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FOUNDATION UNIVERSITY

MEDICAL COLLEGE



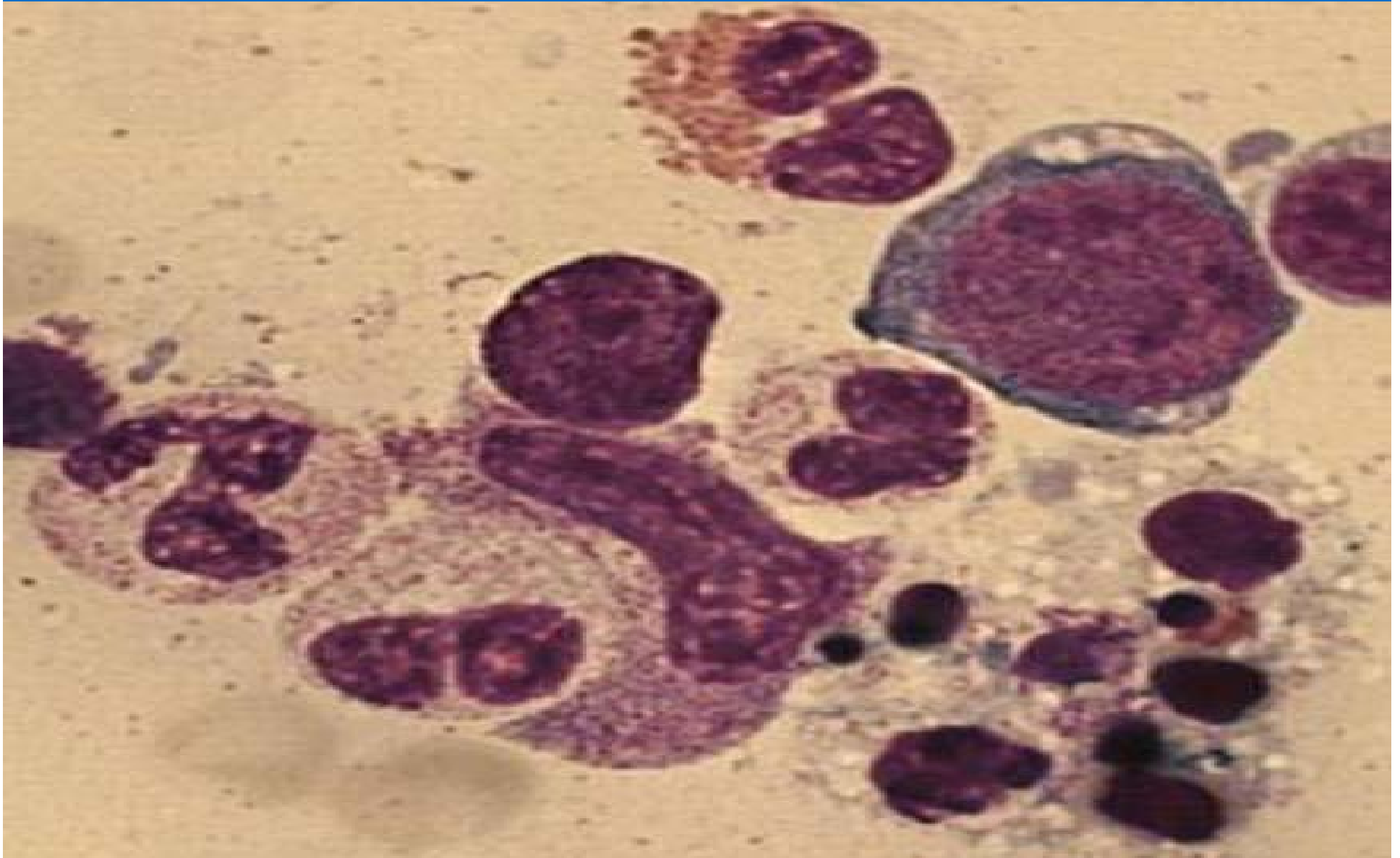
# **Spectrum of Diseases Associated with Haemophagocytosis**

