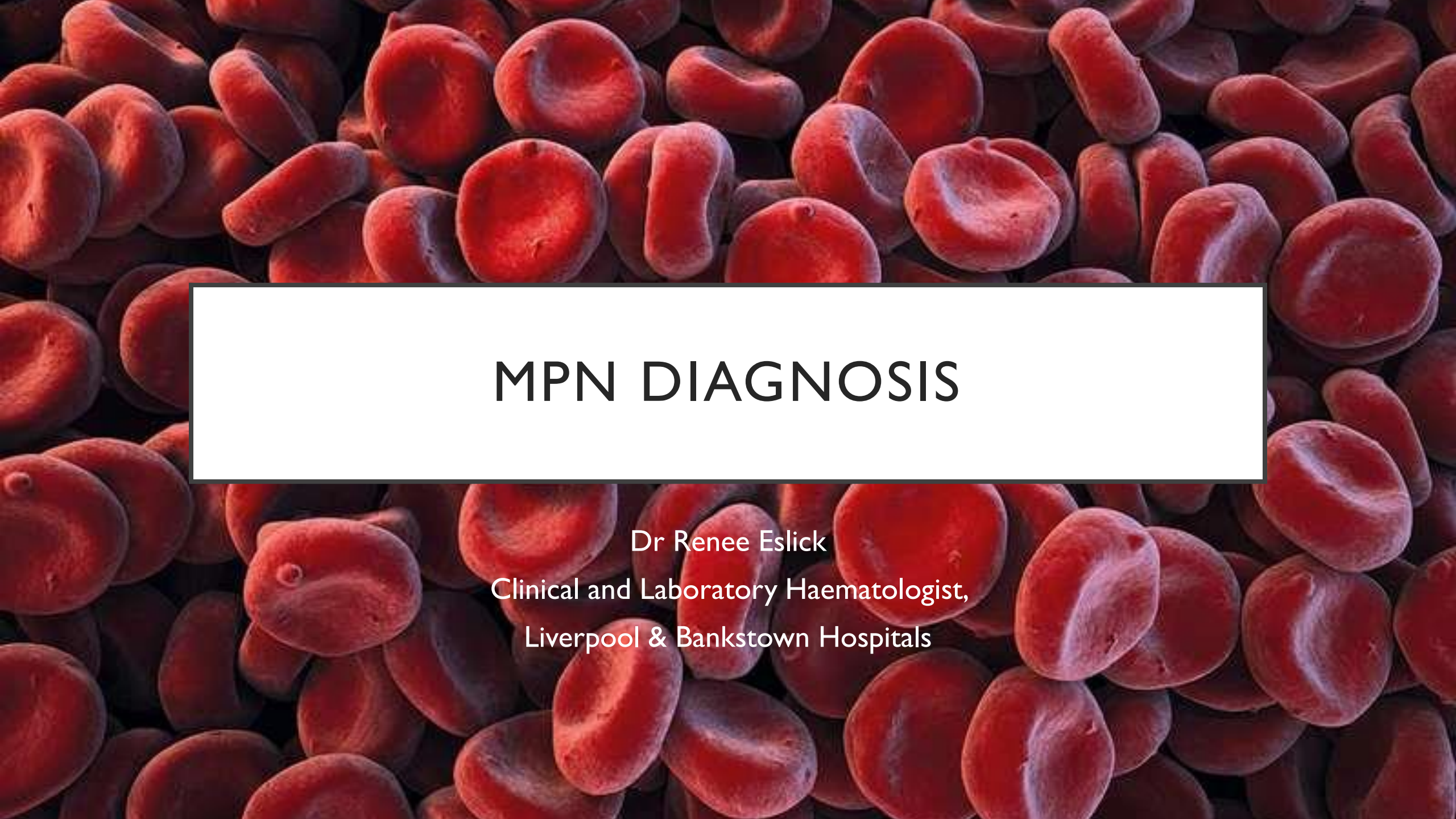


MPN DIAGNOSIS

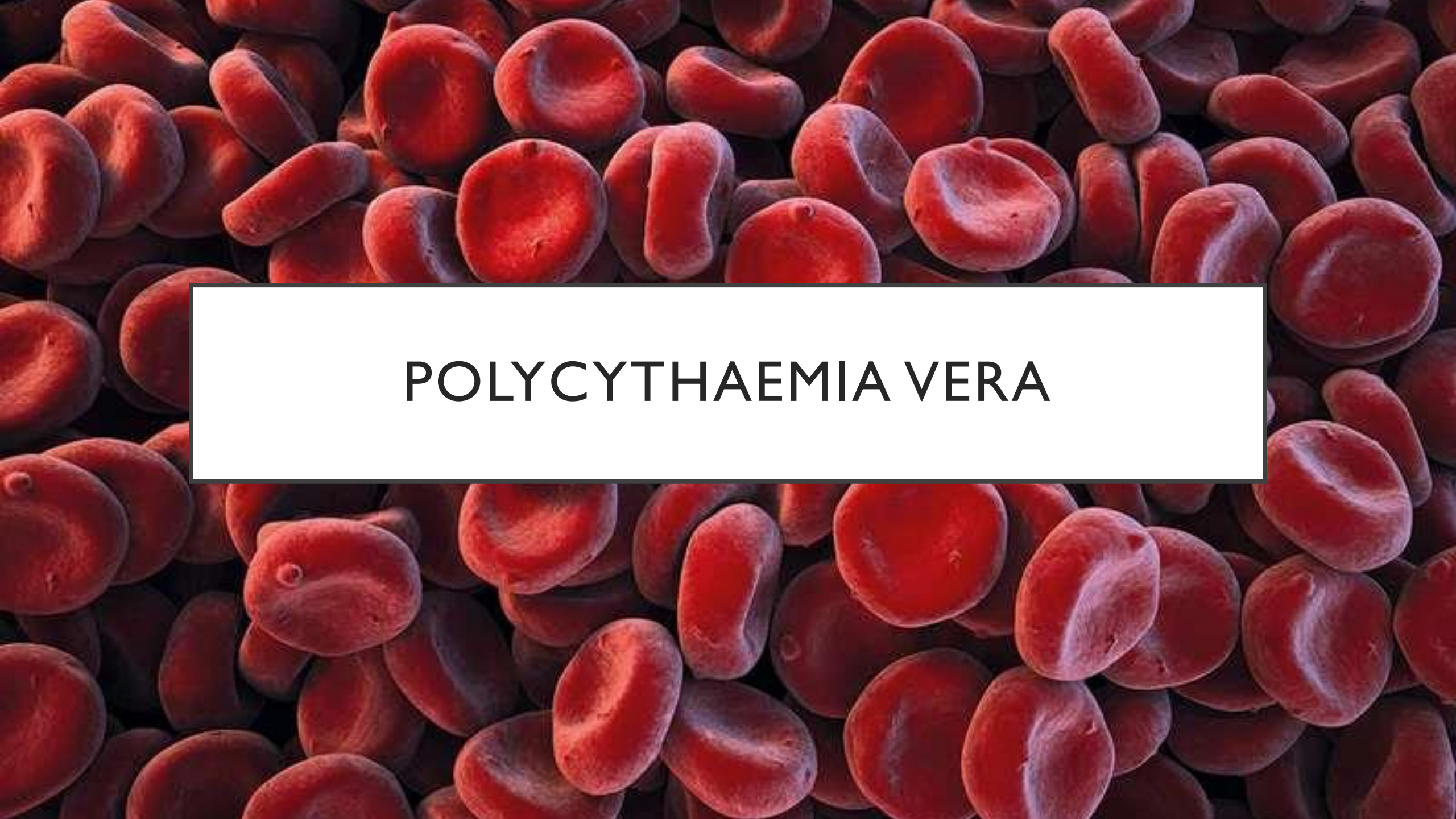
Dr Renee Eslick

Clinical and Laboratory Haematologist,

Liverpool & Bankstown Hospitals

MYELOPROLIFERATIVE NEOPLASMS

- Polycythemia vera
- Essential thrombocythemia
- Primary myelofibrosis
  - PMF, prefibrotic / early stage
  - PMF, overt fibrotic stage
- Chronic myeloid leukaemia (CML)
- Chronic neutrophilic leukaemia
- Chronic eosinophilic leukaemia, NOS
- MPN, unclassifiable

