Haematology Labs: Is it normal?

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Case One

- 25 year old female Maori woman
  - Tired and fatigued
  - Fever and productive cough
- No previous medical history available
- Nil regular medication and NKDA
- Social Hx:
  - Smoker 20/day
  - ETOH within guideline

Investigations

- FBC/CBC

		Ref. Range
Haemoglobin	66	(115 – 155)
RBC	3.98	(3.60 – 5.60)
HCT	0.25	(0.35 – 0.46)
MCV	62	(80 – 99)
MCH	16.6	(27.0 – 33.0)
Platelets	523	(150 – 400)
WBC	5.2	(4.0 – 11.0)
Neutrophils	2.74	(1.90 – 7.50)
Lymphocytes	1.66	(1.00 – 4.00)
Monocytes	0.55	(0.20 – 1.00)
Eosinophils	0.17	(<0.51)
Basophils	0.05	(0.00 – 0.20)

- Iron Study

		Ref. Range
Ferritin	35	(20 – 170)

- Blood Film
  - Microcytic hypochromic anaemia. Thrombocytosis is present. Possible causes include infection or inflammation, iron deficiency, blood loss or recent surgery. Reported by XXXX scientist.

What is going on?

- Microcytic Hypochromic Anaemia
  - Iron deficiency Anaemia
  - Thalassaemia/Haemoglobinopathy
  - Anaemia of chronic disease (functional iron deficiency)
  - Sideroblastic anaemia

- Helpful investigations/parameter to differentiate?
  - Iron studies
  - CBC/FBC parameters
    - Blood film comment
    - Thrombocytosis
    - RDW
    - Reticulocyte Haem (Ret-He)
  - CRP
  - Soluble transferrin receptor (sTFR)

Iron Study

	Serum iron (10 – 30)	Transferrin (1.7 – 3.4)	Transferrin sat (0.15 – 0.50)	Ferritin (20 – 170)
IDA	↓	↑	↓	↓*
Thal	↔	↔	↔	↑↓
FIDA	↓	↔	↓	↔
SA	↔	↔	↔	↔

*Normal in setting of inflammation

- Causes of normal Ferritin in iron deficiency
  - Acute phase reactant
  - Liver disease
  - Renal disease
  - In elderly population (>70) and renal patient ferritin <100 don't exclude iron deficiency

Useful Investigations

	IDA	Thal/Haem	FIDA	SA
Ferritin	↓	↕	↔	↔
Blood Film	Pencil cells Dimorphic*	Target cells Basophilic stipplings	Rouleaux	Dimorphic Dysplasia
Thrombocytosis	↑	↔	↑	↔
RDW	↑	↔	↔	↑
Ret-He	↓↓	↓	↓	↓
CRP	↔	↔	↑	↔
sTFR	↑	↑	↔	↑

Nothing beats clinical correlation!!

Clinical Correlation

- Common things occurs commonly
  - Longstanding abnormal/dysfunctional uterine bleeding

- Management
  - Identify the cause
  - Iron replacement
    - Oral vs Parental
      - Ferric Carboxymaltose (Ferinject) on SA
        - *POAC would cover administration cost if Hb <100g/L*
        - *Those with malabsorption would still need to go through the public hospital*
      - No real indication for IM replacement (unless for specific reason)
  - Repeat FBC/Ferritin in 3 to 6 months' time

Repeat bloods

- FBC/CBC

		Ref. Range
Haemoglobin	137	(115 – 155)
RBC	6.14	(3.60 – 5.60)
HCT	0.44	(0.35 – 0.46)
MCV	72	(80 – 99)
MCH	22.3	(27.0 – 33.0)
Platelets	360	(150 – 400)
WBC	15.0	(4.0 – 11.0)
Neutrophils	10.7	(1.90 – 7.50)
Lymphocytes	3.2	(1.00 – 4.00)
Monocytes	0.8	(0.20 – 1.00)
Eosinophils	0.5	(<0.51)
Basophils	0.0	(0.00 – 0.20)

- Iron Study

		Ref. Range
Serum iron	8	(10 – 30)
Transferrin	2.6	(1.7 – 3.4)
Transferrin sat	0.12	(0.15 – 0.50)
Ferritin	50	(20 – 170)

- Haemoglobinopathy Study

		Ref. Range
Haemoglobin Electrophoresis	Normal	
Haemoglobin A2	2.6%	(1.5 – 3.5)
Haemoglobin F	<2.0%	(0 – 2)
Haemoglobin H	None seen	

- Blood Film
  - Increased number of microcytic hypochromic cells. Reported by XXXX scientist.