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# HAEMOPHAGOCYTOSIS



# HAEMOPHAGOCYTYIC SYNDROME

- HPS is a non neoplastic proliferative disorder often having a fulminant and fatal clinical course.
- It is a clinicopathological condition characterized by increased macrophage activity leading to sepsis –like clinical presentation with hemophagocytosis, causing cytopenias and multi-organ failure.
- It affects all age groups.
- It is not a single disease but can be seen in association with a variety of conditions leading to the same hyperinflammatory phenotype.

# CLASSIFICATION OF HISTIOCYTIC DISORDERS

- **Haemophagocytic Histiocytosis**
  - Familial hemophagocytic histiocytosis
  - Infectious hemophagocytic histiocytosis  
(viral, bacterial, fungal, protozoal)
  - Tumour associated hemophagocytic histiocytosis  
(lymphoma, carcinoma)
  - Drug associated hemophagocytic histiocytosis
- **Sinus Histiocytosis**
- **Clonal Histiocytosis**
  - Langerhan cell histiocytosis
  - Malignant histiocytosis
- **Storage Disorders**

# CLASSIFICATION OF HAEMOPHAGOCYTYC SYNDROMES

## 1. Primary Haemophagocytic Syndromes

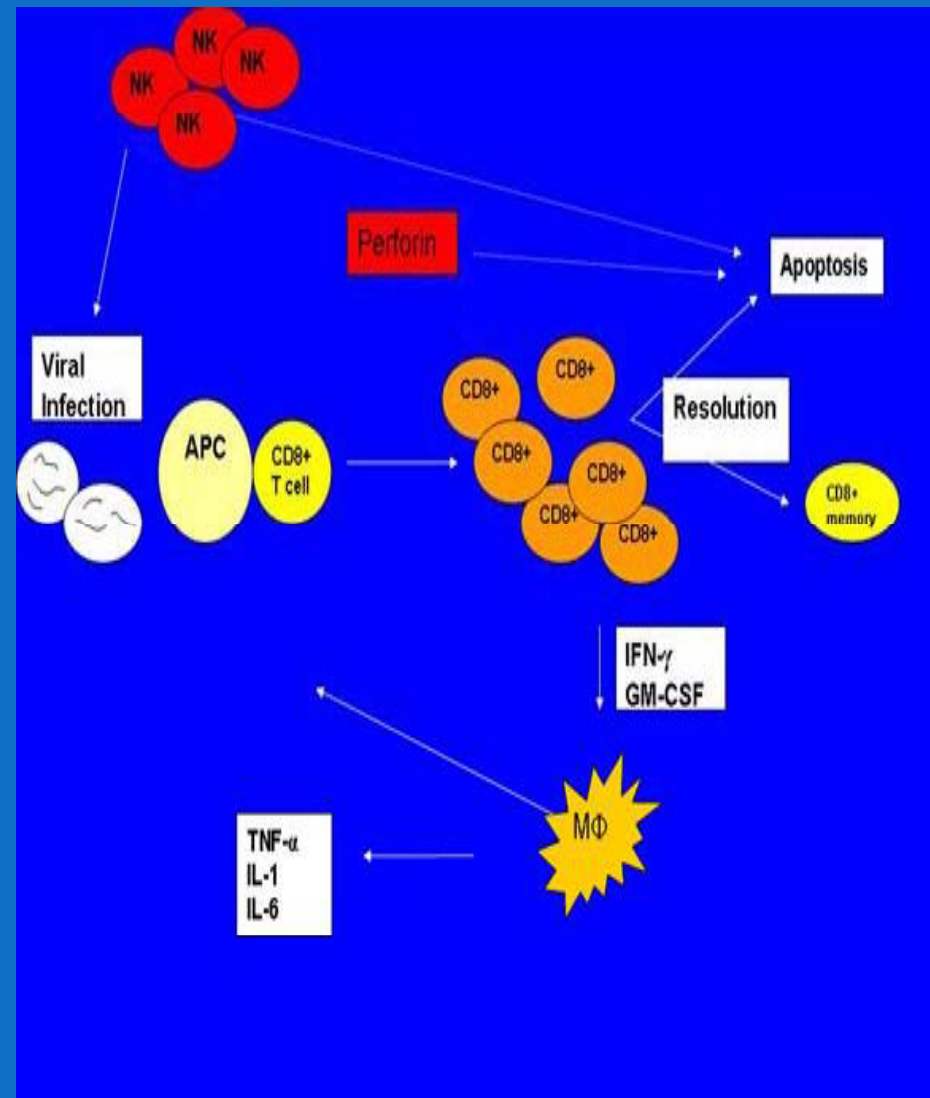
- a. Familial haemophagocytic Lymphohistiocytosis. ( FHL)
- b. Immunodeficiency e.g. Chediak-Higashi Syndrome

