

105.12.10

# 體液檢驗

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CELSVSB

## Body Cavity Fluids

*Filtration of plasma through capillary endothelium.  
Reabsorption by venules and lymphatic vessels.*

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## Body Fluids

- Pericardial effusion
- Pleural effusion
- Peritoneal effusion
- Cerebrospinal fluid
- Synovial fluid

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## Body Cavity Fluids

*In the healthy individual,  
a small amount of fluid  
for lubrication.  
(A potential space)*

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**Body Cavity Fluids**

Fluid (effusion) of sufficient quantity to be aspirated is found only in the presence of disease.

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**Pleural Fluid**

- Hydrostatic pressure (H.P.)
- Oncotic pressure (blood) (O.P.)
- Pleural negative pressure (P.N.P.)
- Pleural oncotic pressure (P.O.P.)

The diagram illustrates the pleural cavity between the parietal pleura (pink) and the visceral pleura (green). It shows the following pressures:

	Parietal pleura	Pleural cavity	visceral pleura
H.P.	30 cm H <sub>2</sub> O		11 cm H <sub>2</sub> O
O.P.	34		34
P.N.P.	5		5
P.O.P.	8		8

Net pressure produce < remove

9 cm H<sub>2</sub>O < 10 cm H<sub>2</sub>O

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**Thoracentesis**

Indications for undiagnosed pleural effusion or for therapeutic benefit to relieve dyspnea caused by effusions

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**Normal Serous Fluid  $\Phi$**

- Appearance : straw color & clear
- pH : 7.4
- Specific gravity : < 1.016
- Total protein : 1~2 gm/dL
- Noncolloidal solutes : same as in plasma
- Clot formation : (-)
- Cells : few lymphocytes and mesothelial cells

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**Mechanisms of Pleural Effusions**

- Lymphatic obstruction
- Increased capillary permeability
- Decreased plasma oncotic pressure
- Increased capillary venous pressure
- Increased negative intrapleural pressure

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**Pleural effusion  
Transudate**

- Congestive heart failure
- Constrictive pericarditis
- Nephrotic syndrome
- Liver cirrhosis
- Peritoneal dialysis
- $\uparrow$  venous pressure
- $\downarrow$  plasma albumin

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**Effusion Exam.**

**Purposes**

- **Transudate (滲出液)**  
An effusion caused by **mechanical factors** influencing formation or reabsorption (a **systemic condition: benign process**)
- **Exudate (滲出液)**  
An effusion caused by **damage** to mesothelial lining (a **serious local process**)

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**Pleural effusion  
Exudate**

- Malignancy
- Infection
- Trauma
- Autoimmune diseases (ex. SLE, RA)
- Pulmonary infarction
- Esophageal rupture
- $\uparrow$  capillary permeability
- $\downarrow$  lymphatic drainage

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Item	Transudate	Exudate
Appearance	clear pale yellow	cloudy, turbid bloody, purulent
Sp. gr.	$\leq 1.015$	$> 1.018$
Protein	$\leq 3 \text{ gm/dL}$ ( $\leq 50\%$ of serum)	$> 3 \text{ gm/dL}$ ( $> 50\%$ of serum) <sup>◊</sup>
LD	$\leq 200 \text{ IU/L}$ ( $\leq 60\%$ of serum)	$> 200 \text{ IU/L}^{\oplus}$ ( $> 60\%$ of serum) <sup>◊</sup>

