

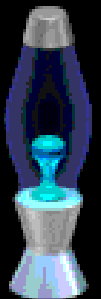
PROLONGED FEVER IN MALIGNANCY

**Reynaldo C. de Castro Jr, MD,
FPPS, FPSBTH**

Fever and Malignancy

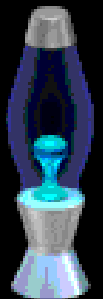
- Fever as a sign of malignancy is more common in adults
- Some malignancy induced fever such as Pel Ebstein fever is uncommon in children
- Most common in hematologic malignancies such as lymphohistiocytic disorders/leukemias

Palazzi, May 2006



American Cancer Society

- Continued, unexplained weight loss
- Headache and vomiting in the morning
- Increased swelling or pain in bones and joints *
- Lump or mass in neck, abdomen *
- Development of eye abnormalities
- Recurrent fever *
- Excessive bruising *
- Noticeable paleness *



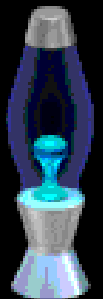
Malignancy

**Fever and
Lymphadenopathies**

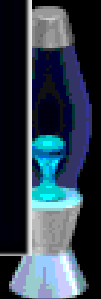
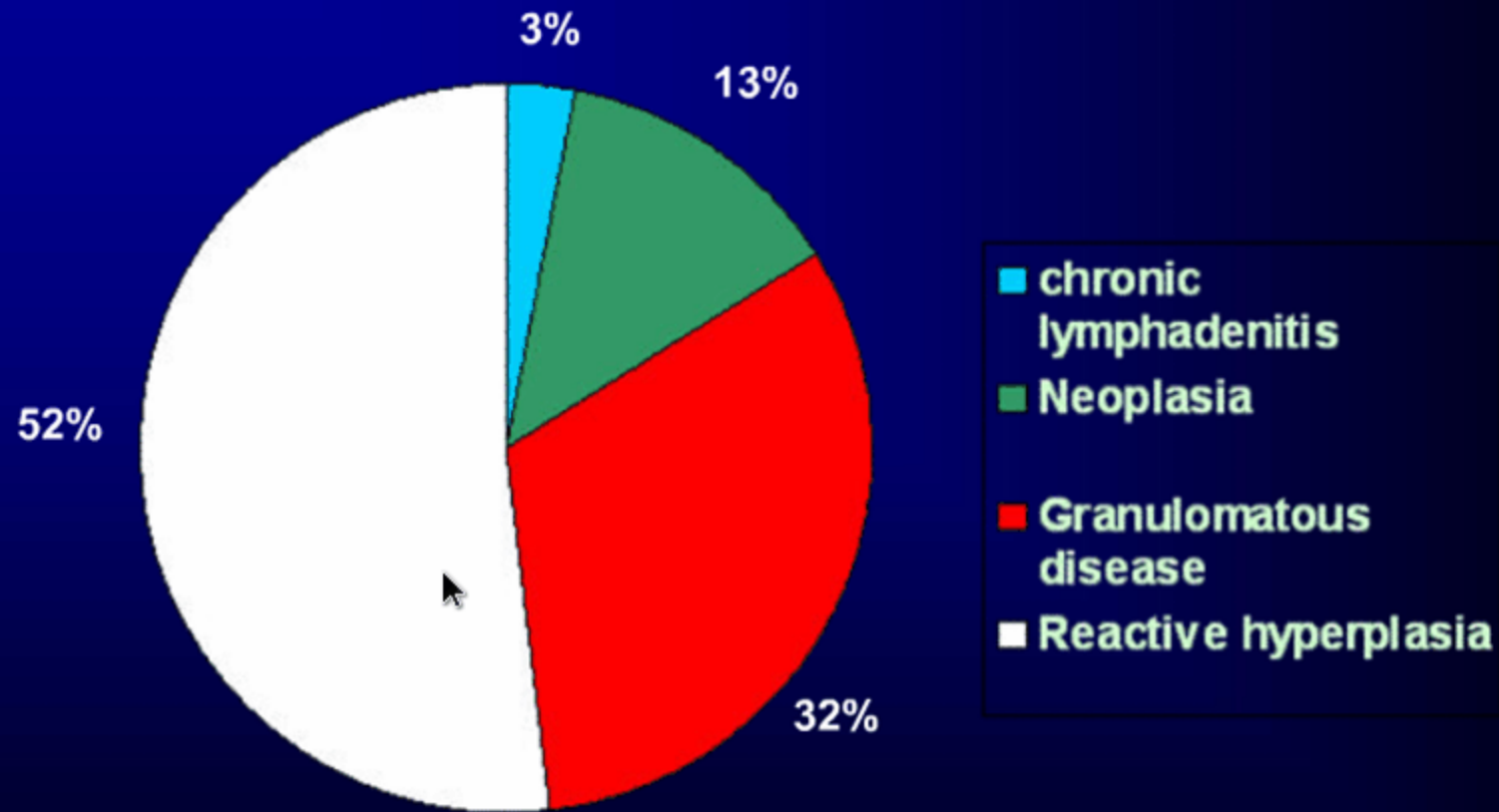
OR