## 2. Secondary (Reactive) Haemophagocytic Syndromes

- a. **Infection** associated haemophagocytic syndrome. (IAHS)  
Virus associated haemophagocytic syndrome( VAHS).  
Bacteria associated haemophagocytic syndrome (BAHS)  
Others; Malaria, Leishmaniasis, Fungal Diseases.
- b. **Malignancy** associated haemophagocytic syndrome  
Lymphoma associated haemophagocytic syndrome (LAHS).  
Others; Multiple myeloma, melanoma, leukaemia, hepatocellular carcinoma.
- c. **Autoimmune** associated haemophagocytic syndrome( AAHS).
- d. **Others**  
Drugs-associated e.g. Phenytoin  
Miscellaneous diseases; Kawasaki disease, Kikuchi disease

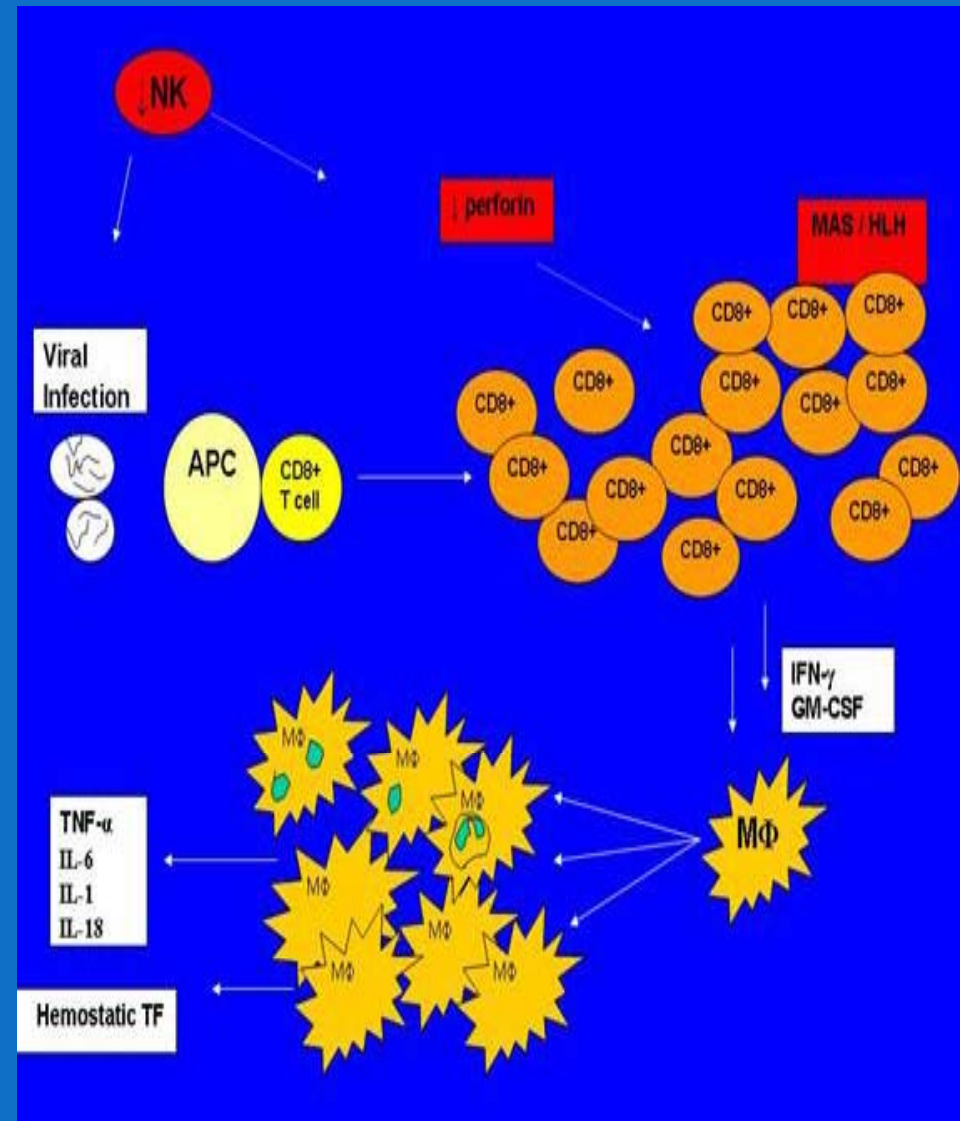
# PATHOGENESIS

- Basic defect is a Cytotoxic T Lymphocyte (CTL) and Natural Killer (NK) cell dysfunction.
- A viral infection or immunological defect is the usual trigger.



# PATHOGENESIS

- Excessive production of cytokines and chemokines capable of stimulating mononuclear phagocytes occurs.
- Enhanced phagocytic activity leads to cytopenias – pancytopenia.



# DIAGNOSTIC CRITERIA

5 out of 8 of the following criteria must be fulfilled in order to label a case as haemophagocytic syndrome.