◊ Light's criteria

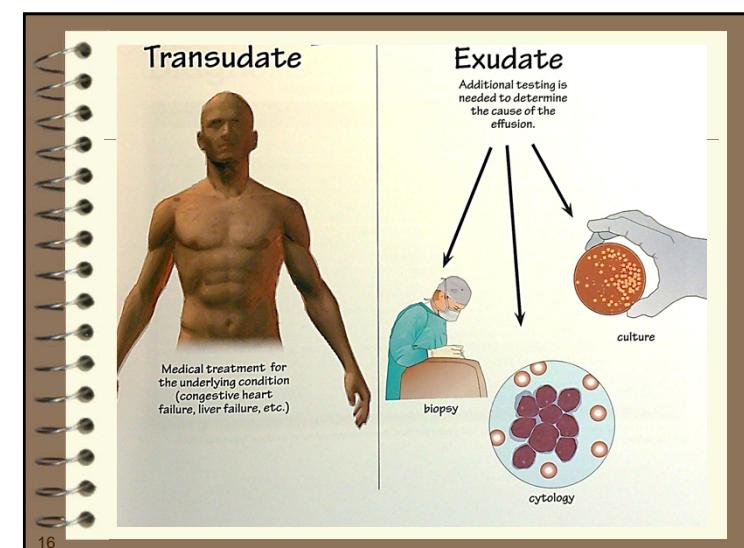
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Item	Transudate	Exudate
RBC	rare	variable from a few cells to bloody
WBC	few	$> 1,000/\text{mm}^3$ to frank pus
Differential count	few lymphocytes, mesothelial cells	lymphocytes, PMN, mesothelial cells

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Item	Transudate	Exudate
Cholesterol	$< 60 \text{ mg/dL}$ ( $< 30\%$ of serum)	$> 60 \text{ mg/dL}$ ( $> 30\%$ of serum)
Bilirubin	$< 60\%$ of serum	$> 60\%$ of serum
Glucose	as in plasma	frequent ↓ due to glycolysis
Fibrinogen	0.3~4 g/dL	4~6 g/dL
Clot	( - )	usually ( + )

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### *Specimen Collection*

- A sample with 3.8% sod. Citrate, heparin, or EDTA
- A sample without anticoagulant
  - Clot formation
- A separate heparinized syringe
  - pH must be measured anaerobically without undue delay.

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### *Routine examination*

- Appearance
- Specific gravity
- Qualitative test of protein
- Cell count
- Differential count

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### *Examination of Puncture*

- Routine examination
- Biochemical examination
- Serological test
- Bacteriologic examination
- Cytological study

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#### *Physical examination*

##### *Appearance*

- Color
  - yellow, red, green, brown
- Transparency
  - clear, turbid, fibrinous, clotting, bloody, chylous



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*Specific gravity*

### Refractometer

**Indirect method**

- ① Refractive index varies with sp.gr.
- ② Temperature (15~40°C) compensation

★Calibration with dd H<sub>2</sub>O, sp. gr. = 1.000

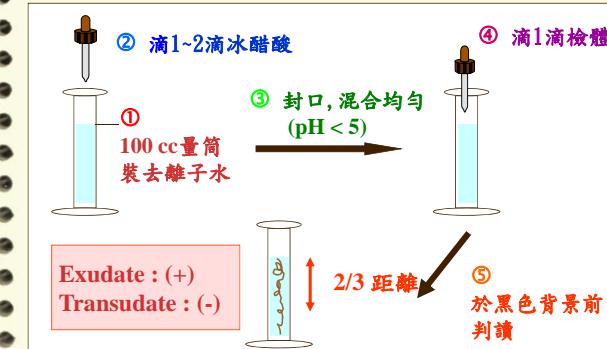


Exudate : > 1.018  
Transudate : ≤ 1.015

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*Routine examination*

### Rivalta's test



② 滴1~2滴冰醋酸  
③ 封口，混合均匀 (pH < 5)  
④ 滴1滴檢體  
⑤ 於黑色背景前判讀

Exudate : (+)  
Transudate : (-)

① 100 cc量筒 裝去離子水

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*Routine examination*

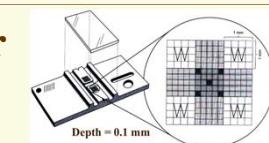
### Protein

- Refractometer - Sp. gr.
- ⌚ (Sp.gr. - 1.007) x 343 = g/dL
- Rivalta's test
- ★ Quantitative test

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### Cell count

- Hemacytometer
- WBC : No. of 10 large squares/mm<sup>3</sup>
- RBC : No. of 5 medium squares X 50/mm<sup>3</sup>
- Automated cell counter: TNC



Depth = 0.1 mm

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**Differential count**

### Purposes

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To determine if the effusion is associated with a **benign or malignant** disease process

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**Differential count**

### Smear preparation

The diagram shows a test tube containing a yellow liquid (effusion) with a red arrow pointing to a red blood cell (RBC) in the sediment. It illustrates three methods for preparing a smear:

- Push smear:** A slide is pushed across the surface of the sediment, creating a thin layer of cells.
- Pull-apart smear:** Two slides are used; one is held horizontally while the other is pulled vertically through the sediment, creating a thicker, more confluent smear.
- Margin free:** A slide is pushed across the sediment, leaving a clean margin at the edge of the slide.