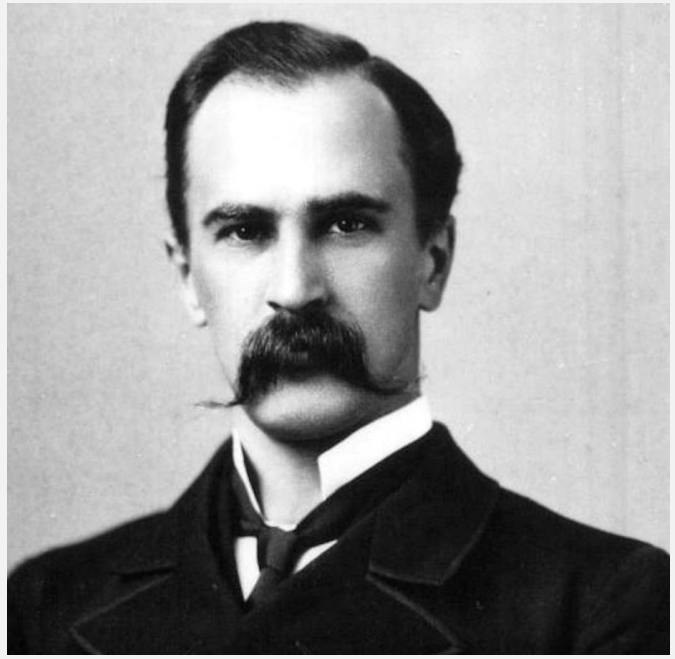


POLYCYTHAEMIA VERA

POLYCYTHAEMIA VERA

- First described in 1892 by Louis Henri Vaquez
- Reported a 40 year old man with chronic cyanosis, distended veins, vertigo, dyspnoea, hepatosplenomegaly, palpitations
- Markedly elevated red cell count

POLYCYTHAEMIA VERA



- William Osler, 1903
- Recognised three types of polycythemia:

1. "True polycythemia" (polycythemia vera)
2. Polycythemia secondary to some other cause
3. Relative polycythemia – red cells appear increased due to a fall in the plasma volume

PV SYMPTOMS

- Incidental finding
- Itchiness, particularly following a bath or shower
- Burning pain in the hands or feet with discolouration
- Visual disturbances
- Gastrointestinal symptoms
- Increased risk of blood clots