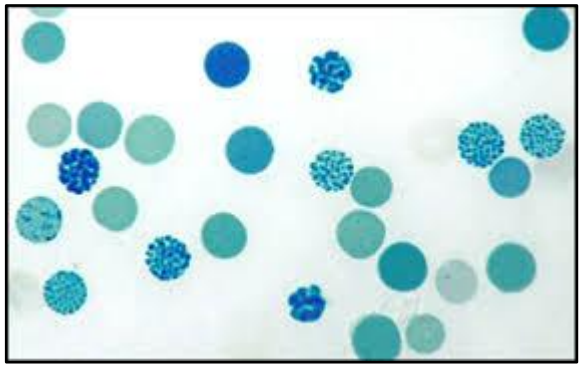
Useful Investigations

	IDA	Thal/Haem	FIDA	SA
Ferritin	↓	↕	↔	↔
Blood Film	Pencil cells Dimorphic*	Target cells Basophilic stippling	Rouleaux	Dimorphic Dysplasia
Thrombocytosis	↑	↔	↑	↔
RDW	↑	↔	↔	↑
Ret-He	↓↓	↓	↓	↔
CRP	↔	↔	↑	↔
sTFR	↑	↑	↔	↑
RBC	↓	↑	↓	↓

- This is highly suspicious for thal/haem

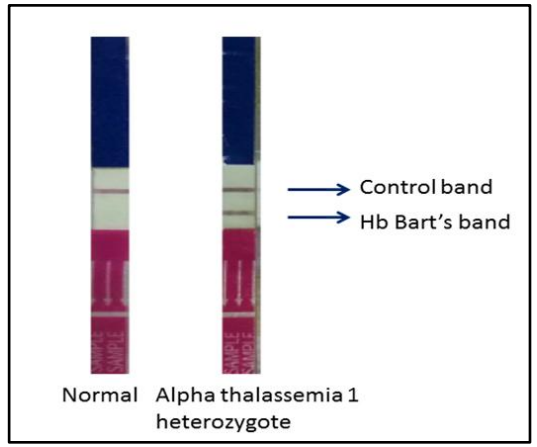
Haemoglobinopathy Study

		Ref. Range
Haemoglobin Electrophoresis	Normal	
Haemoglobin A2	2.6%	(1.5 – 3.5)
Haemoglobin F	<2.0%	(0 – 2)
Haemoglobin H	None seen	



- Does this patient have thalassaemia?
  - α-Thalassaemia

	HbH Sensitivity	Immunochromatographic Test (ICT)
- α/ α α	6%	43%
- α/- α	14%	79%
--/ α α	90% - 100%	100%
--/- α	100%	100%



Continue

- Management
  - Avoid excessive iron replacement
  - Family planning
    - Aim is to avoid 3 or 4 gene deletion of alpha thal

- What do you need to do if she is planning for a family?
  - Test partner
    - FBC and Iron study
      - If NORMAL do nothing
      - If ABNORMAL
        - Refer for genetic counselling
        - Molecular study for alpha genes

Scenario Three

- FBC/CBC

		Ref. Range
Haemoglobin	163	(115 – 155)
RBC	6.34	(3.60 – 5.60)
HCT	0.44	(0.40 – 0.46)
MCV	78	(80 – 99)
MCH	25.8	(27.0 – 33.0)
Platelets	420	(150 – 400)
WBC	8.9	(4.0 – 11.0)
Neutrophils	6.3	(1.90 – 7.50)
Lymphocytes	1.9	(1.00 – 4.00)
Monocytes	0.26	(0.20 – 1.00)
Eosinophils	0.3	(<0.51)
Basophils	0.22	(0.00 – 0.20)

- Iron Study

		Ref. Range
Ferritin	10	(20 – 170)

- Blood Film
  - Increased number of microcytic hypochromic cells. Reported by XXXX scientist.

Time to Vote

1. Iron deficient replace iron.
    - Microcytic hypochromic, low ferritin and thrombocytosis BUT
    - Not anaemic and erythrocytosis (RBC)

2. Thalassaemia/Haemoglobinopathy
    - Microcytic hypochromic and erythrocytosis BUT
    - Not anaemic, low ferritin and thrombocytosis

3. A bit of both?
    - Possible except NOT ANAEMIC

4. Something is not right – ask a friend
    - Polycythaemia
        - Smoking?
        - Either due to JAK2 mutation or increased EPO secretion
            - *Increased erythropoiesis resulting in iron deficiency*

Take home message

- Recommend to do full iron study or ferritin + CRP
  - Normal ferritin do not exclude iron deficiency
- Blood film “can” be helpful
- Please always check response to iron replacement
  - Unmask underlying thalassaemia/haemoglobinopathy or polycythaemia
- Negative thalassaemia/haemoglobinopathy screen do no exclude thal

Case Two

- 66 year old European man admitted under the Gen Surgery
  - Presented with HONK secondary to biliary infection
  - Treated conservatively and responded nicely

  - Given a worrying history of unintentional 10kg weight loss
    - Malignancy screen ensured