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**Routine examination**

### Differential count- Dry smear

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- ⌚ Centrifuge citrated specimen at 1500 rpm for 10 min.
- ↳ Discard supernatant.
- ↳ Smear sediment or buffy coat on slides.
- ↳ Air dry.
- ↳ Stain with Liu's stain.

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**Differential count**

### Cytocentrifugation

A photograph of a Cytospin machine, which is a specialized centrifuge designed for cytocentrifugation. A sample slide is shown being processed inside the machine.

**Cytospin  
800 rpm  
5 min**

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**Differential count**

### **Smear staining**

- Liu's stain
- Wright-Giemsa stain
- Papanicolaou stain
- Immunocytochemical stain

**★ For morphological observation & identification of the cells**

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**Differential count**

### **Classification**

- 100 nucleated cells including Lymphocyte, Neutrophil, Mesothelial cell, Histiocyte
- L : N : M : H = 90 : 4 : 1 : 5
- L : N : M : H = 90 : 2 : 7 : 1
- Eosinophil (E), basophil (B)

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**Differential count**

### **Smear staining**

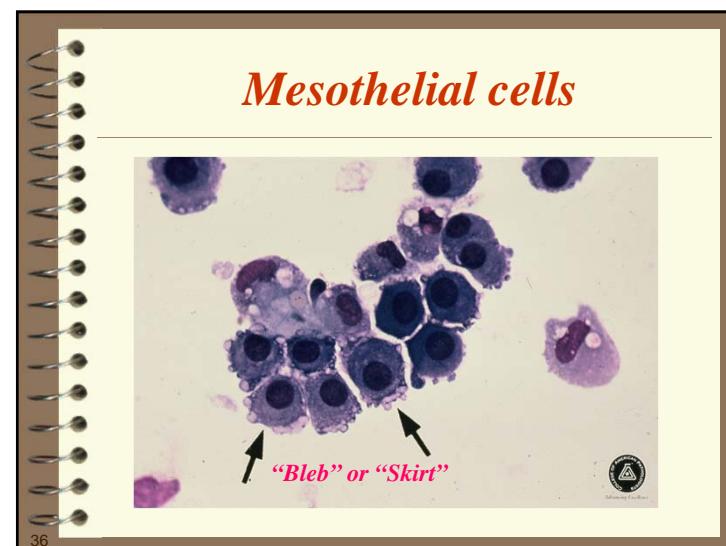
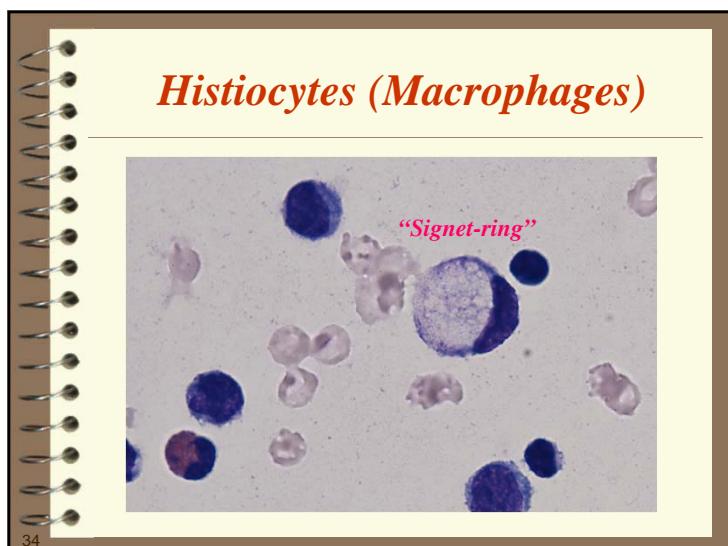
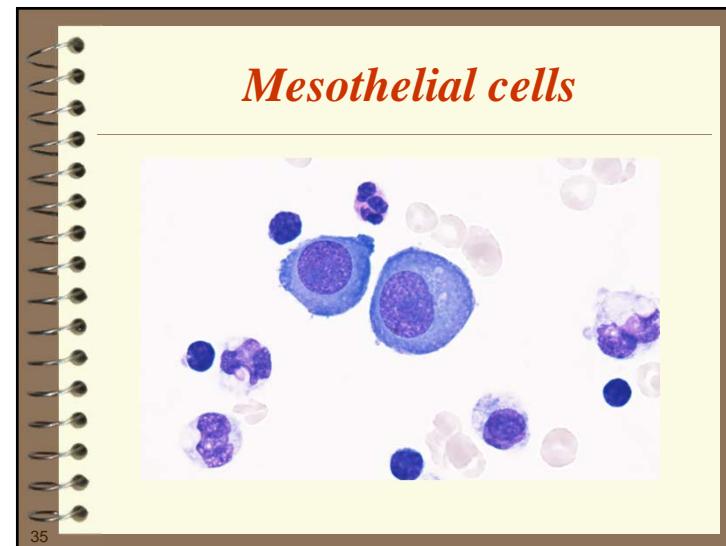
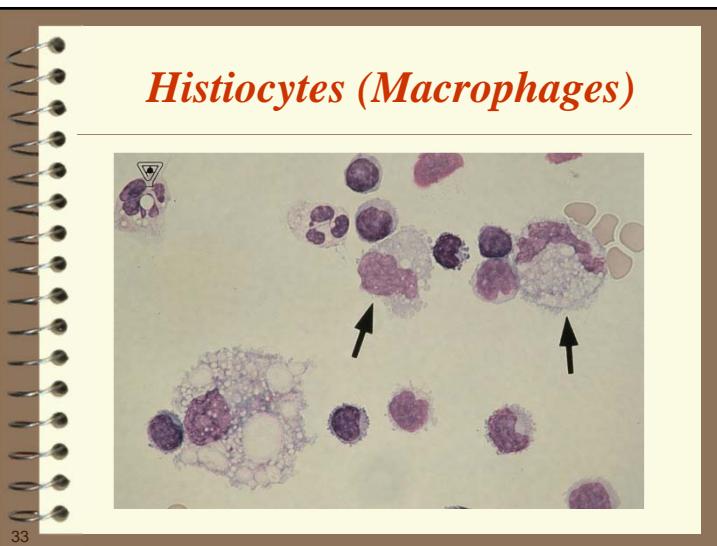
**Liu's stain**