CURRENT DIAGNOSTIC CRITERIA

THE UPDATED WHO CLASSIFICATION OF HEMATOLOGICAL MALIGNANCIES

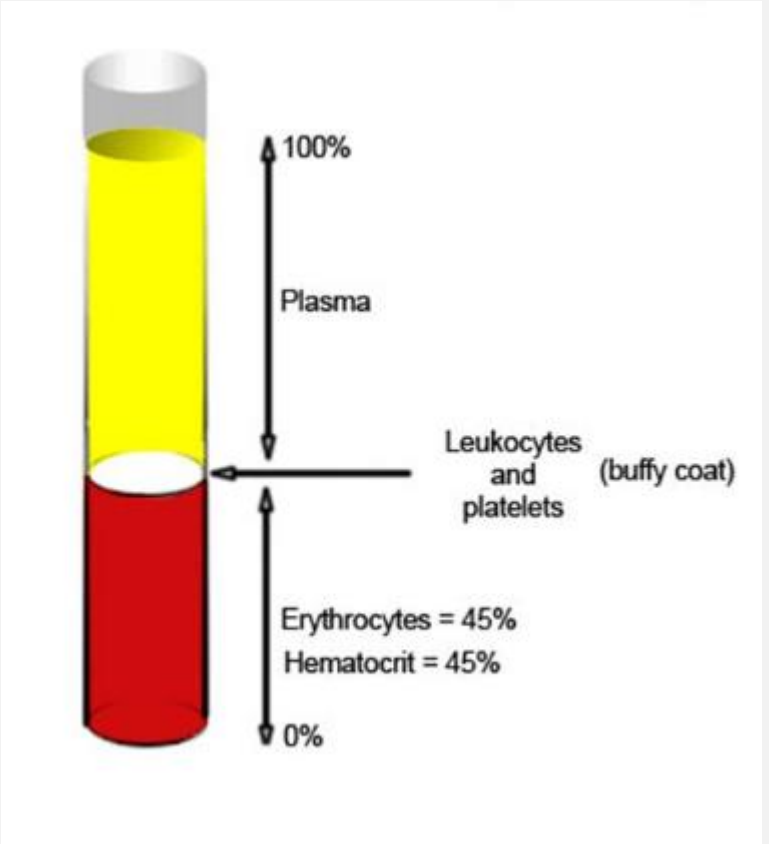
The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia

Daniel A. Arber,[1] Attilio Orazi,[2] Robert Hasserjian,[3] Jürgen Thiele,[4] Michael J. Borowitz,[5] Michelle M. Le Beau,[6] Clara D. Bloomfield,[7] Mario Cazzola,[8] and James W. Vardiman[9]

2016 WHO CRITERIA

MAJOR CRITERIA

- Haemoglobin >165g/L in men
- Haemoglobin >160g/L in women
- *Or*
- Haematocrit >49% in men
- Haematocrit >45% in women
- *Or*
- Increased red cell mass



RED CELL MASS MEASUREMENTS

- Rarely done
- Nuclear medicine scan
- “Label” the red cells and plasma with a radioactive marker

2016 WHO CRITERIA

MAJOR CRITERIA

- 2. Bone marrow biopsy:
  - Increase in all types of blood cells (“panmyelosis”)
  - Increased number of blood cells (“hypercellular”)
  - Platelet precursors (“megakaryocytes”) are differently sized

2016 WHO CRITERIA

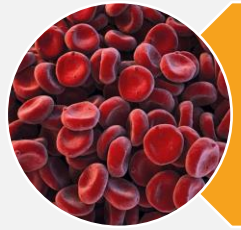
MAJOR CRITERIA

- 3. Presence of JAK2 V617F
- Or presence of JAK2 exon 12 mutation

MINOR CRITERIA

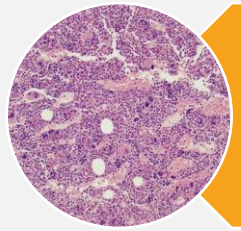
- Subnormal serum erythropoietin level

1. ALL THREE MAJOR CRITERIA



Haemoglobin >165g/L (men) or >160g/L (women)

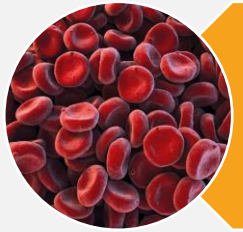
Haematocrit >49% (men) or >48% (women)



Bone marrow biopsy

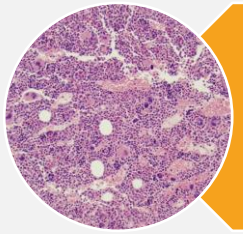
JAK2 V617F or JAK2 exon 12

2. FIRST TWO MAJOR & MINOR CRITERION



Haemoglobin >165g/L (men) or >160g/L (women)

Haematocrit >49% (men) or >48% (women)

