Cytopaenias in HIV

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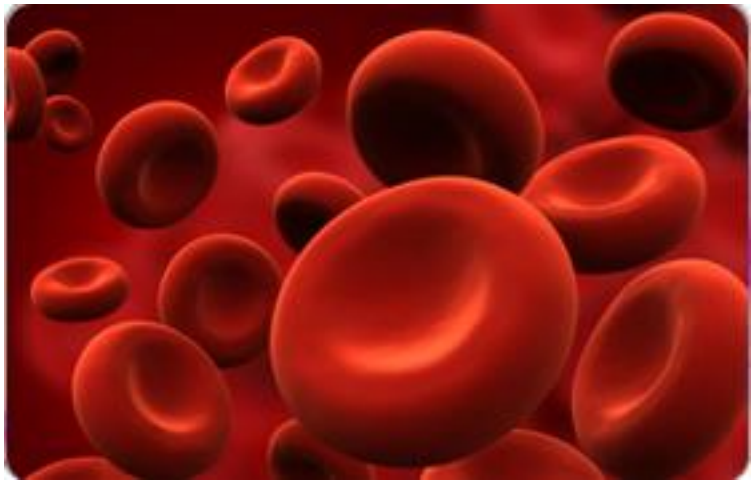
Introduction

- Cytopaenias in HIV are common
- Anaemias – multifactorial causes
- Thrombocytopaenias may be the first manifestation of HIV



Laboratory approach to cytopaenia

- FBC, diff, smear
- Retic count (RPI)→ haemolysis/peripheral loss or production problem
- UE/LFT/CMP/LDH
- Nutritional deficiencies: B12/Folate/Iron studies
- Hepatitis B/EBV/Parvo
- BMAT low threshold

Some common causes of anaemia

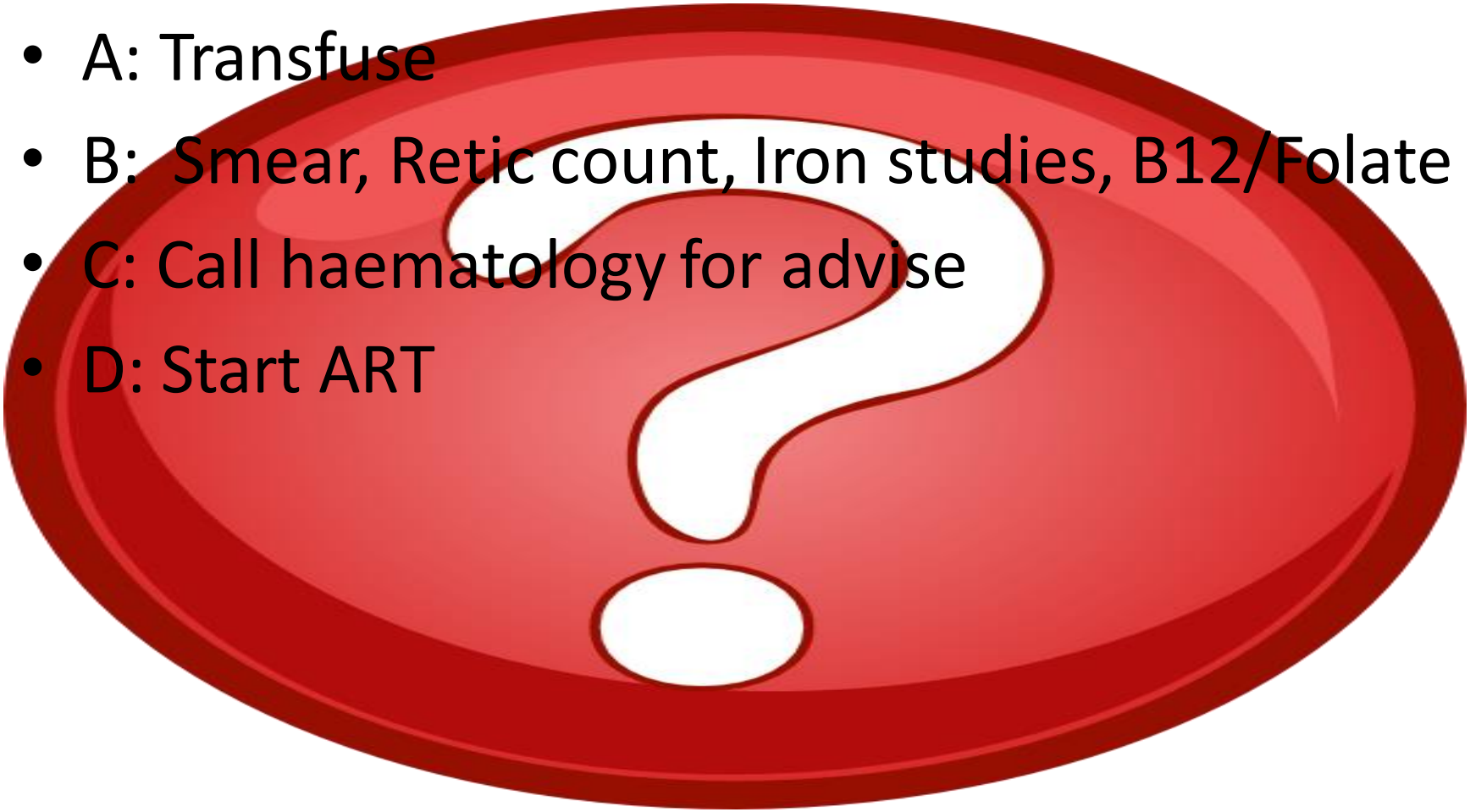
Decreased RBC production	Increased RBC loss
HIV itself	Haemolysis
Opportunistic infections	Blood loss
Drugs	Hypersplenism
Nutritional deficiencies	
Malignancy	