**Abnormal Blood picture
OR**

Bone pains



Common Causes of Lymphadenopathy



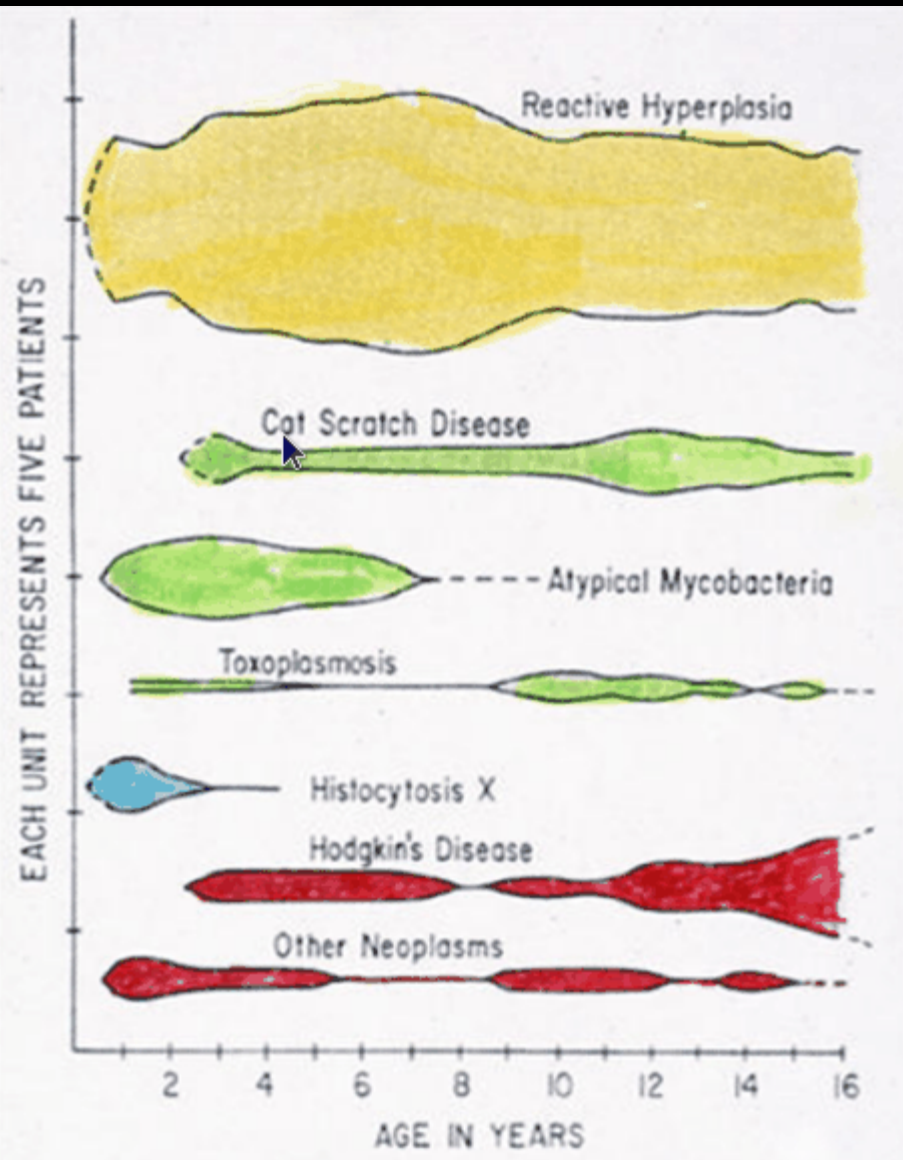
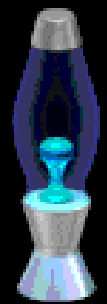
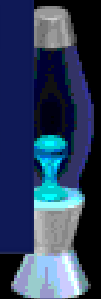
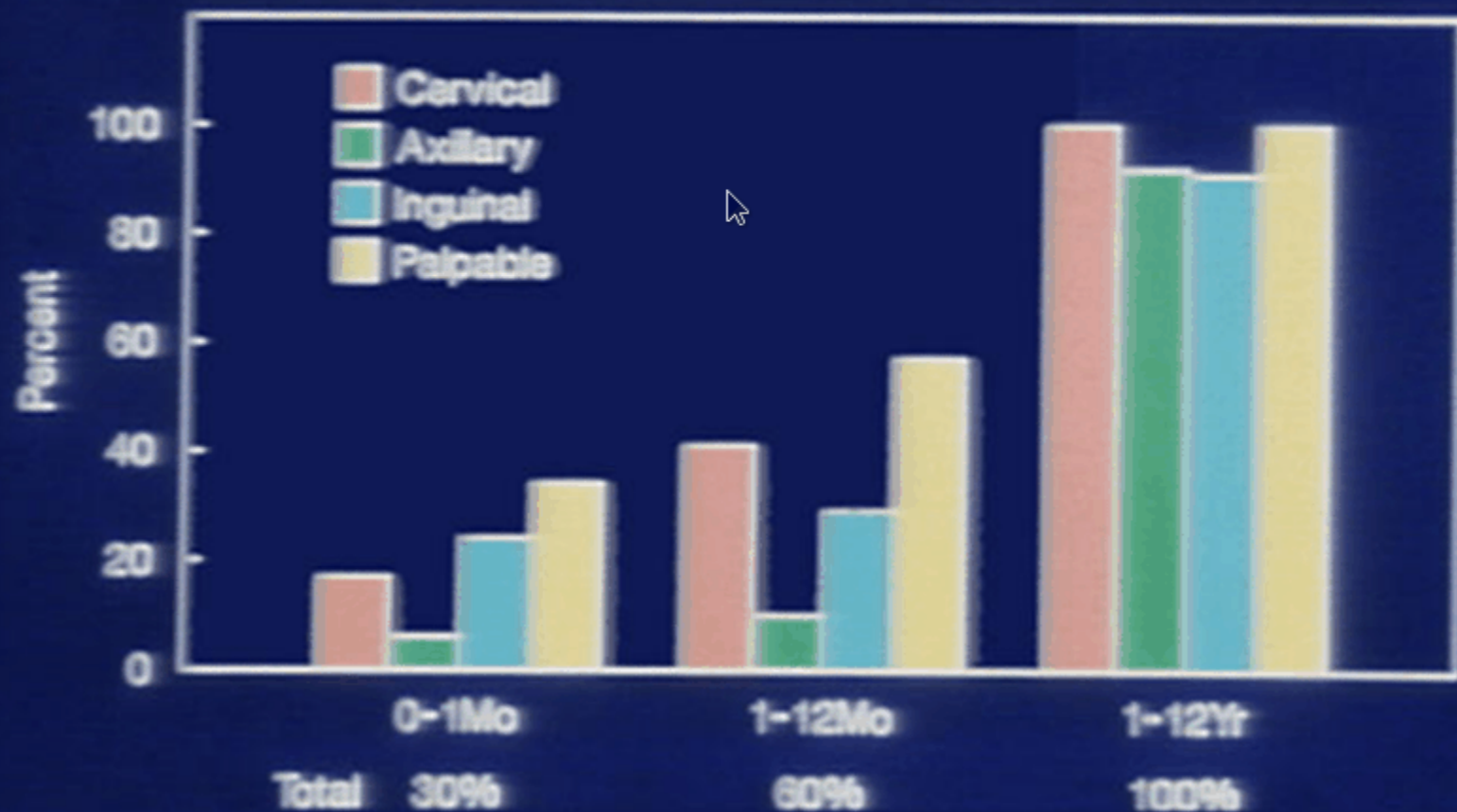