- PMHX
  - T2DM on oral hypoglycaemic

Bloods

- FBC/CBC

		Ref. Range
Haemoglobin	88	(130 – 175)
RBC	3.52	(4.30 – 6.00)
HCT	0.28	(0.40 – 0.52)
MCV	78	(80 – 99)
MCH	25.0	(27.0 – 33.0)
Platelets	547	(150 – 400)
WBC	11.2	(4.0 – 11.0)
Neutrophils	9.8	(1.90 – 7.50)
Lymphocytes	0.8	(1.00 – 4.00)
Monocytes	0.4	(0.20 – 1.00)
Eosinophils	0.1	(<0.51)
Basophils	0.00	(0.00 – 0.20)
Immature Granulocytes	0.1	(0.0 – 0.06)

- General Chemistry

		Ref. Range
Sodium	136	(135 – 145)
Potassium	3.9	(3.5 – 5.2)
Chloride	100	(95 – 110)
Urea	11.4	(3.2 – 7.7)
Creatinine	176	(60 – 105)
Calcium (adjusted)	2.60	(32 – 48)
Albumin	21	(32 – 48)
Protein	80	(66 – 84)
Globulin	59	(25 – 41)
CRP	164	(0 – 5)

- Iron Study

		Ref. Range
Serum iron	7	(10 – 30)
Ferritin	1671	(20 – 170)

What do you think is going on?

- What further investigation would you do?
  - Microcytic hypochromic anaemia
  - Hypercalcaemia
  - Renal impairment
  - Elevated globulin
  - Reactive changes
    - Thrombocytosis, neutrophilia with left shift, elevated CRP, extremely high ferritin

- "Spoke to your registrar and advice for this patient to be reviewed in the haematology outpatient clinic ? MGUS ?? Myeloma"

Further Investigations

- Immunoglobulin + SPE

		Ref. Range
IgG	17.8	(7 – 16.0)
IgA	4.8	(0.8 – 4.0)
IgM	1.1	(0.4 – 2.5)
Electrophoresis	*	
Immuno Fixation	*	

* Immuno Fixation: There is a moderate polyclonal immune response, with an oligoclonal banding pattern in the gamma region.

- Serum Free Light Chain

		Ref. Range
Free Kappa	135	(3.5 – 19.5)
Free Lambda	66	(6.0 – 26.0)
Kappa/Lambda Ratio	2.05	(0.26 – 1.65)
Creatinine	176	(60 – 105)
Test performed at Waitemata DHB Laboratory		

- Bence Jones Protein

		Ref. Range
Protein Urine	0.21	(0 – 0.15)
Urine (elph)	Refer to Immuno Fixation comment.	
Immuno Fixation	A mixed tubuloglomerular proteinuria is seen.	

Does he have MGUS or Myeloma?

1. Yes

2. No
   - In order to diagnose MGUS or Myeloma you need to show clonality
     - Only one globulin should be increased while the other can be normal or suppressed
       - IgG and IgA are both high
     - Electrophoresis/Immuno Fixation
       - Negative in both serum and urine
     - Serum free light chain
       - Skewed ratio!

Serum Free Light Chain

		Ref. Range
Free Kappa	135	(3.5 – 19.5)
Free Lambda	66	(6.0 – 26.0)
Kappa/Lambda Ratio	2.05	(0.26 – 1.65)
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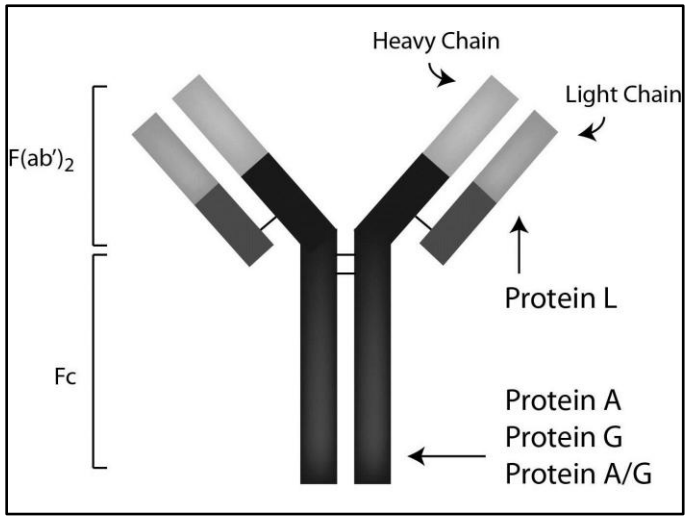

- Serum Free Light Chain
  - Two things that goes against clonality
    - Both kappa and lambda light chain is increased
      - Reflect infection/inflammation
    - Renal impairment
      - Increase serum kappa LC
      - Normal range can be up to ~3.5
  - Much more sensitive than Bence Jones protein
    - I no longer do Bence Jones protein
  - Intra-laboratory variation of up to 25%
    - Significant variation inter-laboratory!
    - Trend is much more important than absolute number unless there is a significant increase.

Take home message

- Serum free light chain should replace Bence Jones protein
  - K/L ratio can be increased in renal impairment
  - K and L light chain is increased in inflammation
    - Increase ≠ clonal
  - Significant inter and intra-laboratory variation