Case 1

- 32y old male – CD4 =102, not on ART
- Non specific symptoms
- Examination: Pallor, no lymphadenopathy, no organomegally,
- Pancytopaenia
- Hb 7.6 MCV/MCH normal Plts 31 WCC 2.5
- Normal UE, Albumin 24

What's the next step? Do you…

- A: Transfuse
- B: Smear, Retic count, Iron studies, B12/Folate
- C: Call haematology for advise
- D: Start ART



Answer: B

- Smear: Macrocytosis
- Retic Production Index 0.6 (low)
- B12/ Folate low
- Iron studies: Iron low/ Transferrin low /% saturation low / Ferritin was high
- Cause of cytopaenias: Multifactorial
- → Anaemia of chronic disease
- → B12/ folate deficiency

Distinguishing Iron deficiency anaemia (IDA) from Anaemia of Chronic disease (ACD)

	IDA	ACD
Iron	Decreased	Decreased
Transferrin saturation	Decreased	Decreased
Serum Transferrin (TIBC)	increased	Decreased
Ferritin	Decreased	Normal/ Increased

Nutritional deficiency

- Common
- Look for cause
- If concerned about iron deficiency : Trial of iron
- Expect 1g/dl increase after 1/12 and if no increase then likely Anaemia of chronic disease
- Also: Expect Retic count to improve as well
- Replace B12 appropriately: 1000mg x 5/7→ weekly x 4/52→ monthly

Case 2

- 30y old female on ART with a CD4 255, undetectable VL
- Symptomatic anaemia
- Hb 3.3 (Normocytic normochromic)
- Clinically NAD
- Initial workup normal

Considerations now??

- ? Haemolysis: Retic count, COOMBS, Bilirubin. LDH

- Red cell aplasia
  - Drugs (AZT)
  - Infections Parvovirus

Case 2 continued

- BMAT was suggested with Parvovirus PCR
- Findings: Arrest in maturation of erythroid series suggestive of red cell aplasia
- Parvovirus PCR was positive

Case 3

- 59 year old female
- ART for 2 years CD4 202, VL undetectable
- On TB treatment (uncertain how diagnosis was made)
- Lower back pain and dyspnoea 2/52
- Clinically : Not looking well, uncertain if axillary lymphadenopathy
- Obese, uncertain if organomegaly
- Normocytic normochromic anaemia Hb 6,8

Immediate Investigations

- UE: Mildly deranged
- LFT: TP 92 Albumin 30
- Ca 3,1
- LDH mildly elevated
- Nutritional studies pending
- Viral screen pending

- A: Multiple Myeloma
- B: Lymphoma + Tumour Lysis Syndrome
- C: Drug resistant TB
- D: A + B + C

Answer:

- Consider ALL possiblities
- Lymphoma with imminent tumour lysis syndrome ESP BURKITTS LYMPHOMA!!
- MDR TB is a strong possibility
- Multiple Myeloma: CRAB criteria

Next step:

- Examine again for lymphadenopathy
- CXR
- Ultrasound to exclude organomegaly
- Urate level, UE, Calcium, phosphate and LDH monitoring for tumour lysis
- Microbiological evidence of resistant TB
- SPEP looking for MONOCLONAL peak
- BIOPSY