Fig 2. Cause of lymphadenopathy vs age. Shaded area within curves is proportional to age-related frequency of major causes of lymphadenopathy.



Percentage of Healthy Infants and Children with Palpable Lymph Nodes



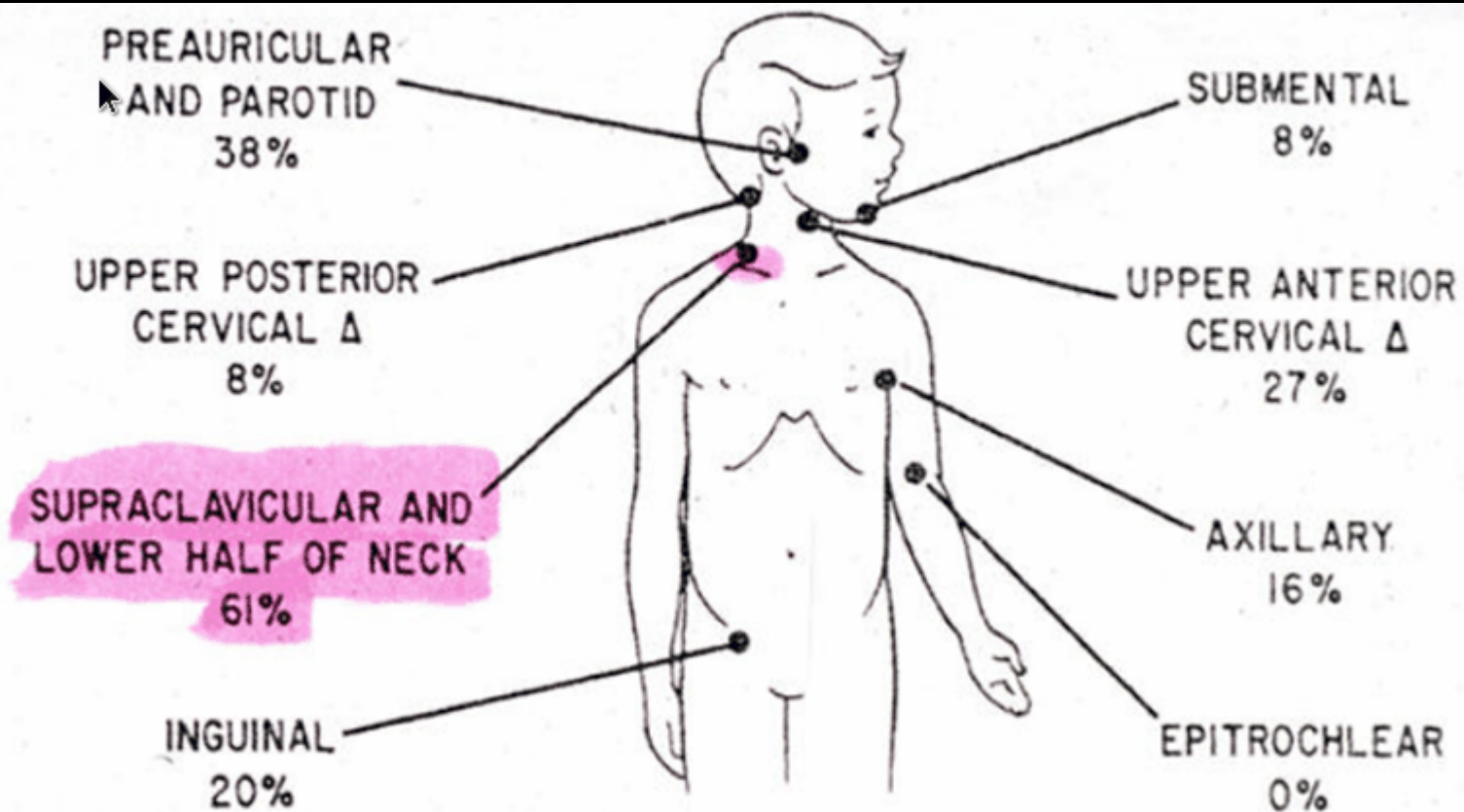
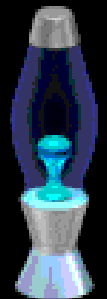
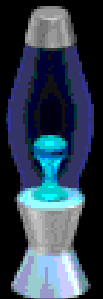