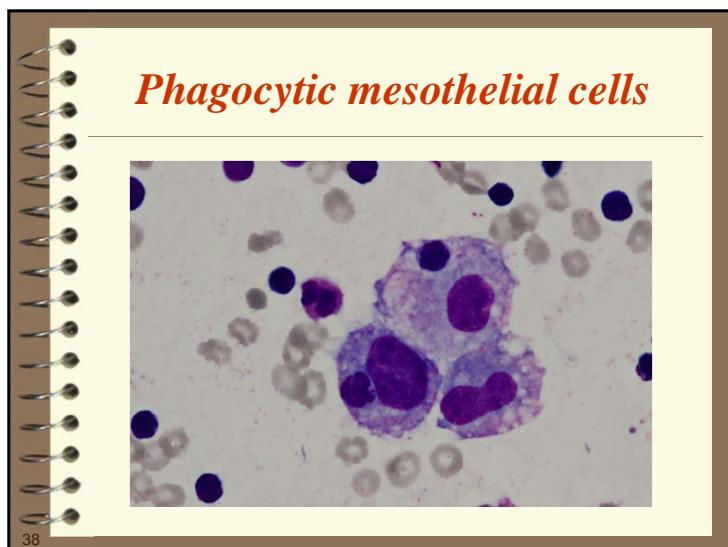
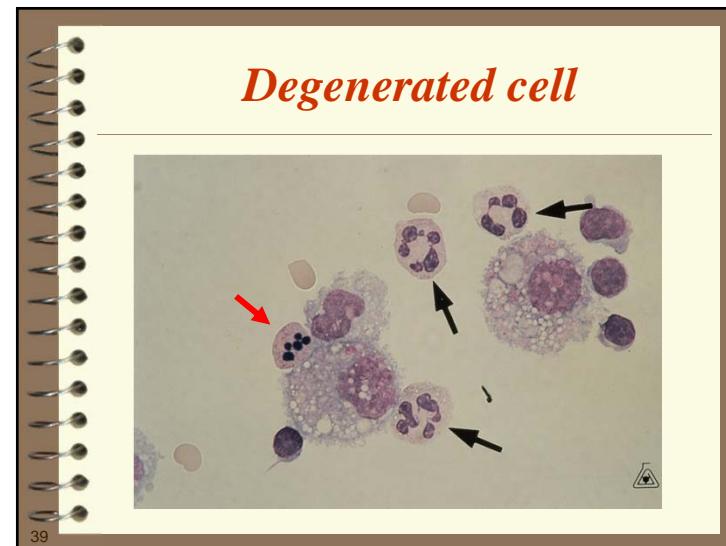
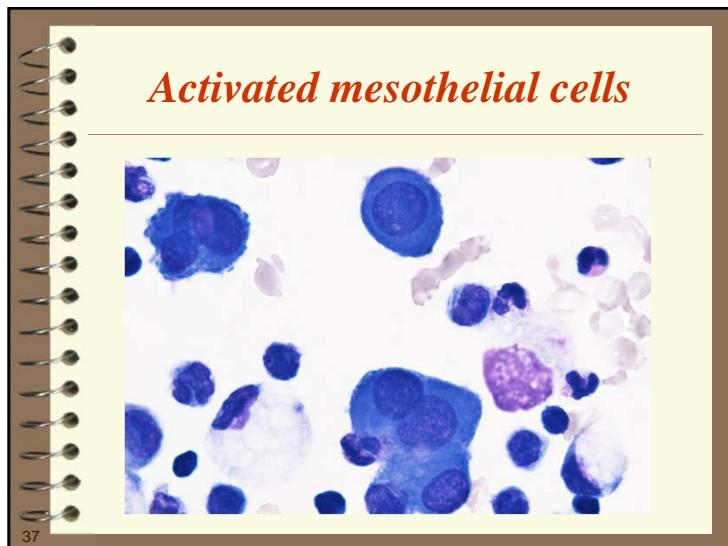
① Liu A 5 滴  
② 15~30 秒  
③ Liu B 10 滴  
④ 1分30秒~2分  
⑤ 沖洗