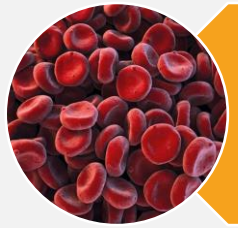


Bone marrow biopsy

JAK2 V617F o[illegible]AK2 exon 12

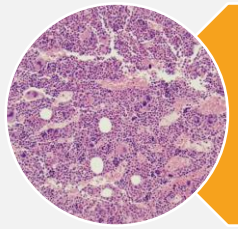
Reduced serum erythropoietin level

3. DIAGNOSIS WITHOUT A BONE MARROW



Haemoglobin **>185**g/L (men)
or **>165**g/L (women)

Haematocrit **>55.5%** (men)
or **>49.5%** (women)



Bone marrow biopsy

JAK2 V617F or JAK2 exon 12

Reduced serum erythropoietin level

ESSENTIAL THROMBOCYTHAEMIA

HISTORY

- Described in 1924 by Austrian pathologists Epstein and Goedel
- Patient with extremely elevated platelet count, minimal change in the red cells, and mucocutaneous bleeding
- Primary (essential thrombocythemia) and secondary (due to other causes) described in 1954

ET SYMPTOMS

- Incidental finding
- "Vasomotor symptoms"
  - Headache
  - Dizziness / fainting
  - Numbness of fingertips and toes
  - Burning pain in hands and feet with redness and warmth
  - Transient visual changes

ET SYMPTOMS

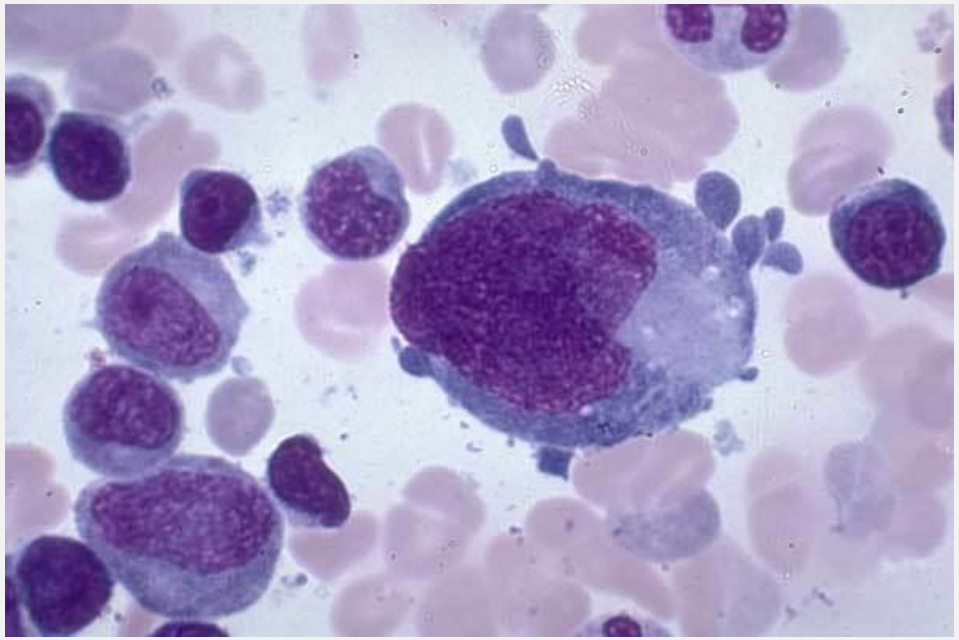
- Blood clot – venous or arterial
- Bleeding symptoms

2016 WHO CRITERIA

MAJOR CRITERIA

- 1. Platelet count ≥ 450 x 10^9/L

- 2. Bone marrow biopsy
  - Increased megakaryocytes (platelet precursors)
  - Enlarged, mature, hyperlobated
  - *No* increase in the white or red blood cell precursors
  - *No* fibrosis / scarring of bone marrow (or only very minor)



2016 WHO CRITERIA

MAJOR CRITERIA

- 3. Not meeting WHO criteria for CML, PV, PMF, MDS or other myeloid neoplasms
  - Makes this a 'diagnosis of exclusion'
  - Essentially, rule out other conditions first