Fig 3. Cause of lymphadenopathy vs site of lymphadenopathy. Percent at each site of adenopathy is therapeutic yield for that location. High yield from supraclavicular adenopathy was due to Hodgkin disease, whereas that in upper cervical and preauricular areas was due to atypical mycobacteria.



Lymphadenopathies

- > 15mm in size
- Postauricular, supraclavicular and epitrochlear
- Absence of inflammation
- Weight loss and hepatosplenomegaly
- No progression in size after 2-3 months of observation

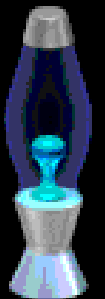


Bone Pains

Any child with suspected arthritis

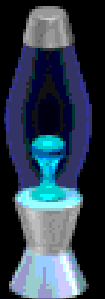
- whose diagnosis is not definitive or
- who has abnormal peripheral blood picture,
- elevated SLDH or
- steroid therapy is contemplated

→ **SHOULD UNDERGO A BMA**



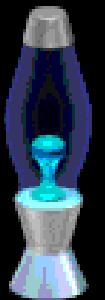
ABNORMAL PERIPHERAL BLOOD PICTURE

- Anemia with reticulocytopenia
- Leukocytosis/leukopenia, lymphocytosis and neutropenia
- Thrombocytopenia
- BLASTS in the smear

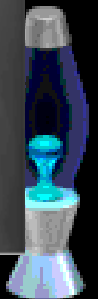
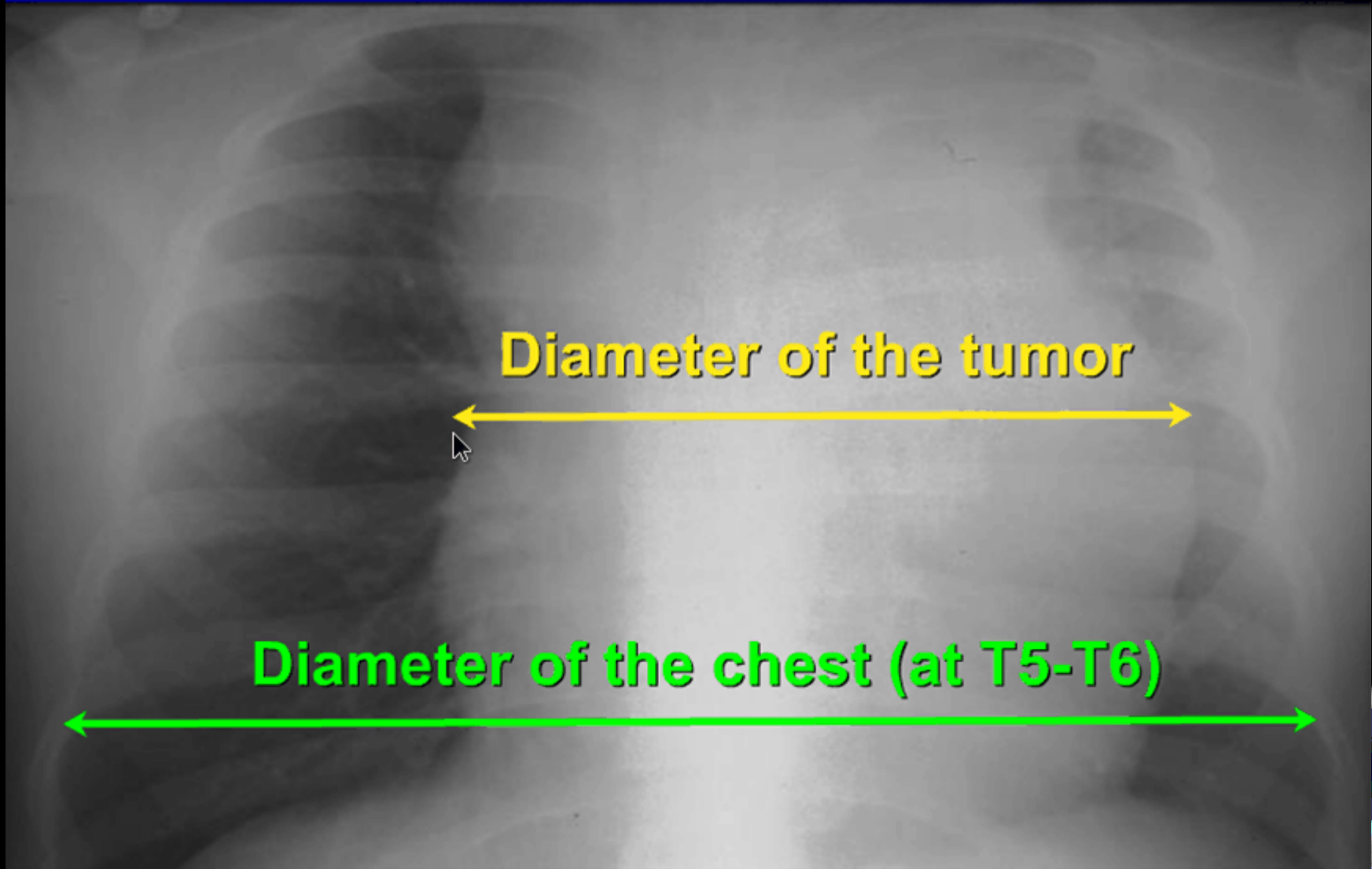