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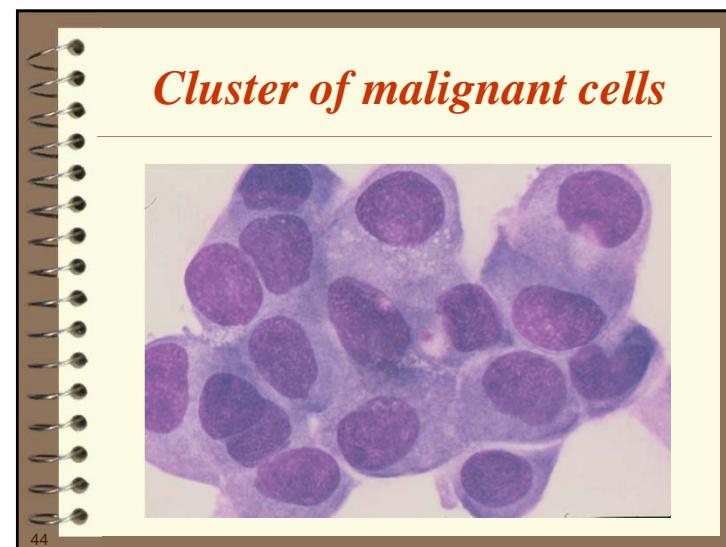
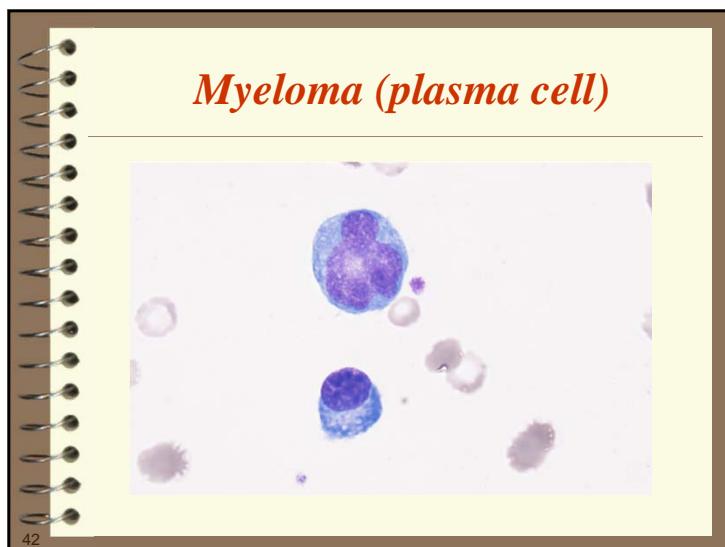
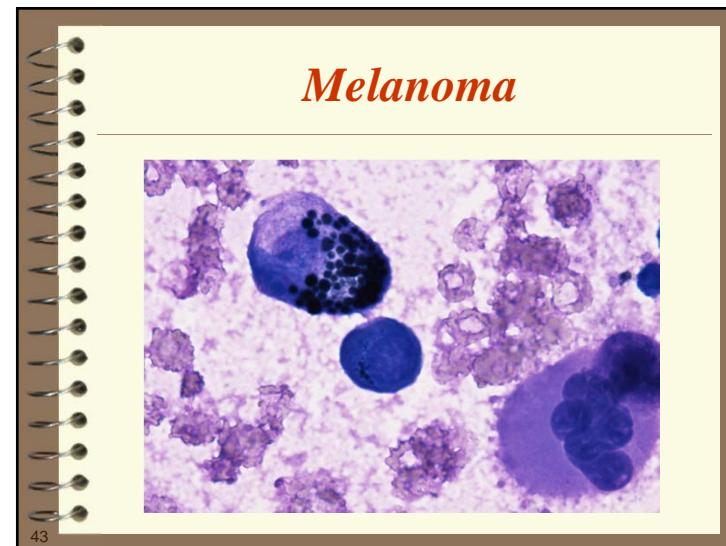
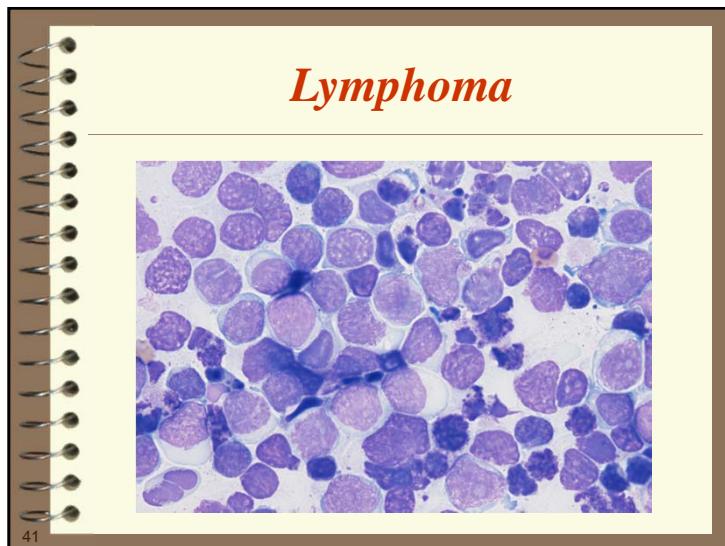
### **Leukocytes**

