Lessons learnt in a 17 year old with PUO: Haemophagocytic lymphohistiocytosis- the most fatal outcome of EBV infection.



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Aims

- Present a case of EBV-HLH
- Describe the diagnosis and treatment of EBV-HLH
- Reflect on lessons learnt

The case

P/C:

-17 year female

-4 day hx of **fevers**, **sore throat**, **vomiting**

PMH:

IgG subclass deficiency

Bronchiectasis

Viral meningitis

Findings

On examination:

Tachycardic

Febrile- 39 C

CVS: NAD

Chest: clear

Abdomen: no organomegaly

Petechial rash on uvula

No lymphadenopathy

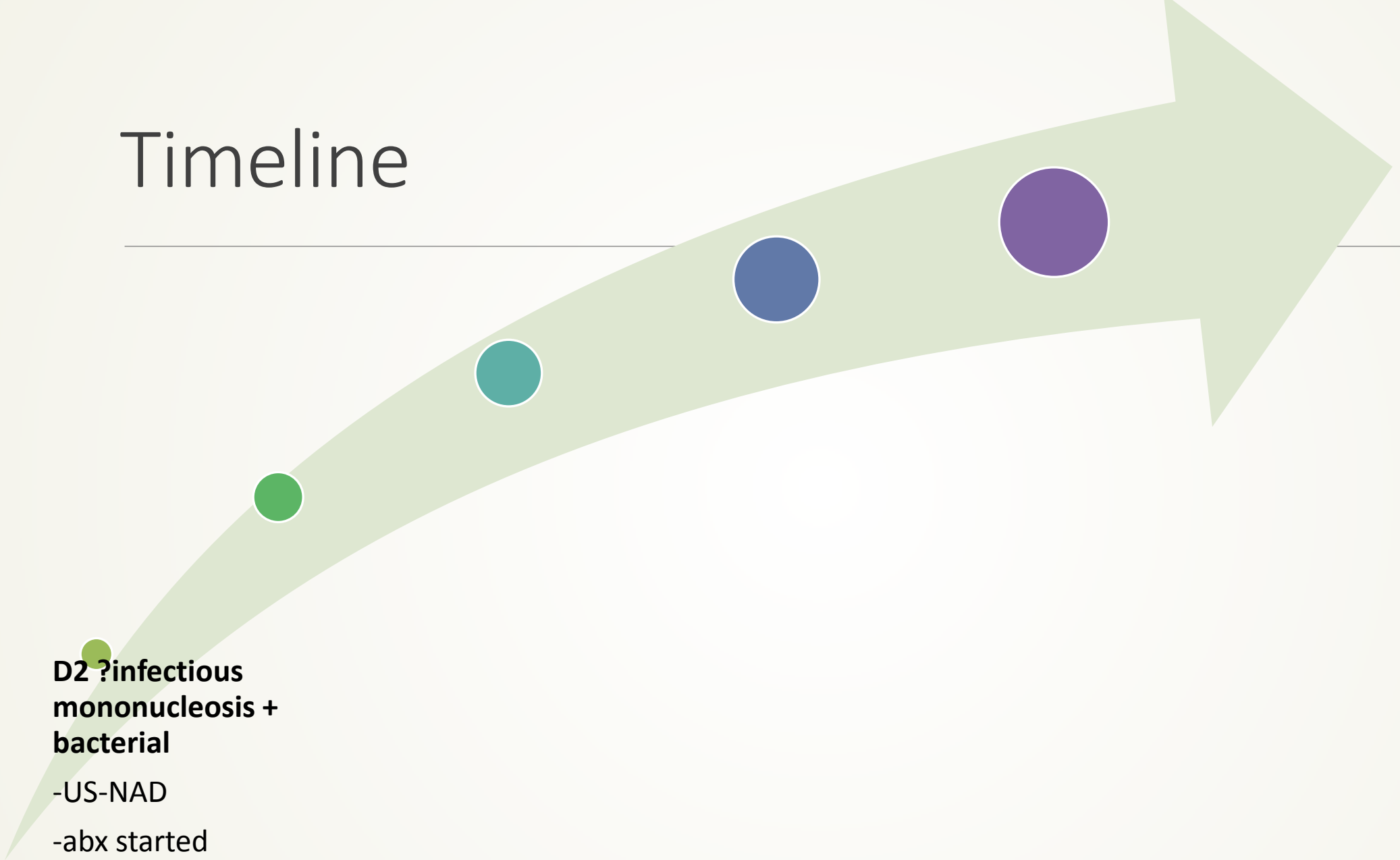
Initial Ix

ECG: normal

CXR: NAD

Hb	WCC	Plts	CRP	ALP	AST	EBV
121	1.4	86	32	300	326	**Monospot + 53000 copies**

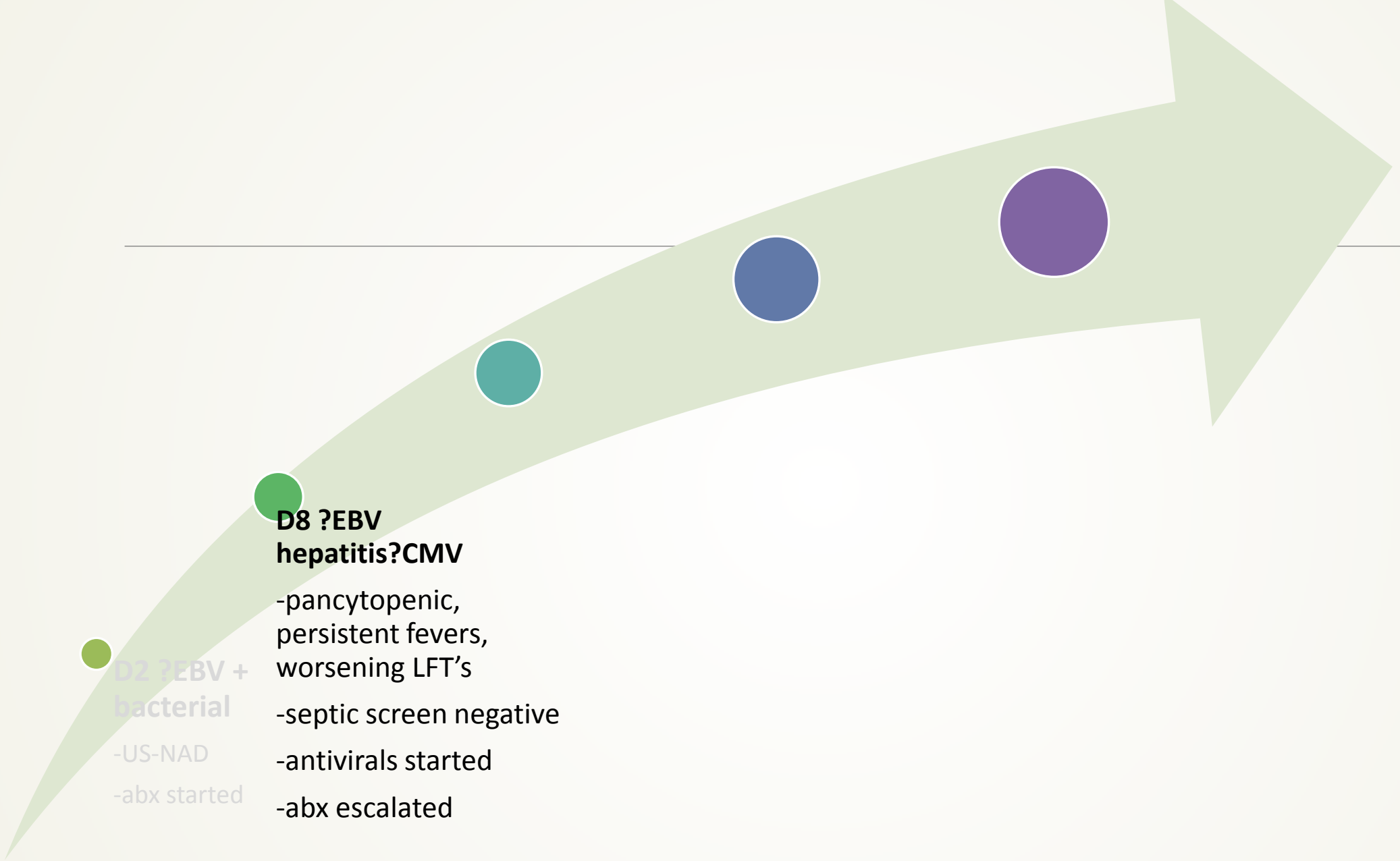
Timeline



D2 ?infectious mononucleosis + bacterial

-US-NAD