Basic Tests

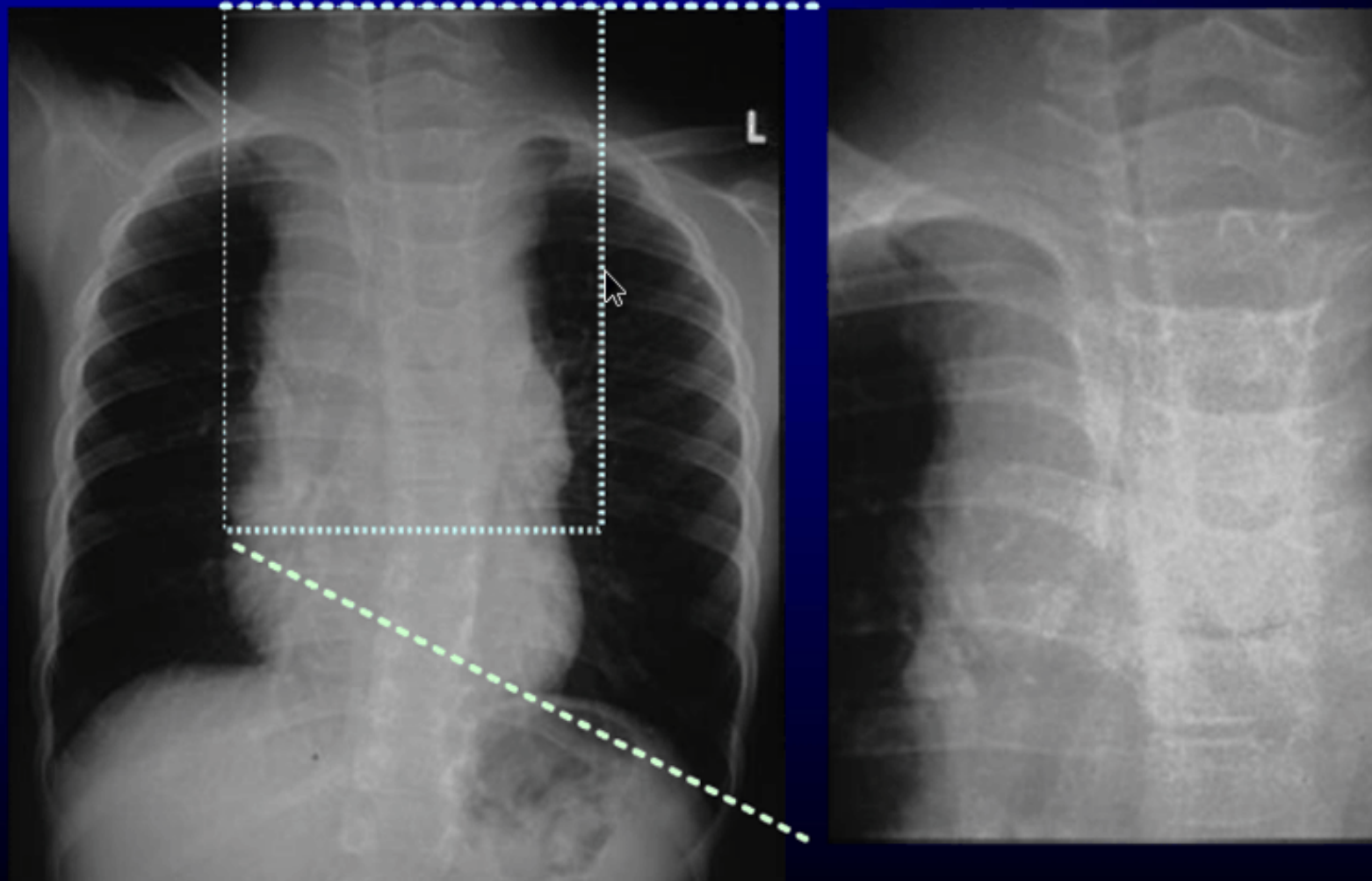
- CBC
- SLDH
- Chest X-ray



Chest Radiograph – Mediastinal Thoracic Ratio



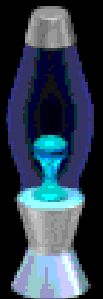
Chest X-ray



Pitfalls in the Diagnosis of leukemia in Children (1997-2002)

Most common signs

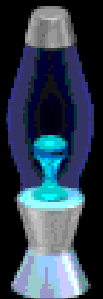
1. Hematologic Abnormalities
 - A. Anemia – 94.9%
 - B. Thrombocytopenia – 73%
 - C. Lymphocytosis – 70%



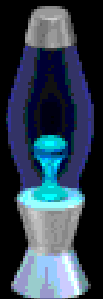
Pitfalls in the Diagnosis of leukemia in Children (1997-2002)

Most common signs

1. Hematologic abnormalities
2. Fever – 68.5%
3. Organomegaly – 68%
4. Bone Pains – 30%

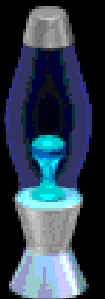


- Majority of the 160 patients (81.2%) were misdiagnosed.
- Mean time of delay in diagnosis is 2.1 months or 63 days.