2016 WHO CRITERIA

MAJOR CRITERIA

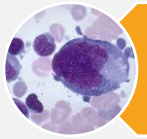
- 4. Presence of JAK2, CALR or MPL
  - JAK2 – 60-65%
  - CALR – 20-25%
  - MPL – 5%
  - "Triple negative" – 10-15%

MINOR CRITERIA

- Presence of another clonal marker (eg ASXL1, EZH2, TET2, IDH1/IDH2, SRSF2, SR3B1)
- OR no other cause for raised platelet count found

1. FIRST FOUR MAJOR CRITERIA

Platelets ≥ 450



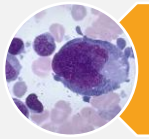
Bone marrow biopsy

Not meeting WHO criteria for other conditions

Presence of JAK2, CALR or MPL

2. FIRST THREE MAJOR CRITERIA & MINOR CRITERION

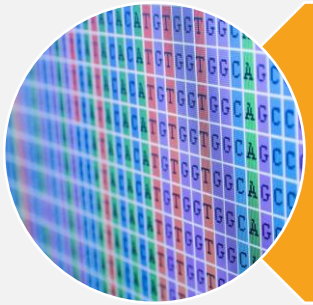
Platelets ≥ 450



Bone marrow biopsy

Not meeting WHO criteria for other conditions

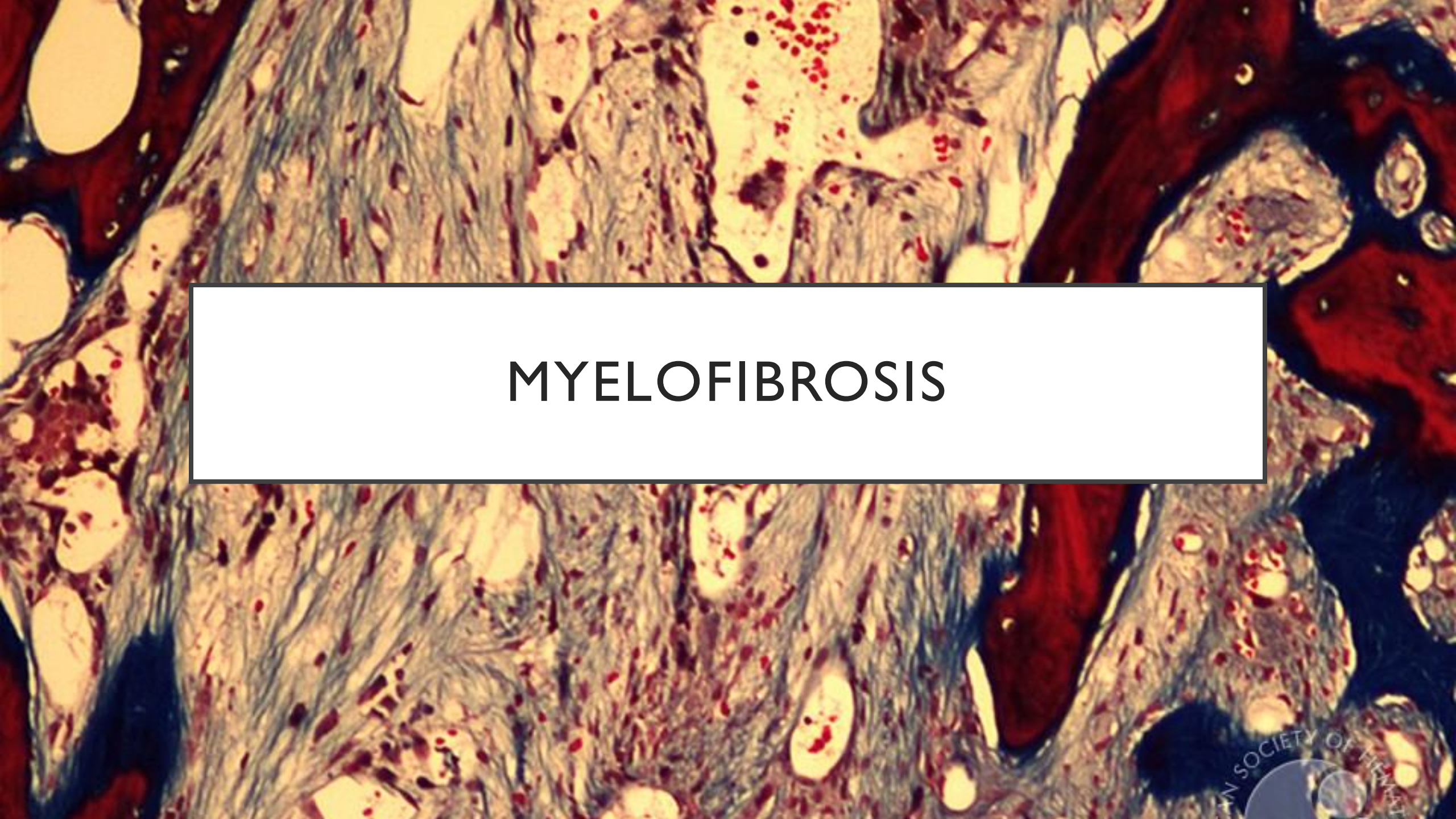
Presence of [illegible]2, CALR or [illegible]