- Fever
- Splenomegaly
- Cytopenia of at least 2 lineages .
- Hyperferritinemia of  $\geq$  to 500 ug/L
- Hypertrygliceridemia and or hypofibrinogenemia  
fasting tryglicerides  $\geq$  3mmol/L fibrinogen  $\leq$ 1.5 g/L
- sCD25  $\geq$  to 2400 U/ml
- Decreased or absent NK cell activity.
- Presence of haemophagocytosis in bone marrow spleen or lymph nodes

# EXPERIENCE AT FAUJI FOUNDATION HOSPITAL RAWALPINDI

- Data Collected is from October 2007- October 2008.
- We performed a total of 360 bone marrows in this time period.
- Out of 360 bone marrow aspirations 67 were positive showing haemophagocytosis of varying degree.
- 18.6% Positive

<b>Associated Diseases</b>	<b>Number of Cases</b>
Non Hodgkin Lymphoma	16
Hodgkin Lymphoma	5
Acute Leukemia	8
Multiple Myeloma	2
Myelodysplastic Syndrome	1
ITP	2
Hypersplenism	2

<b>Associated Diseases</b>	<b>Number of Cases</b>
Mixed Deficiency Anaemia	6
Megaloblastic Anaemia	7
Iron Deficiency Anaemia	3
Hemolytic Anaemia	3
Anaemia of Chronic Disorder	2
Pyrexia of unknown origin / Infections	6
Autoimmune Disorder	4

