)
Platelets	224	(150 – 400)
WBC	5.6	(4.0 – 11.0)
Neutrophils	3.62	(1.90 – 7.50)
Lymphocytes	1.23	(1.00 – 4.00)
Monocytes	0.52	(0.20 – 1.00)
Eosinophils	0.16	(<0.51)
Basophils	0.03	(0.00 – 0.20)
Reticulocyte	123	(10 – 100)

- Iron Study

		Ref. Range
Ferritin	22	(20 – 170)

- Blood Film
  - Markedly increased target cell, microcytes, fragmented cells, spherocytes and blister cells.

Microcytic Anaemia

	IDA	Thal/Haem	ACD	SA
Ferritin	↓	↑↓	↔	↔
Blood Film	Pencil cells Dimorphic*	Target cells Basophilic stippling	Rouleaux	Dimorphic Dysplasia
Thrombocytosis	↑	↔	↑	↔
RDW	↑	↔	↔	↑
Reticulocyte	↑↓	↑	↓	↑
CRP/ESR	↔	↔	↑	↔
sTFR	↑	↑	↔	↑
RBC	↓	↑	↓	↓

IDA = Iron Deficiency Anaemia SA = Sideroblastic Anaemia REt-He = Reticulocyte Haem sTFR = Soluble Transferrin Receptor

Case 2

- FBC/CBC

		Ref. Range
Haemoglobin	92	(115 – 155)
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Monocytes	0.52	(0.20 – 1.00)
Eosinophils	0.16	(<0.51)
Basophils	0.03	(0.00 – 0.20)
Reticulocyte	123	(10 – 100)

- Haemoglobinopathy Screen

		Ref. Range
HbA2	0.9%	(2.2 – 3.3)
HbH	Numerous inclusion	
HbA	92.4%	

- Diagnosis?
  - Alpha thalassaemia

Question?

Case 3

- FBC/CBC

		Ref. Range
Haemoglobin	54	(115 – 155)
RBC	2.28	(3.60 – 5.60)
HCT	0.19	(0.35 – 0.46)
MCV	83	(80 – 99)
MCH	23.7	(27.0 – 33.0)
Platelets	143	(150 – 400)
WBC	3.0	(4.0 – 11.0)
Neutrophils	1.36	(1.90 – 7.50)
Lymphocytes	1.32	(1.00 – 4.00)
Monocytes	0.26	(0.20 – 1.00)
Eosinophils	0.05	(<0.51)
Basophils	0.0	(0.00 – 0.20)
Reticulocyte	57	(10 – 100)

- Additional Test

		Ref. Range
Ferritin	84	(20 – 170)
Creatinine	77	(45 – 90)
TSH	1.6	(0.30 – 4.00)
CRP	<1	(0 – 5)

- Blood Film
  - Normocytic normochromic anaemia, marked rouleaux and background staining.

Normocytic Anaemia

	Blood Loss	Haemolysis	ACD	Renal Disease	Bone marrow	Drug
Retic	↑	↑	↑↓	↑↓	↑↓	↑↓
Haptoglobin	↔	↓	↑↓	↔	↔	↔
Urea	↑↓	↔	↔	↑	↔	↔
Cr	↔	↔	↔	↑	↔	↔
Film	Polychromasia Leucoerythroblastic	Polychromasia Various	Normal	Echinocytes	Normal Malignant cells Leucoerythroblastic	Normal

- Consider myeloma screen

Case 3

- FBC/CBC

		Ref. Range
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RBC	2.28	(3.60 – 5.60)
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Reticulocyte	57	(10 – 100)

- Additional Test

		Ref. Range
Ferritin	84	(20 – 170)
Creatinine	77	(45 – 90)
TSH	1.6	(0.30 – 4.00)
CRP	<1	(0 – 5)

		Ref. Range
Bilirubin	14	(<25)
ALP	34	(40 – 130)
GGT	18	<50
ALT	11	<45
Total Protein	127	(66 - 84)
Globulin	101	(25 – 41)

Case 3

		Ref. Range
IgG	3.8	(7.0 – 16.0)
IgA	62.9	(0.8 – 4.0)
IgM	0.2	(0.4 – 2.5)
Paraprotein	78g/L of IgA Lambda	
Kappa SFLC	5	(3 – 19)
Lambda SFLC	914	(6 -26)
Calcium	2.57	(2.10 – 2.55)

- Diagnosis?
  - IgA myeloma

Question?