Case 4

- 50 year old male
- Newly diagnosed with a CD4 65
- Shotty inguinal lymphadenopathy
- Anal mass which is ulcerating x 2/12
- Constitutional symptoms
- FBC: Pancytopaenia
- Hb 8,9 / Plt count 65 / WCC 2,9

What do you consider

- A: Tuberculosis
- B: Lymphoma
- C: Doing biopsy
- D: A, B and C

Answer

- Consider all 3: strong possibility Plasmablastic lymphoma
- Occurs when CD4 low
- Often has bone marrow involvement, hence cytopaenias
- No standarised treatment protocols
- Prognosis is dismal

Case 5

- 35 y old female
- CD4 278, VL undetectable→ HAART for 2 years
- Dyspnoea, poor appetite and constitutional symptoms
- Clinically: Lymphadenopathy
- Hb 6,2 Normocytic normochromic
- Platelet count 32
- Ultrasound shows multiple abdominal lymphadenopathy, splenomegaly

What do you consider

- A: Tuberculosis
- B: lymphoma
- C: Evans Syndrome: Autoimmune haemolytic anaemia and thrombocytopaenia
- D: A and B

Answer

- D: TB and lymphoma
- C could also be correct as a manifestation of lymphoma

Steps to follow

- Smear: Fragments
- Reticulocyte count: Haemolysis, production problem
- LFT: Look at Bilirubin
- Calcium and LDH → Lymphoma
- Microbiological evidence of TB
- Coombs: Autoimmune problem

HIV associated lymphomas (HAL)

- 60-200x increased risk of Non Hodgkins Lymphoma (NHL)
- 4% - will have NHL at diagnosis
- 10% will develop a lymphoma during course of the illness
- Introducing ART has decreased incidence and improved the outcome

HAL Pathogenesis

- Chronic antigenic stimulation
- Genetic abnormalities
- Cytokine dysregulation (IL-6, IL-10)
- Co-infection with oncogenic viruses- EBV and HHV8

HIV associated NHL

Good prognosis	Poor prognosis
Mild Immunodeficiency Moderate CD4	Severe immunodeficiency Low CD4
Post ART	Pre-ART
Burkitts Lymphoma (25-30%)	DLBCL -Immunoblastic subtype (10%)
DLBCL -Centroblastic subtype (25%)	Plasmablastic Lymphoma
	Primary Effusion Lymphoma

HIV associated Hodgkins Lymphoma (HL)

- Commonest non-AIDS defining malignancy
- Manifests especially during first few months after ART initiation as CD4 increases and VL decreases
- Sudden drop in CD4 count may herald onset, not necessarily a sign of treatment failure
- EBV associated

Lymphomas in a Nutshell

- Consider at all times, irrespective of CD4 and if on HAART or not
- Often present with cytopaenias
- EXCISIONAL Biopsy is very important

Thrombocytopaenia

- 30% of patients will present with it at some point
- Need to exclude TTP
- Consider ITP
- BMAT necessary?

Case 6

- 36y old female presents to casualty with headache and “dizziness”
- Newly diagnosed HIV, CD4 136, meant to start ART 2 months ago but wants to try alternative medications first

- Urgent FBC: Hb 7,6 (previously noted that 9,7)
- Plts 5 (previously noted to be 187)

Case 6 continued…

- Biochemistry unavailable
- Now patient complaining of worsening headache
- Concerned about intracranial bleed

What do you do?

- A: Transfuse blood and platelets
- B: Call the laboratory for urgent smear
- C: Refer to next level of care
- D: Start prednisone