Misdiagnosis

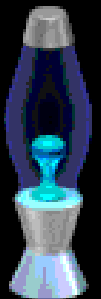
1. Rheumatic fever – 27%
2. Nutritional anemia – 21.5%
3. Infection – 14.7%
4. PTB – 10%



- ANA, ESR or ASO titer that supported the initial physician : diagnosis gave a false sense of security

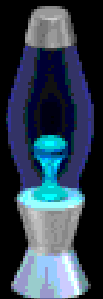
1984

Saulsbury, J Ped



HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

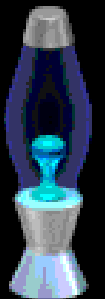
- Prolonged fever
- Pancytopenia
- Coagulopathy
- Hepatosplenomegaly
- Failure to thrive



Types

Familial

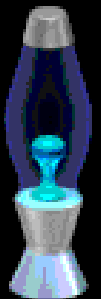
- Usually 3-4 yrs of age
- Usually made when a second sibling is affected
- Prolonged fever and failure to thrive



Types

Infection Associated

- Associated with viral, bacterial, fungal and parasitic infection
- Immunodeficient patients
- SAME manifestation as familial but coagulopathy pronounced



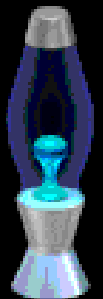
Diagnostic criteria

- Fever : $> 38.5\text{ C}$, > 7 days
- Splenomegaly > 3 cms

AND

2 of the following

- Anemia
- Thrombocytopenia
- Neutropenia



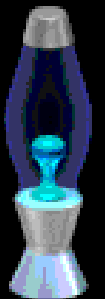
Diagnostic Criteria

One of the following

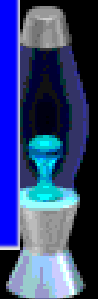
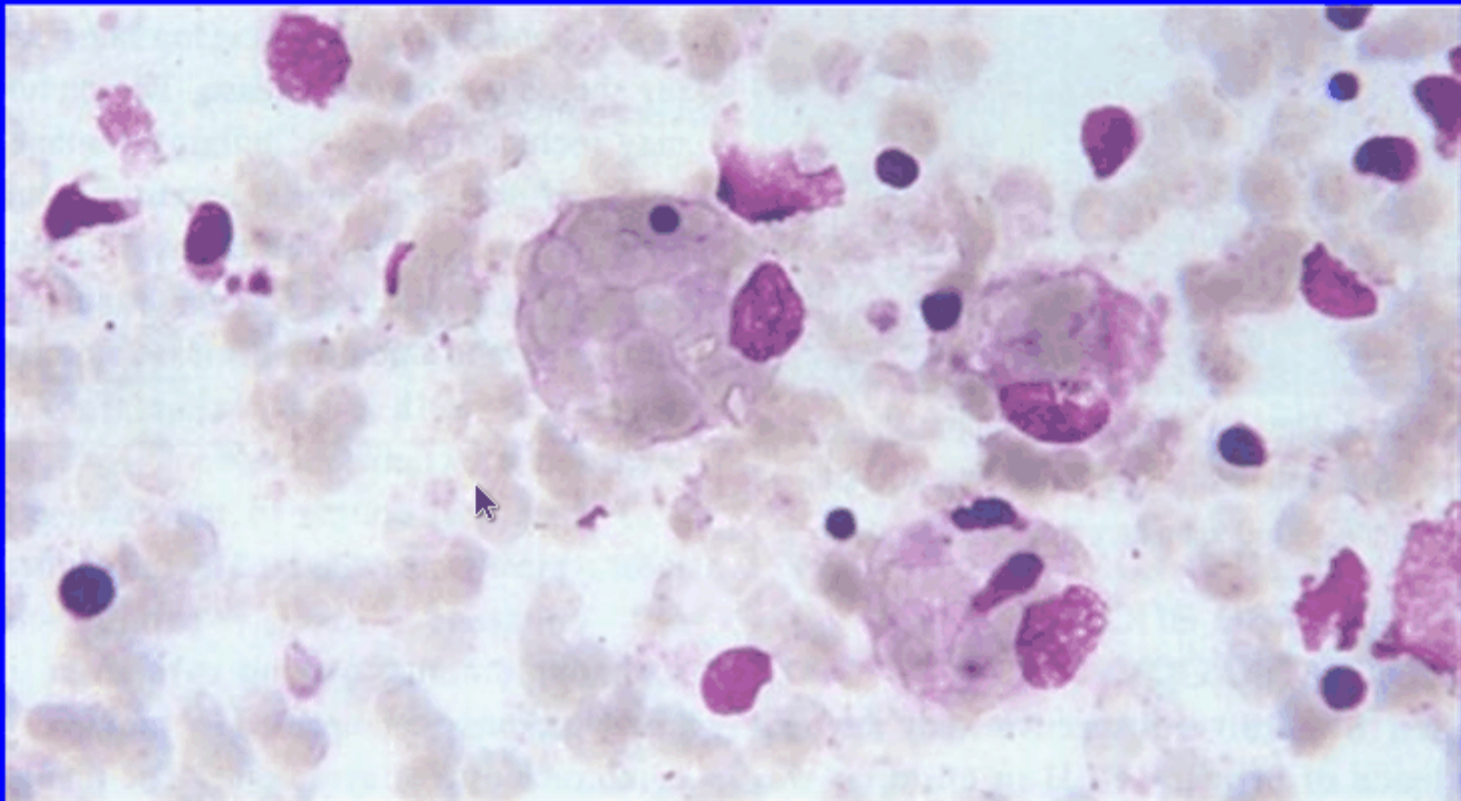
- Hypertriglyceridemia
- Hypofibrinogenemia