-abx started



D2 ?EBV + bacterial

-US-NAD

-abx started

D8 ?EBV hepatitis?CMV

-pancytopenic, persistent fevers, worsening LFT's

-septic screen negative

-antivirals started

-abx escalated

EBV load vs symptoms



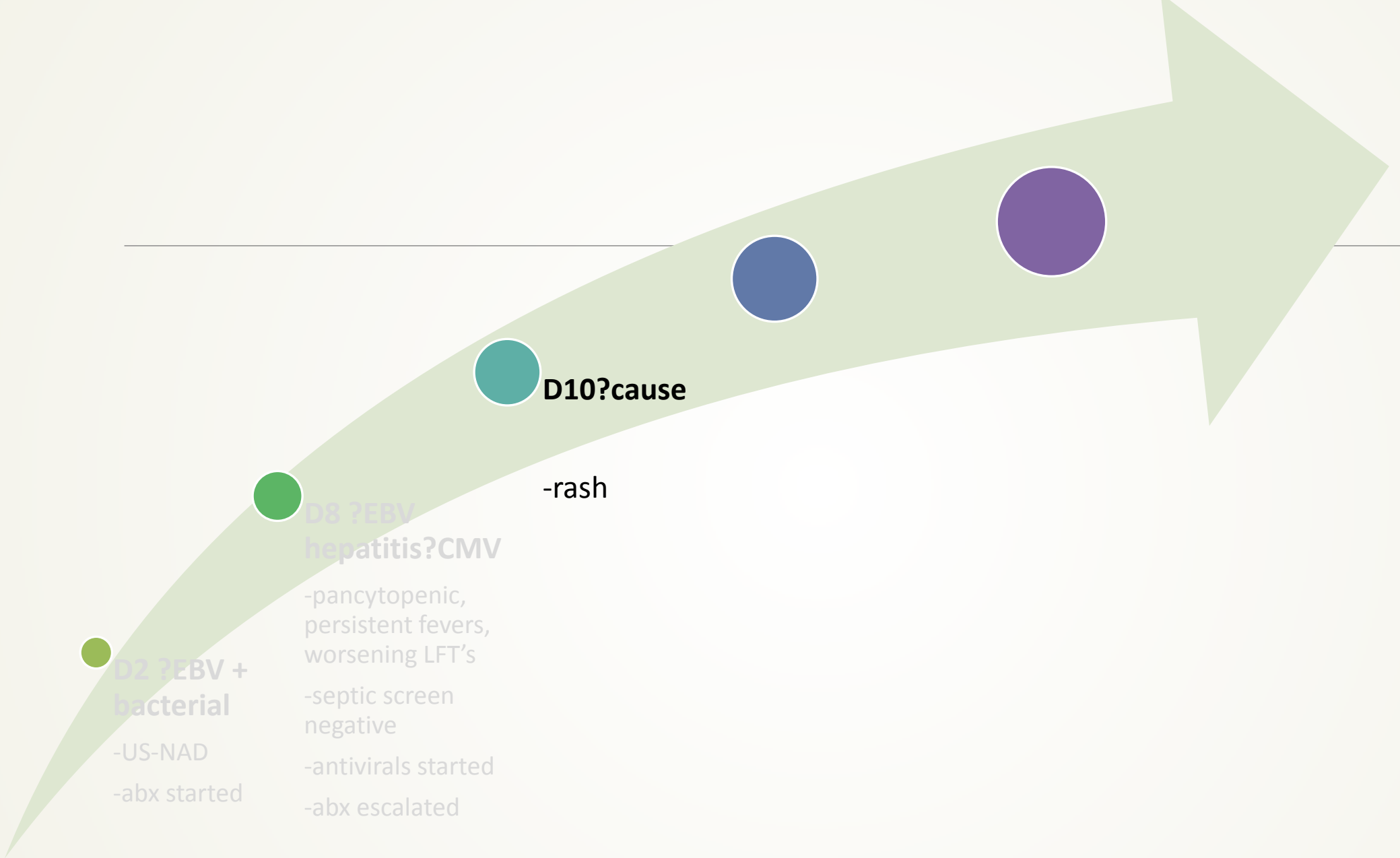
Persistent fevers

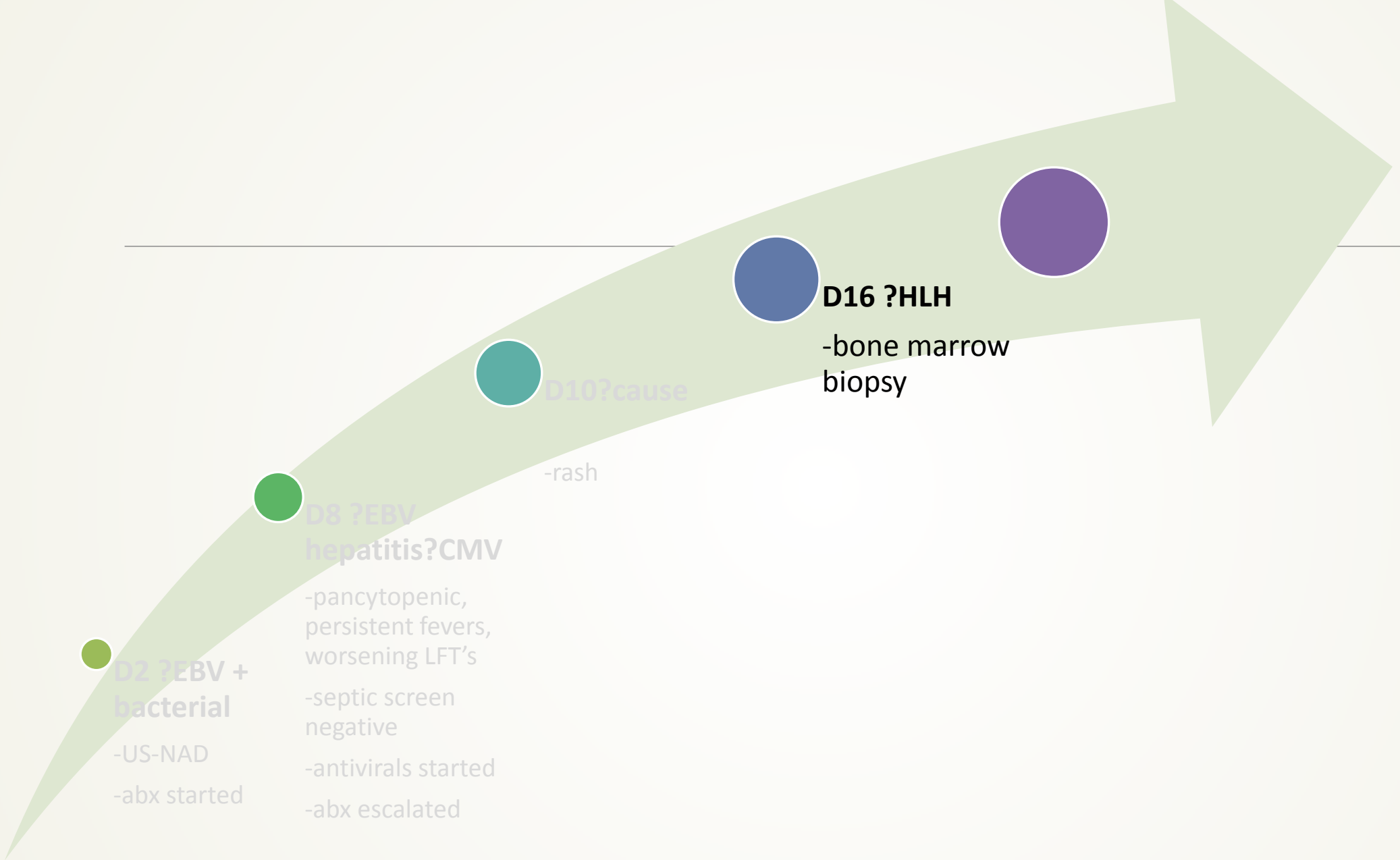
Worsening LFT’s

Clinically deteriorating

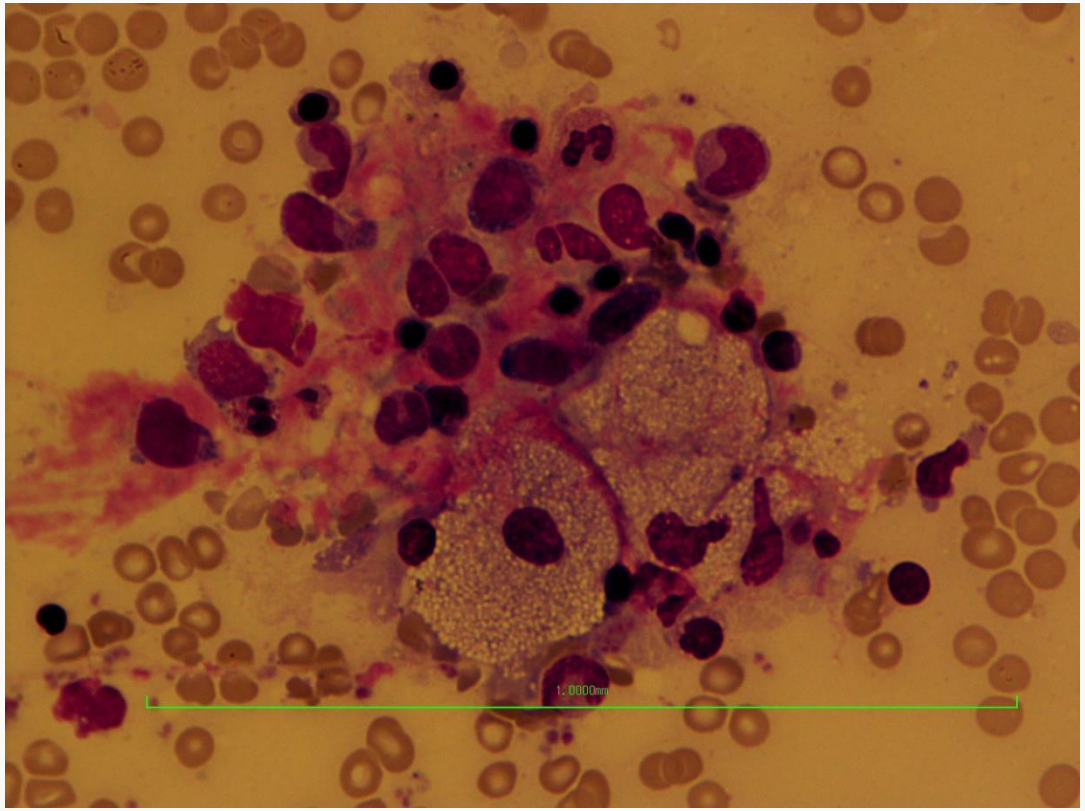