# EXPERIENCE AT FAUJI FOUNDATION HOSPITAL RAWALPINDI

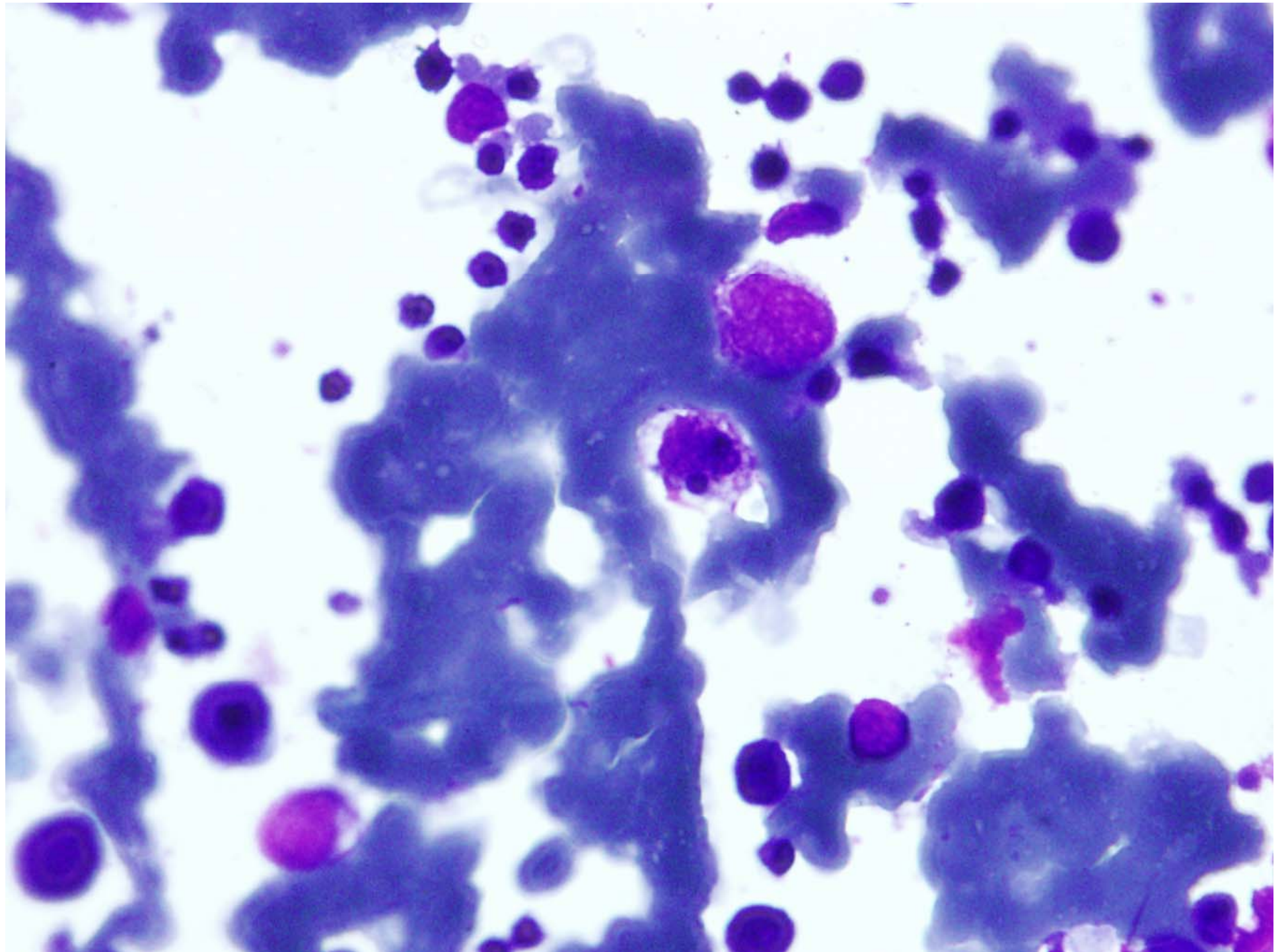
- Non-Hodgkin lymphoma 16 cases (23.8%)
- Hodgkin lymphoma 5 cases (7.4%)
- Leukaemias 8 cases (11.9%)
- Different types of anemias collectively 21 cases (31.3%)
- Immune disorders 4 cases (5.9%)
- Infections 6 cases (8.8%)
- Miscellaneous disorders 7 cases (10.4%)