Answer

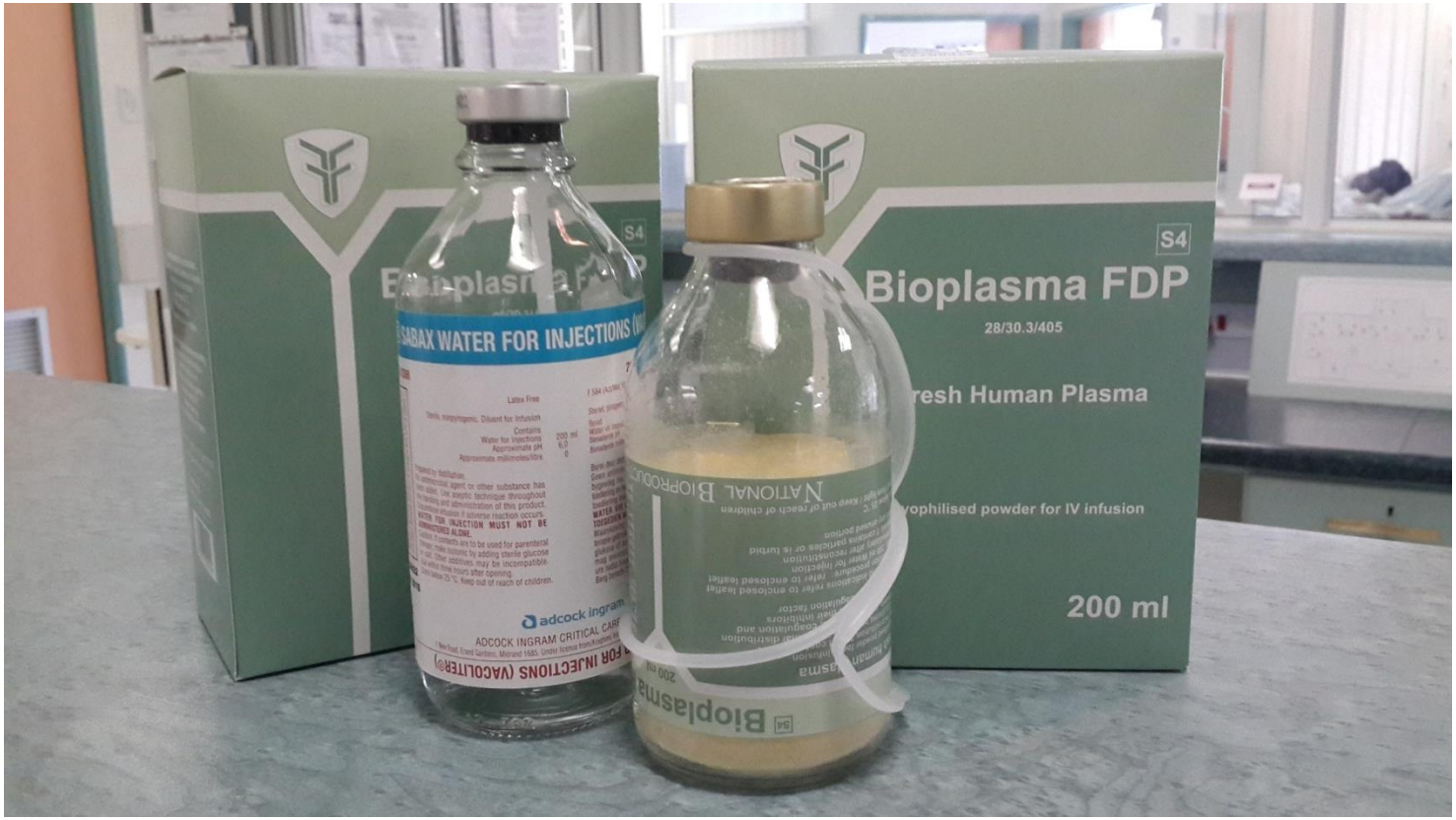
- B: Call laboratory for urgent smear

- Could be TTP
- → Haemolytic anaemia + Thrombocytopaenia

- Medical emergency
- Platelets are contraindicated
- Headache evidence of thrombosis