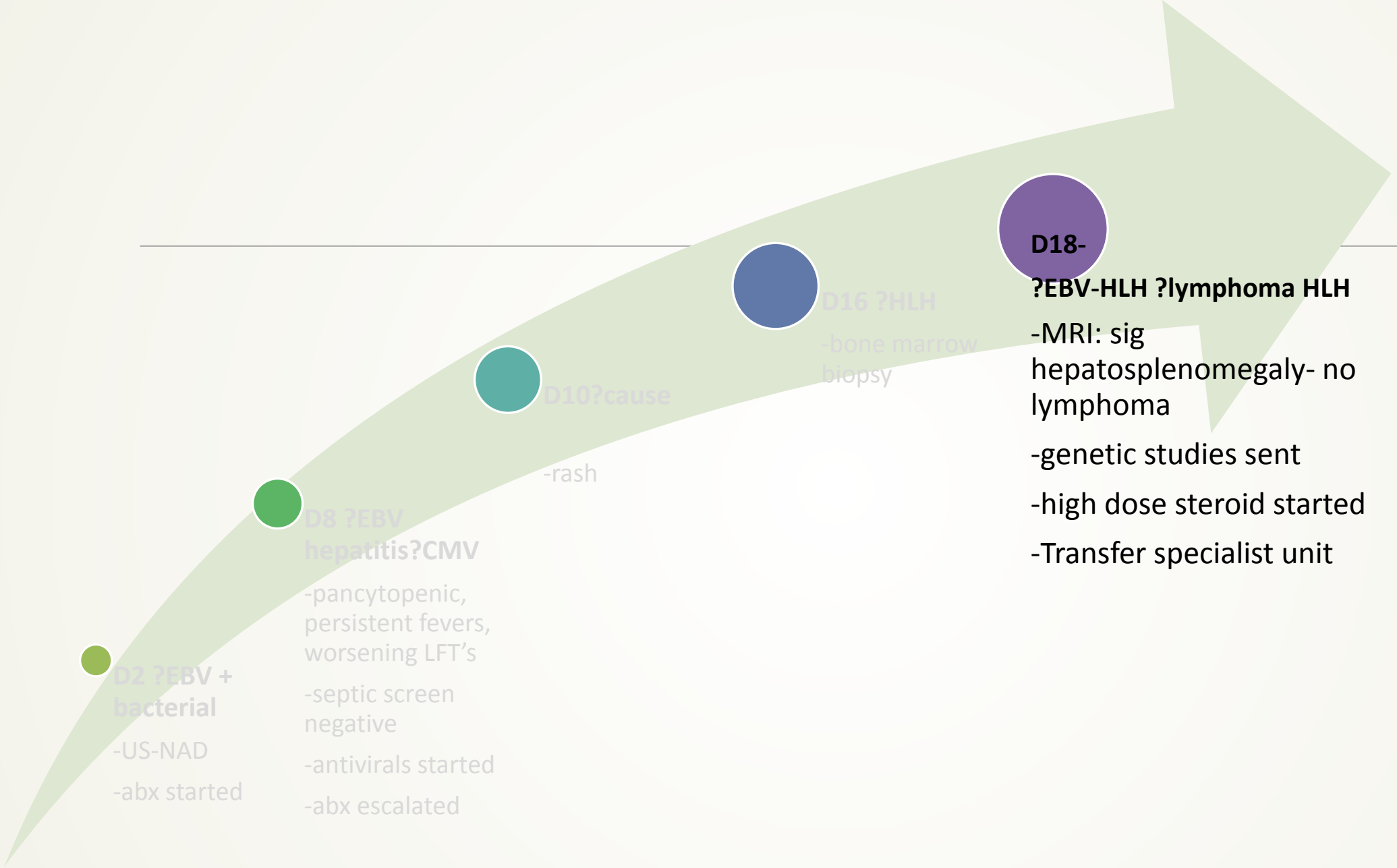
Reducing EBV viral load

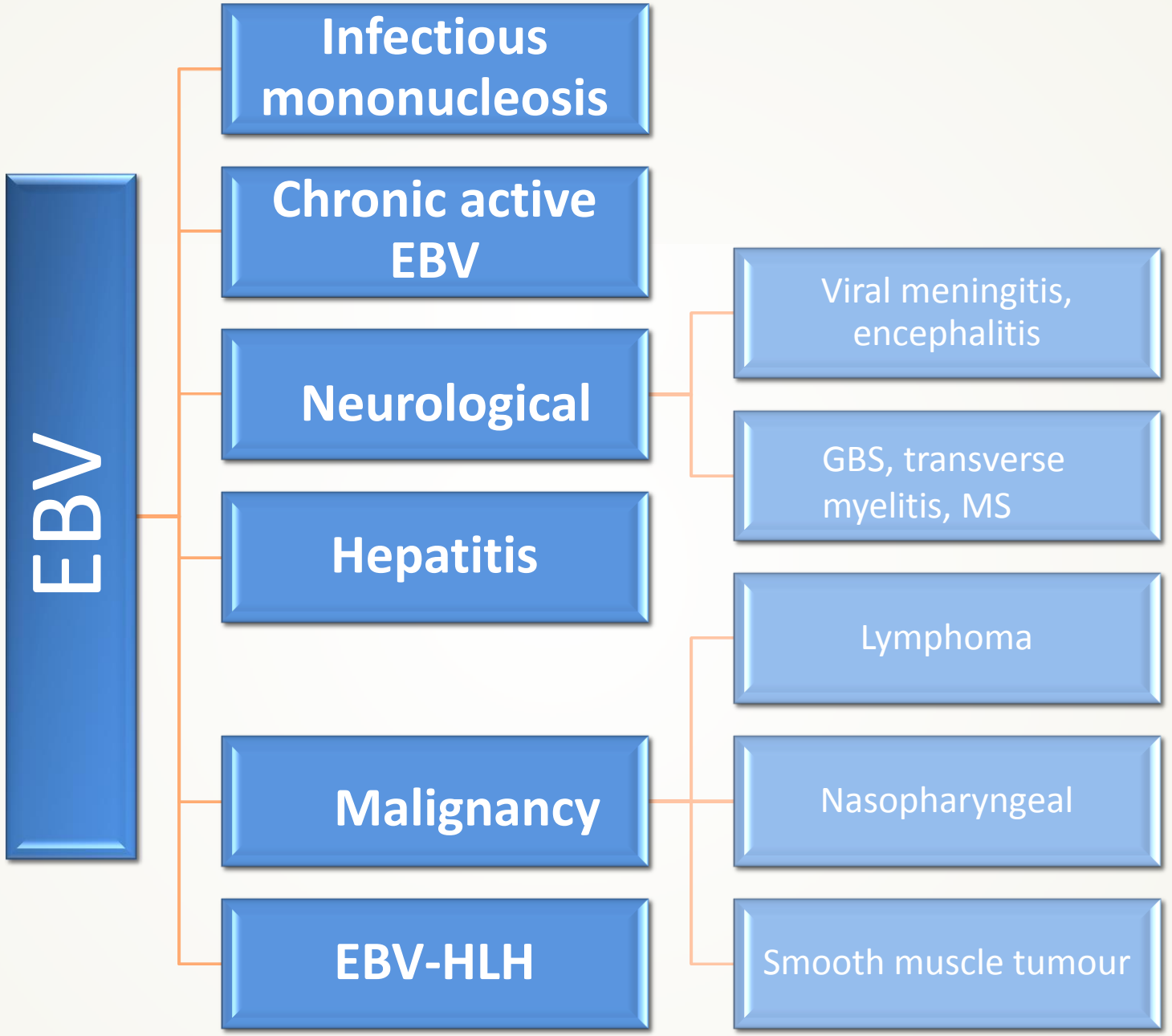

D10?cause
-rash
D8 ?EBV hepatitis?CMV
-pancytopenic, persistent fevers, worsening LFT's
-septic screen negative
-antivirals started
-abx escalated
D2 ?EBV + bacterial
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D10?cause
-rash
D16 ?HLH
-bone marrow biopsy

D16 Bone marrow aspirate




D2 ?EBV + bacterial
-US-NAD
-abx started
D8 ?EBV hepatitis?CMV
-pancytopenic, persistent fevers, worsening LFT's
-septic screen negative
-antivirals started
-abx escalated
D10?cause
-rash
D16 ?HLH
-bone marrow biopsy
D18-
?EBV-HLH ?lymphoma HLH
-MRI: sig hepatosplenomegaly- no lymphoma
-genetic studies sent
-high dose steroid started
-Transfer specialist unit


EBV
Infectious mononucleosis
Chronic active EBV
Neurological
Viral meningitis, encephalitis
GBS, transverse myelitis, MS
Hepatitis
Malignancy
Lymphoma
Nasopharyngeal
Smooth muscle tumour
EBV-HLH

EBV-HLH

- HLH can be 1^0 (familial) or 2^0 (malignancy, viral)
- Rare and aggressive syndrome
- Excessive activation of T cells, NK cells + Macrophages → **cytokine storm**
- Cause haemophagocytosis, cellular damage and organ dysfunction
- Most typical findings are fever, cytopenias, deranged liver function & hepatosplenomegaly