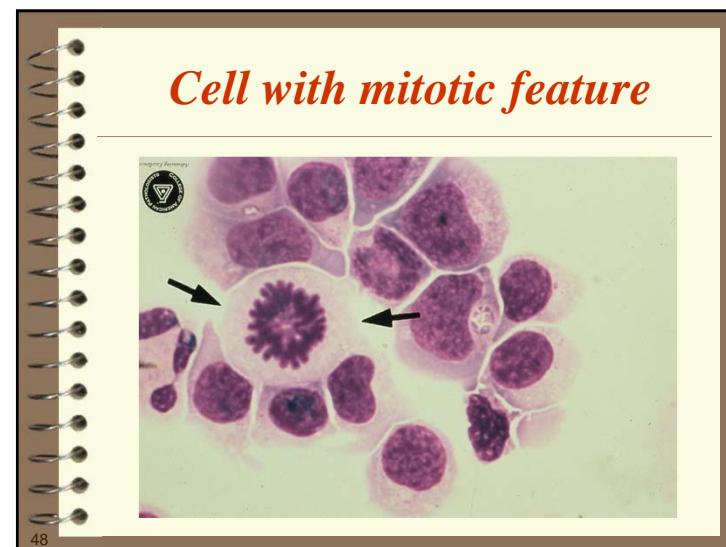
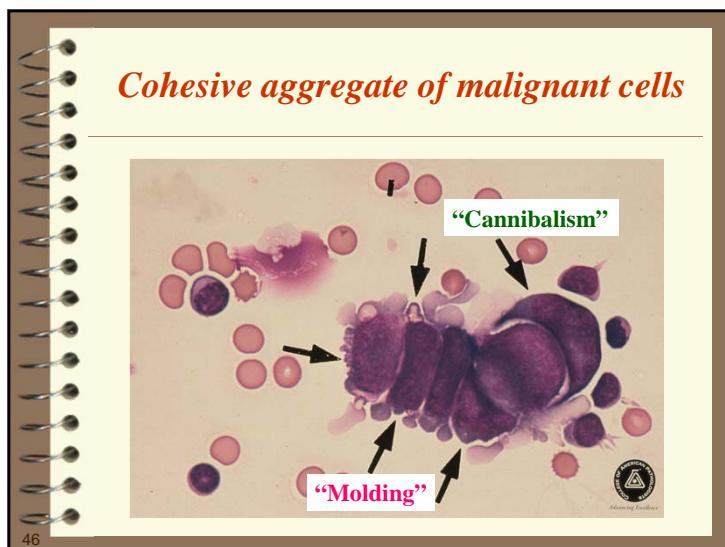
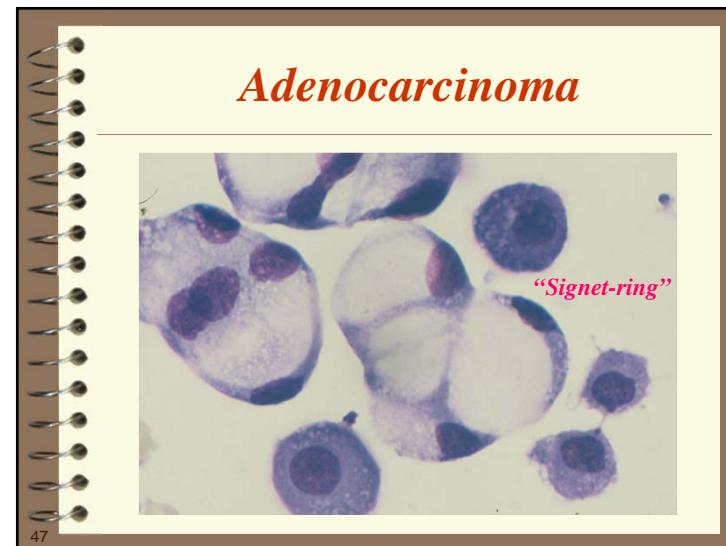
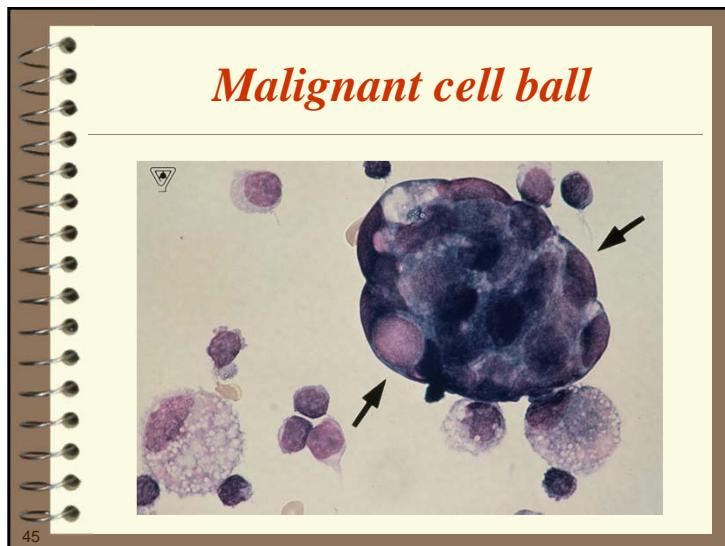
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- *Differential count*
- Malignant cells*
- Morphology of nucleus, chromatin & cytoplasm
  - Clusters of tumor cells
  - Tumor cell ball
  - Cannibalism feature
- ☆ ***Detection rate: 50-70%***
- 40