Outcome case 6

- Smear shows fragments
- Concerned that TTP
- Considering plasma exchange
- Problem: Far from next level of care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Bioplasma FDP
28/30.3/405
resh Human Plasma
ophilised powder for IV infusion
200 ml
SABAX WATER FOR INJECTIONS
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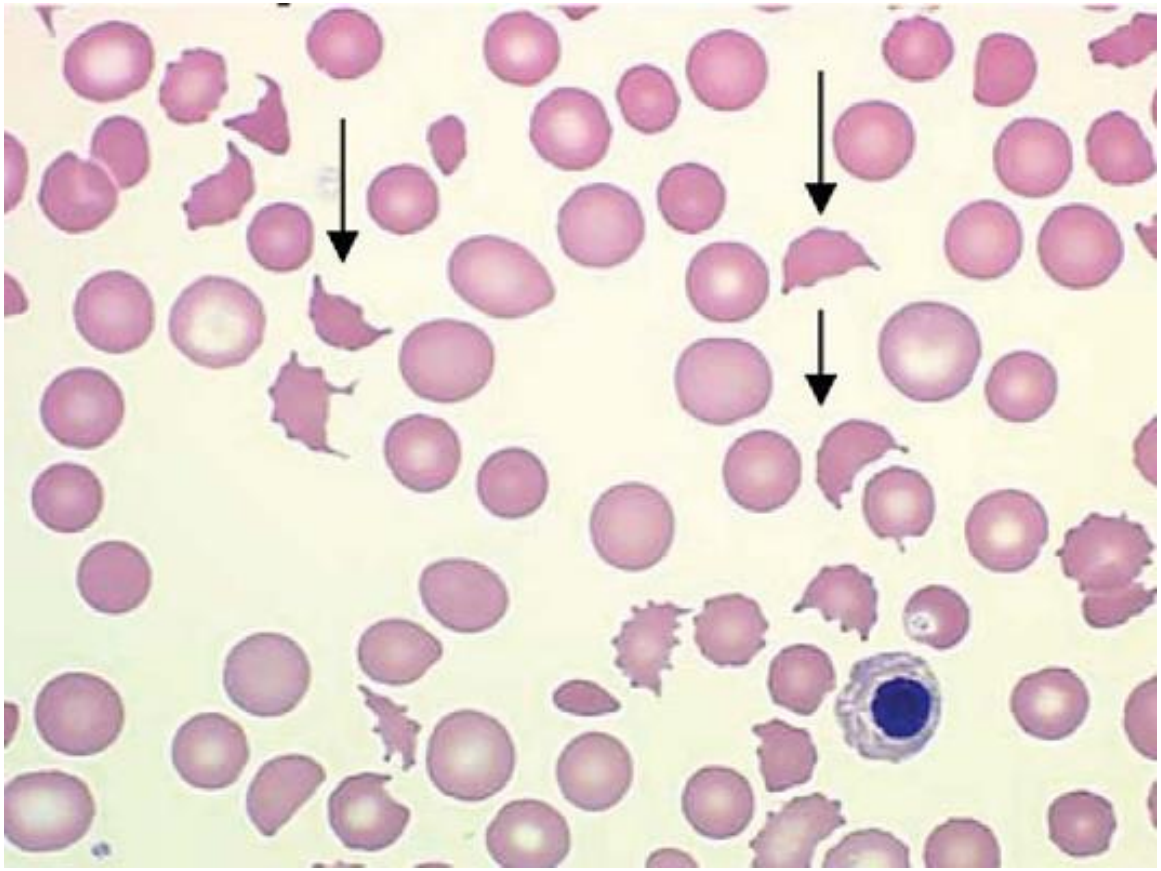
ADCOCK INGRAM CRITICAL CARE
NATIONAL BIOPRODUCTS

Treatment of HIV-TTP

- Plasma infusion
  - FDP (Freeze dried plasma) 30ml/kg/day (can add loop diuretic)

- Adjunctive corticosteroids
  - Prednisone 1mg/kg/day
- Folate
- Aspirin once plts > 100

- If no response in 48- 72 hours→ plasma exchange



Peripheral Smear

Fragments, true thrombocytopaenia

Lesson

- If Thrombocytopaenia and Anaemia
- Need to exclude haematologial emergency: TTP
- Smear: Look for fragments
- Evidence of haemolysis (**high RDW**)
- Don't start platelets until see smear
- Monitor response to treatment: FBC, Bilirubin and LDH

Case 7

- 25y old female CD4 237, not on ART
- Presents with severe PV bleeding
- Otherwise completely well
- Hb 8,9 Plts 13, WCC 4.1
- Basic workup completely normal , including smear which shows no fragments

What's the immediate next step

- A: Platelet transfusion
- B: Start HAART
- C: Start Prednisone
- D: Book Bone Marrow aspirate and trephine

Answer

- A : Start platelet transfusion

- Prednisone 1mg/kg/day
- Low threshold to do a BMAT
- Might pick up Bone marrow infiltrations or opportunistic infections
- Polygam if need rapid response

Differences between ITP and TTP

	ITP	TTP
Clinical	Bleeding	“Clotting” Multi-organ involvement
Laboratory	No fragments	Fragments
Treatment	HAART steroids	HAART Steroids FDP Plasma exchange

In Conclusion….Indications for BMAT in HIV+

- Unexplained anaemia, abnormal red cell indices, cytopenias
- Isolated thrombocytopenias
- Unexplained organomegaly or presence of mass lesions inaccessible for biopsy
- Microbiological culture for investigation of PUO
- Staging in Lymphoma

References

- OPIE, Jessica. Haematological complications of HIV Infection.SAMJ, [S.l.], v. 102, n. 6, p. 465-468, mar. 2012.
- BJH 2005: Thrombotic thrombocytopenic purpura in patients with retroviral infection is highly responsive to plasma infusion therapy
- ASH 2012: Guidelines on the diagnosis and management of TTP and other thrombotic microangiopathies
- ASH 2012: How to approach thrombocytopenia
- ASH 2013: Update on the treatment of HIV-associated haematological malignancies