Diagnosis

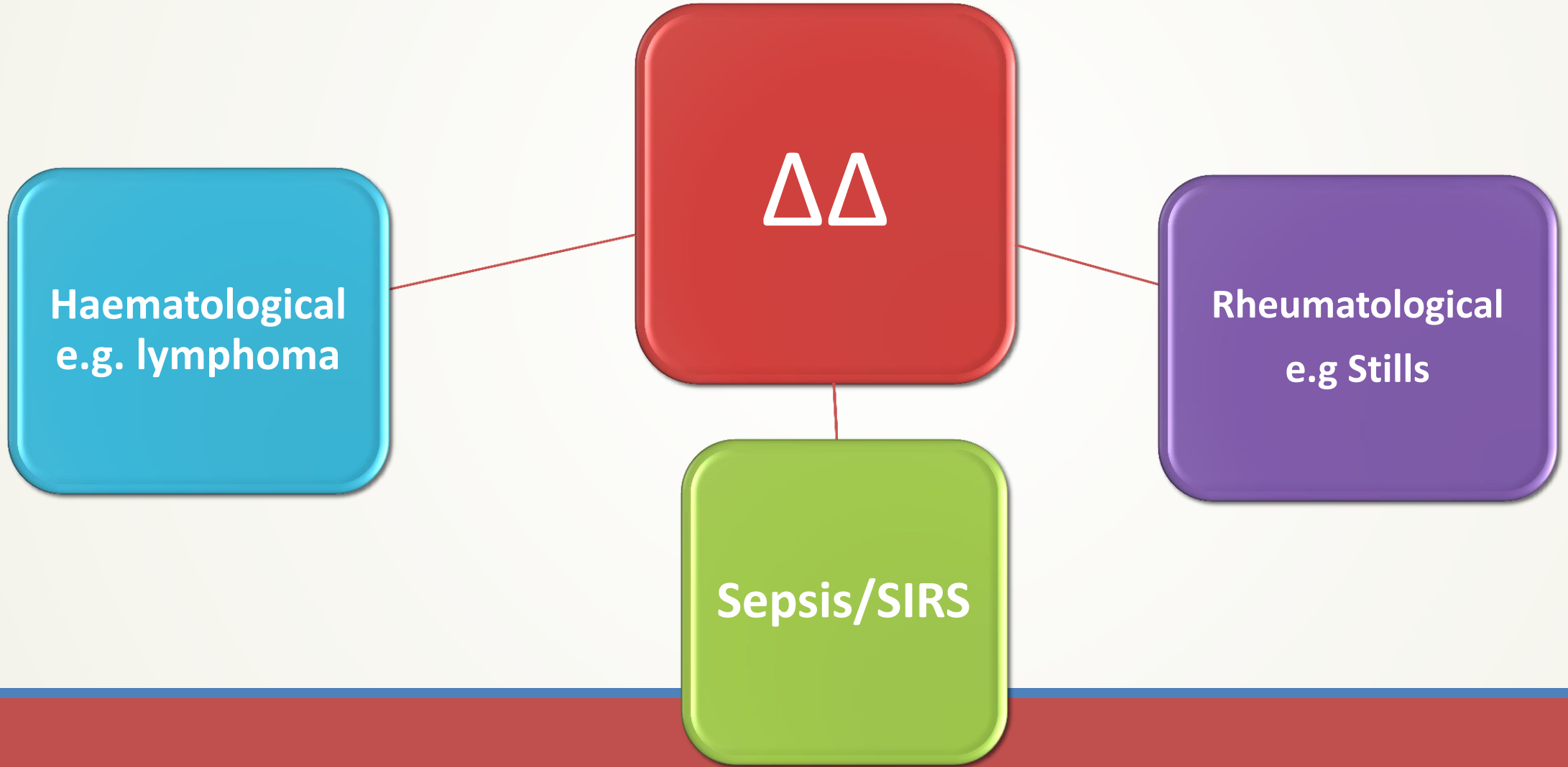
1) Molecular diagnosis consistent with HLH

Or

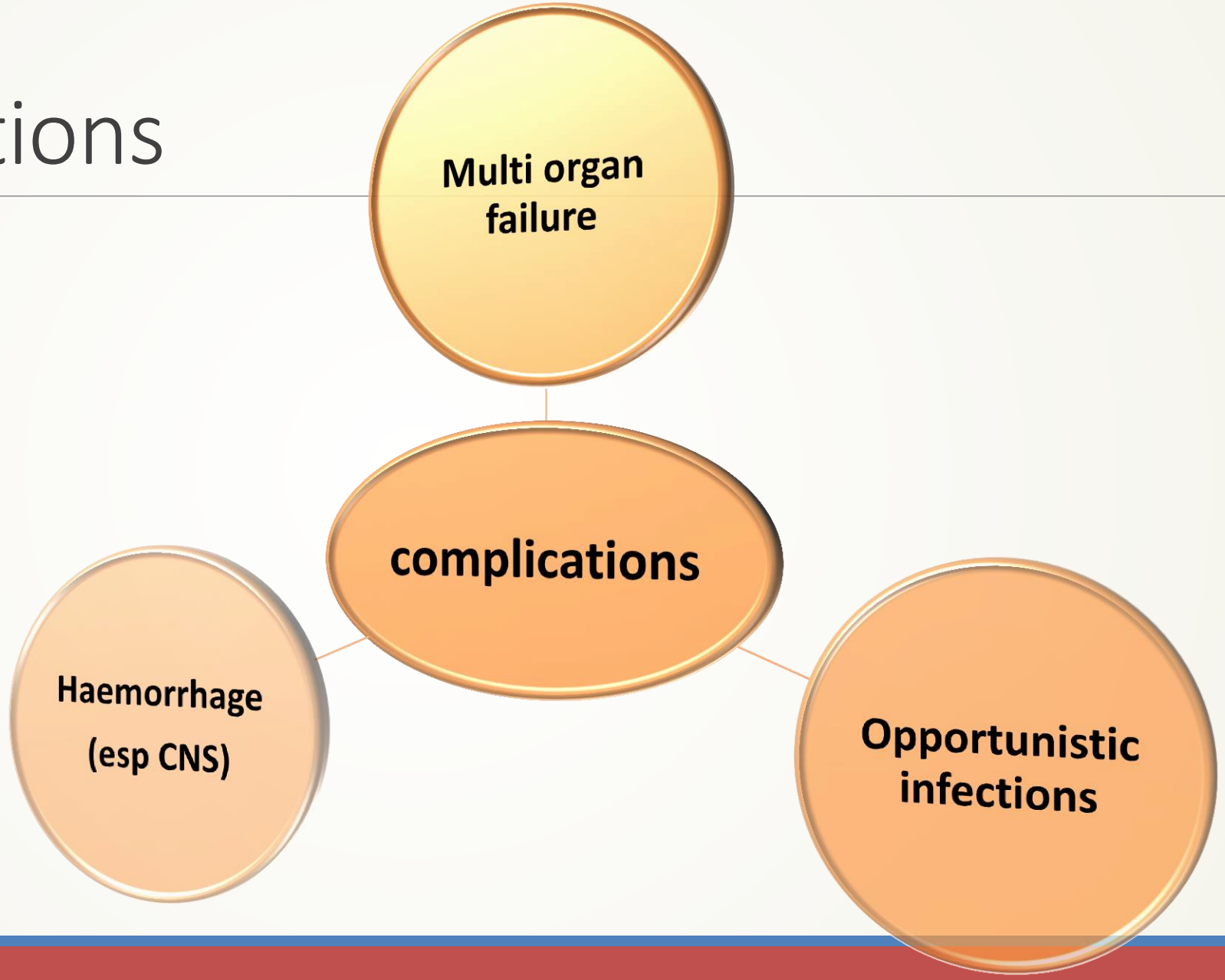
2) Fulfills at least 5 of the criteria in the table