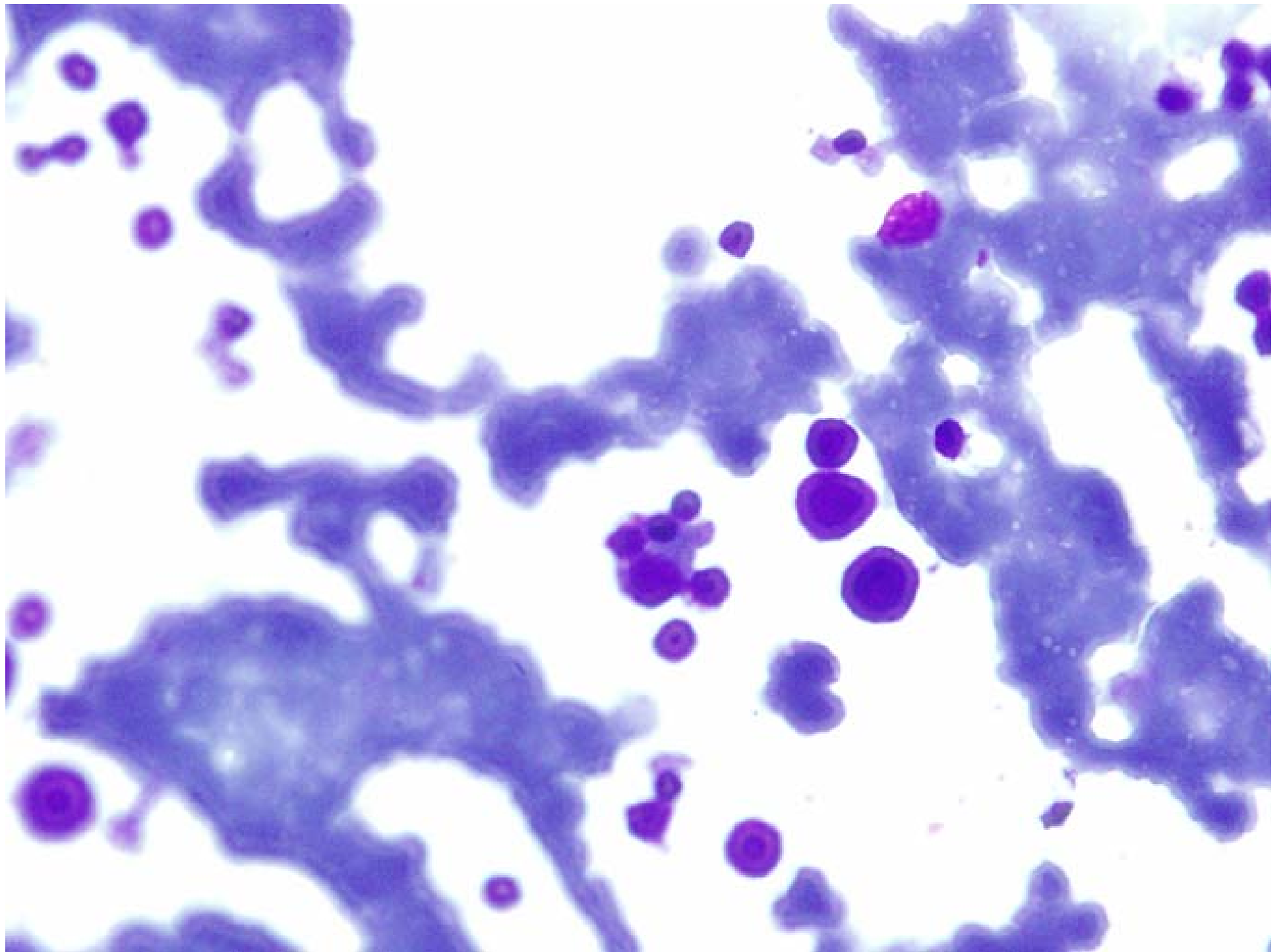
46%

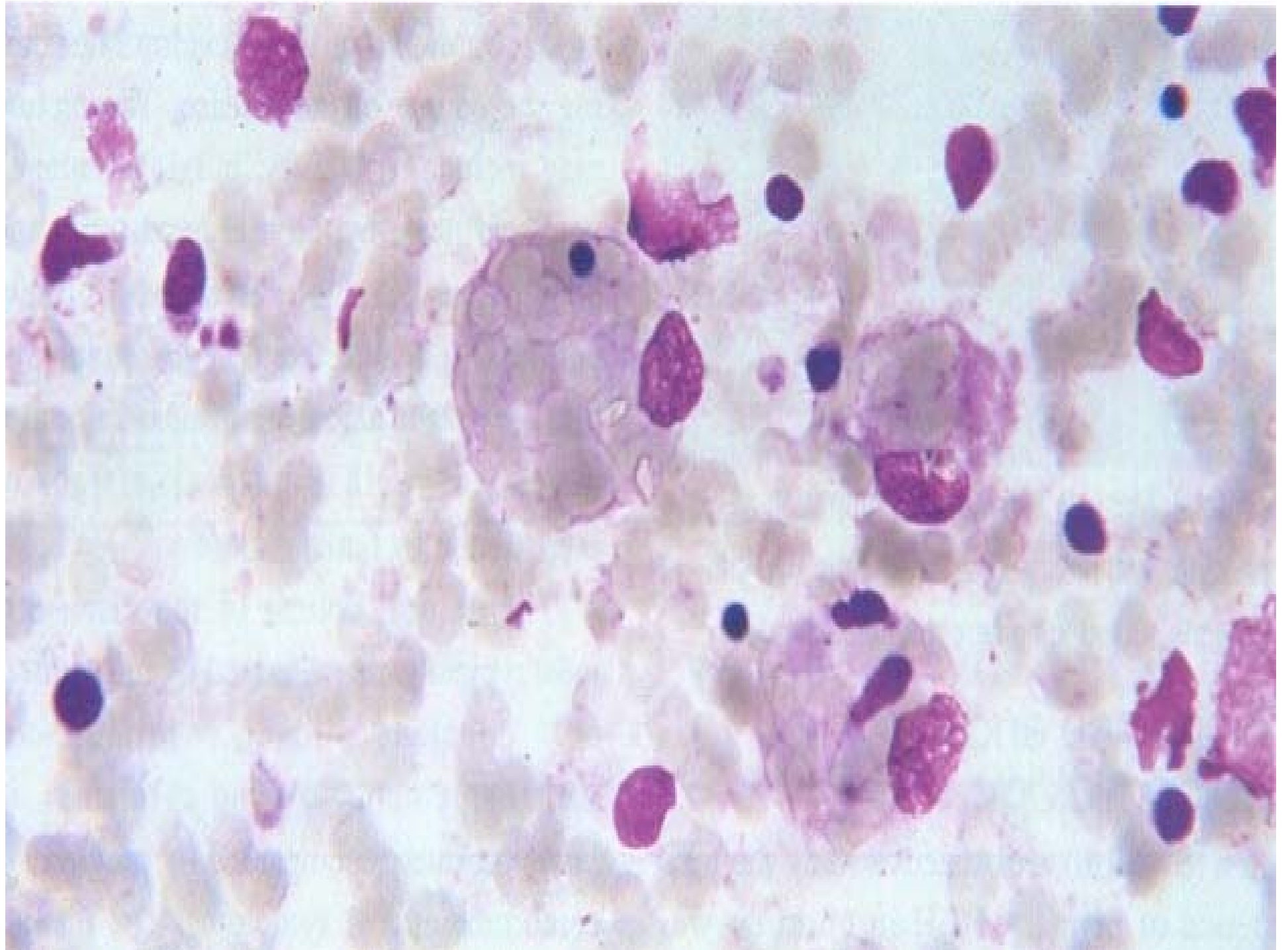
**2 Patients fulfilled criteria for HPS (2.9%)**