AND

- Hemophagocytosis in BMA, spleen or lymph node
- No evidence of neoplasia



Hemophagocytosis is found in
60% of patients at the diagnosis



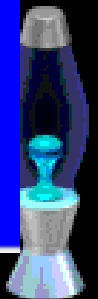
HLH - Main clinical features

- M/F 1:1
- Fever 114/122 (93%)
- Hepato-splenomegaly 119/122 (97%)
- Lymphadenomegaly 39/122 (31%)
- Skin rash 30/122 (24%)



HLH - Main laboratory features

• Thrombocytopenia	104/122	(85 %)
• Triglycerids ↑	78/ 97	(80%)
• Fibrinogen ↓	66/101	(65%)
• Neutropenia	73/122	(59%)
• CSF Pleocytosis	55/94	(58%)
• ALT ↑	55/104	(53%)
• Ferritin >500µg/L	26/31	(83%)

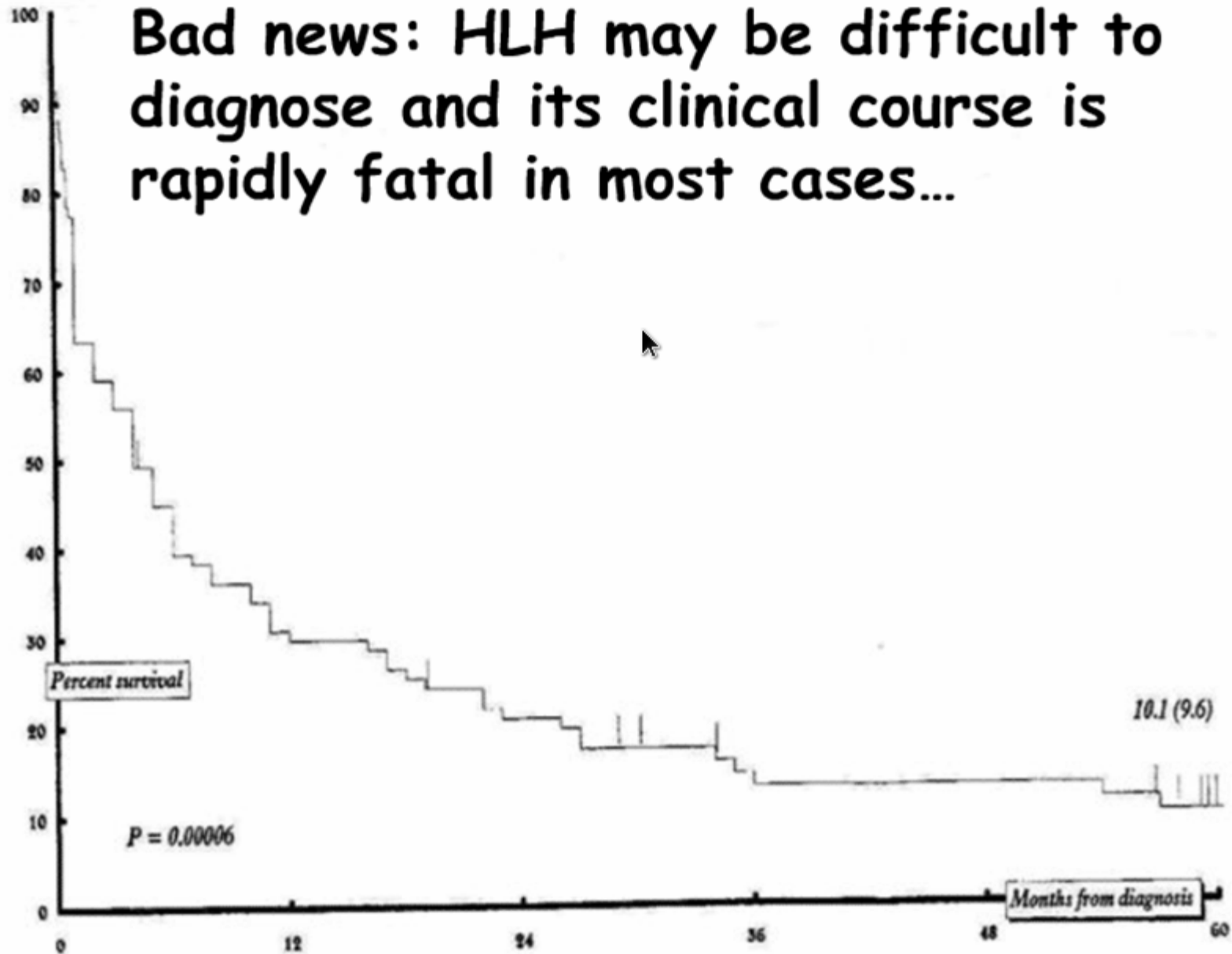


HLH: a difficult diagnosis

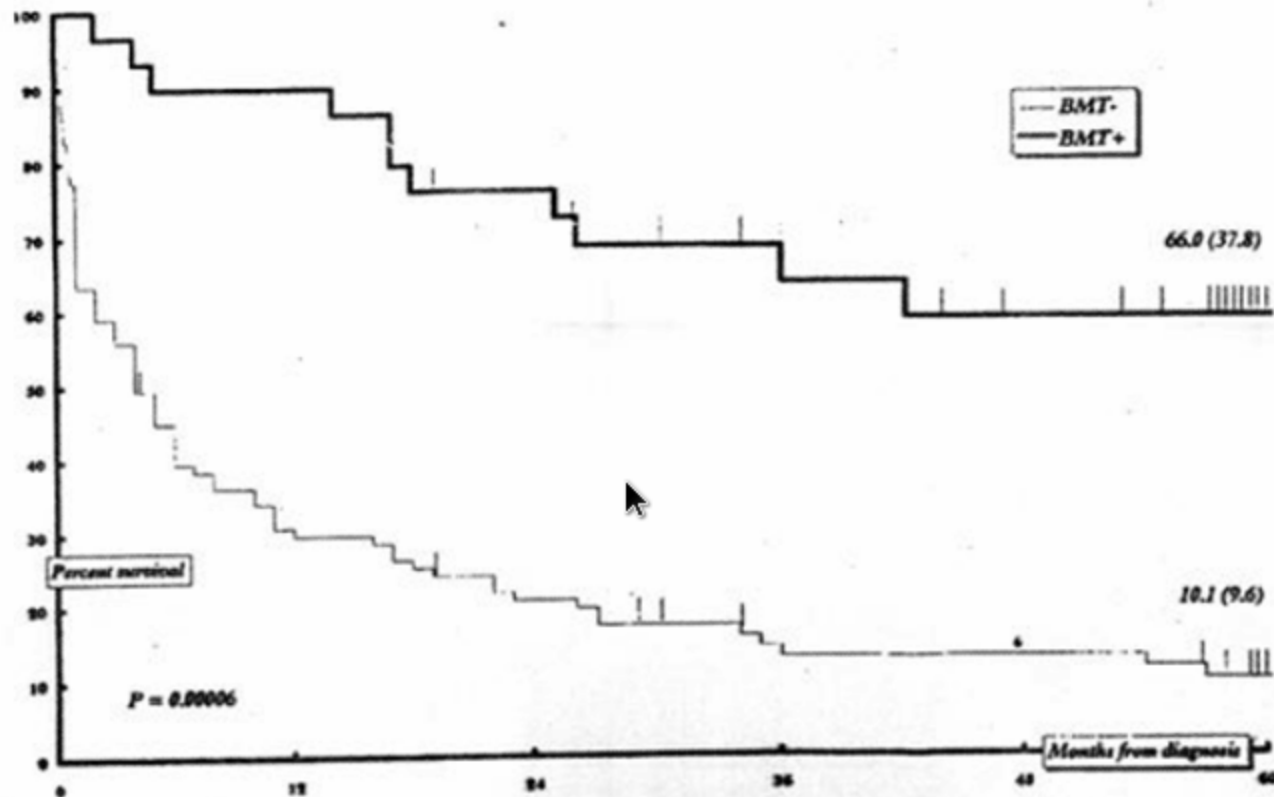
- Clinic:
 - looks like leukemia....
 - looks like septicemia....
 - looks like viral infection....
- Laboratory:
 - Nothing specific!



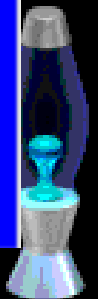