Criteria	Did our patient have?
Fever	✓
Splenomegaly	✓
Cytopenias	✓
Hypertriglyceridemia +/- hypofibrinogenemia	✓
Haemophagocytosis in BM, spleen or lymph nodes	✓
Hyperferritinemia	✓
Low or absent NK cell cytotoxicity	**N/A**
Elevated sCD25 levels	**N/A**

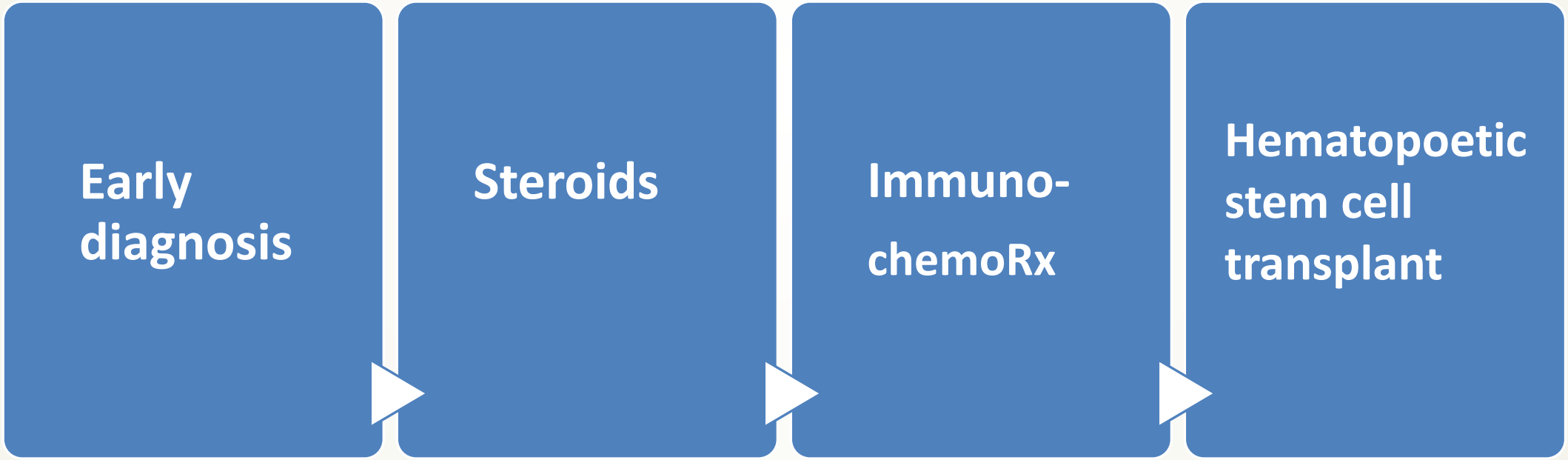
Differentials?



Complications



Treatment


Early diagnosis
Steroids
Immuno-chemoRx
Hematopoetic stem cell transplant

Antiviral therapy?

- In 1980's Sullivan et al- successful Rx of x2 cases EBV-HLH with 10 days acyclovir

- No concrete evidence for role of acyclovir

Key lessons

1

- EBV-HLH mimics other inflammatory/infectious conditions
- Should be prompted by signs of unexplained fever, cytopenia, splenomegaly and deranged liver function.

2

- HLH is the most fatal complication of EBV.
- High mortality rate due to delayed diagnosis.

3

- Rx includes steroids,immuno chemotherapy, stem cell transplant.
- Early involvement of haematologists is paramount.