Another clonal marker

Or

No other cause of raised platelets found



MYELOFIBROSIS

MYELOFIBROSIS

- First described in 1879 by Gustav Heuck
  - Noticed bone marrow scarring coupled with blood cell production outside of the bone marrow
- Recognised as related to the other myeloproliferative conditions in 1951

PMF SYMPTOMS

- Fatigue
- Scarring of the bone marrow → leads to blood cells being made elsewhere, causing enlargement of the spleen and/or liver
- Spleen related symptoms
- Low grade fever, night sweats, weight loss
- Bony tenderness / joint pain
- Blood clots

WHO CRITERIA

- Two entities recognised:
- 1. Pre-fibrotic primary myelofibrosis
  - *Important to distinguish from essential thrombocythaemia*

- 2. Overt primary myelofibrosis

PRE-FIBROTIC PMF

MAJOR CRITERIA

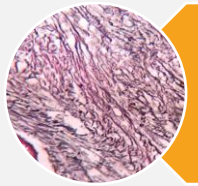
- 1. Bone marrow: Increased abnormal platelet precursors (megakaryocytes)
  - Increased cellularity with increased white blood cell precursors
  - Red cell precursors might be reduced
  - NO significant fibrosis (MF grade 1 or less)
- 2. Not meeting WHO criteria for other condition (eg PV, ET)
- 3. Presence of JAK2, CALR, MPL, **or** another clonal marker, **or** no other cause of minor fibrosis found

PRE-FIBROTIC PMF

MINOR CRITERIA

- At least 1 of:
- Anaemia
- Raised white cell count ≥ 11
- Palpable enlarged spleen
- Raised LDH