S. No	Patient Name	Sex	Age	Presenting Complaint	Associated Disease	Orgaonomegaly	Blood CP	Bone marrow Findings	Others
1	Zaib-un-Nisa	Female	58 Yrs	1. Fever 2. Bleeding gums 3. Bruises	HCV/CLD	Splenomegaly	Hb 8.5g/dl WBC 3.27 x 10 <sup>9</sup> /L platelets 30 x 10 <sup>9</sup> /L	Marked Hemophago-cytosis	PT18/14 Sec APTT 35/28 Sec INR 1.33 Bilirubin 23 umol
2	Kashaf Zohra	Female	19 Yrs	1. High grade fever 2. Progressive pallor	PUO	Splenomegaly	Hb 9.5g / dl WBC 1.3 x 10 <sup>9</sup> /L platelets 125 x 10 <sup>9</sup> /L	Hemophago-cytosis	Blood culture Urine culture No organism grown
3	Shabina Bibi	Female	31 Yrs	1. High grade fever 2. Joint pains	Rheumatoid Arthritis	Splenomegaly	WBC 3.9 x 10 <sup>9</sup> /L Hb 9.3g/dl platelets 94 x 10 <sup>9</sup> /L	Hemophago-cytosis	ESR 22 Bilirubin 1.90/MI
4	Saifullah	Male	55 Yrs	1. Fever 2. Migrating arthralgia	Felty's Syndrome	Splenomegaly	WBC 2.94 x 10 <sup>9</sup> /L Hb 9.8g /dl platelets 84 x 10 <sup>9</sup> /L	Hemophago-cytosis	---

5	Nosheen Akhtar	Female	25 Yrs	1. Fever 2. Cough	Past History of Brucellosis / Tuberculosis	Hepatosplenomegaly	WBC 10.17 x 10 <sup>9</sup> / L Hb 8.39/dl platelets 432 x 10 <sup>9</sup> / L	Hemophagocytosis	Bilirubin 290 umol Blood culture Pseudomonas
6	Kiran	Female	14 Yrs	1. Fever 2. Cervical Lymphadenopathy	Hodgkin's Disease (Nodular Sclerosis) (bulky Disease)	Hepatosplenomegaly	Hb 125g WBC 4.7 x 10 <sup>9</sup> / L platelets 500 x 10 <sup>9</sup> / L	Hemophagocytosis seen	LDH 455 u/L PT/APTT Normal ALT 290/L7
7	Ehtesham	Male	13 Yrs	1. Fever 2. Cervical Lymphadenopathy	Hodgkin's lymphoma Hypereosinophilic Syndrome	Hepatosplenomegaly	WBC 31.07 x 10 <sup>9</sup> / L Hb 8.4g 10/L PLT 344 x 10 <sup>9</sup> / L	Hemophagocytosis marked eosinophilia	ESR 120 mm
8	Imtiaz Begum	Female	50 Yrs	1. Fever 2. Vomiting 3. Diarrhea	HCV/CLD	Splenomegaly	WBC 8.5 x 10 <sup>9</sup> / L Hb 5.7g /dl platelets 161 x 10 <sup>9</sup> / L	Hemophagocytosis Seen	ESR 140 mm







# CONCLUSION

- Haemophagocytosis is present in a significant number of our patients undergoing bone marrow aspiration.
- The possibility of HPS should always be considered in non-resolving infections and in patients with cytopenias, fever and hepatosplenomegaly with haemophagocytosis.
- Awareness is important for early diagnosis and prompt treatment.



Shangri-La  
Heavens on Earth