Bad news: HLH may be difficult to diagnose and its clinical course is rapidly fatal in most cases...



.. and the only way to rescue them is BMT



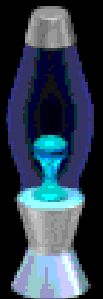
3 Kaplan-Meier survival estimates of 122 HLH children treated with or without BMT.



COURSE AND TREATMENT

Familial

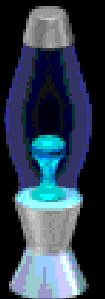
- Highly fatal
- May respond with chemotherapy But long term prognosis is guarded
- BMT



COURSE AND TREATMENT

Infection Associated

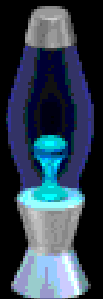
- High fatality rate
- Immunosuppressive chemotherapy may be harmful
- Acyclovir



PCMC Data

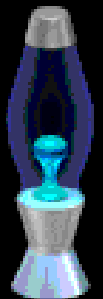
1999-2007

- 8 patients
- Prolonged fever (100%)
- Splenomegaly (55%)
- Pancytopenia (73%)
- Hemophagocytosis in BMA (67%)
- Mortality (60%)



PCMC Data

- 2 reported cases of Familial Type
- Prolonged fever > 2 months, hepatosplenomegaly, jaundice and bleeding
- Both died



**THANK YOU
AND
GOOD DAY !!!**