ALL 3 MAJOR & 1 MINOR CRITERIA



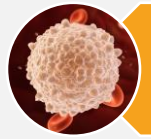
Typical bone marrow findings

Not meeting other WHO diagnoses

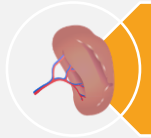
Clonal marker

Or no other cause of fibrosis found

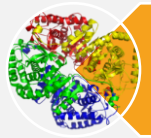
Anaemia



White cells >11



Palpable spleen



LDH high

OVERT PMF

MAJOR CRITERIA

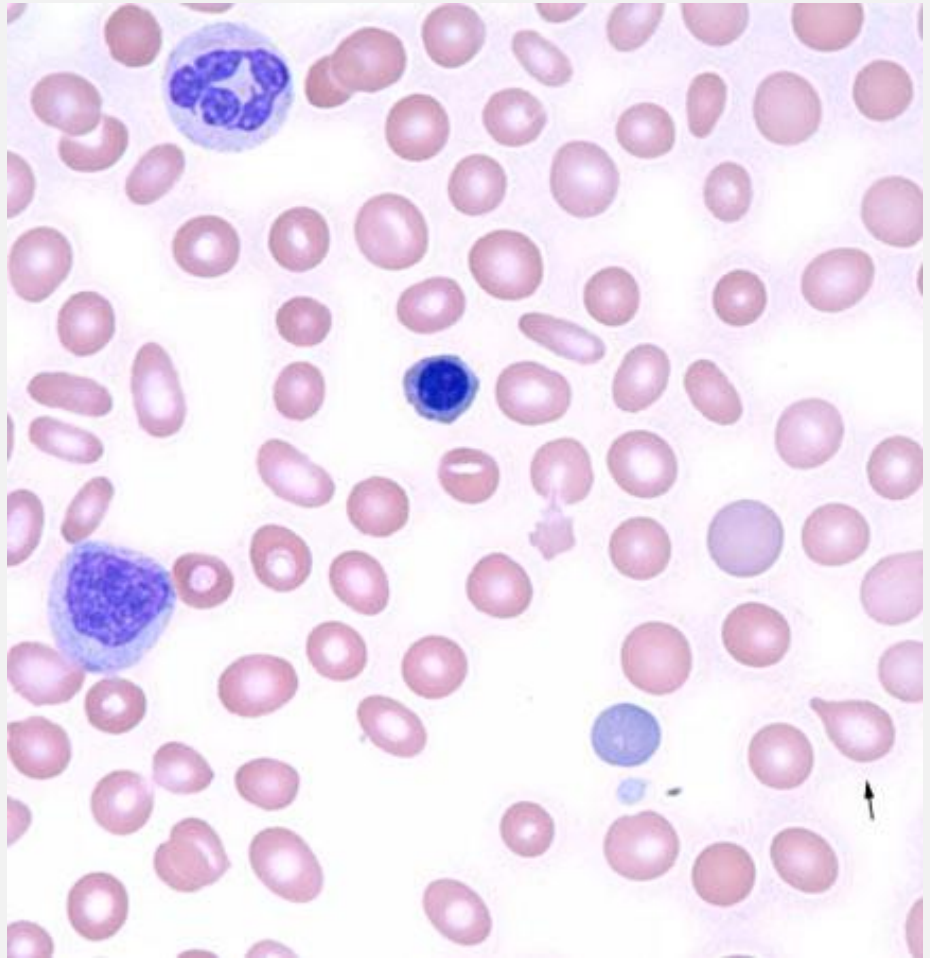
- 1. Increased platelet precursors (megakaryocytes) and/or atypia, plus significant fibrosis
- 2. Not meeting WHO criteria for other conditions
- 3. Presence of JAK2, CALR, MPL; **or** another clonal marker; **or** no other cause of fibrosis found
  - JAK2 – 65%
  - CALR – 15-30%
  - MPL – 8%

OVERT PMF

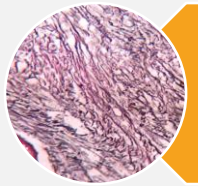
MINOR CRITERIA

- At least 1 of:
- Anaemia
- White cells ≥ 11
- Palpable enlarged spleen
- LDH above normal
- Leukoerythroblastosis (immature blood cells found in the blood)

LEUKOERYTHROBLASTOSIS



ALL 3 MAJOR & 1 MINOR CRITERIA



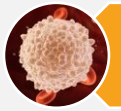
Typical bone marrow findings

Not meeting other WHO diagnoses

Clonal marker

Or no other cause of fibrosis found

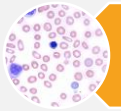
Anaemia



White cells >11

Palpable spleen

LDH high



Leukoerythroblastosis

QUESTIONS?