### Biochemical examination

- Protein
- Glucose
- Lactate dehydrogenase (LD)
- Triglyceride & cholesterol
- Amylase
- Tumor markers: CEA, CA-125

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### Bacteriological examination

- Gram stain
- Acid-fast stain
- Culture
  - Routine culture
  - TB culture

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### Serological test

- Rheumatoid factors
  - Rheumatoid disease
- Antinuclear antibodies
  - Systemic lupus erythematosus

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### Exam. of Punctate Purposes

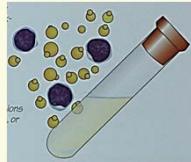
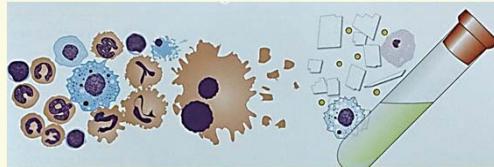
- Chylous effusion

It is due to damage or obstruction of thoracic duct. (e.g. trauma, lymphoma, carcinoma)
- Pseudochylous effusion

It is usually caused by tuberculosis and contains cholesterol crystals.

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*Exam. of Punctate Purposes*

- Chylous effusion 
- Pseudochylous effusion 

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*Chylous effusion*

- Triglyceride < 50 mg/dL  
→ Rule out chylous effusion
- Triglyceride 50~110 mg/dL  
Lipoprotein EP : chylomicrons (+)  
→ Chylous effusion
- Triglyceride > 110 mg/dL  
→ Probable chylous effusion

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*Cholesterol*



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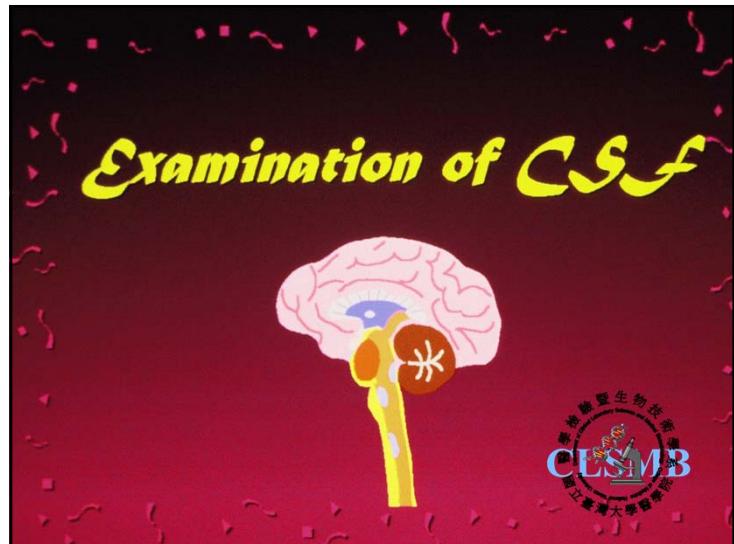
*Exam. of chylous effusion Ether extraction*

- ★ Put 1 mL specimen in glass tube.
- ↳ Add 2~3 drops of diluted HCl.
- ↳ Add 1 mL ether (or chloroform).
- ↳ Shake well.
- ↳ Stand or centrifuge to separate specimen and ether.

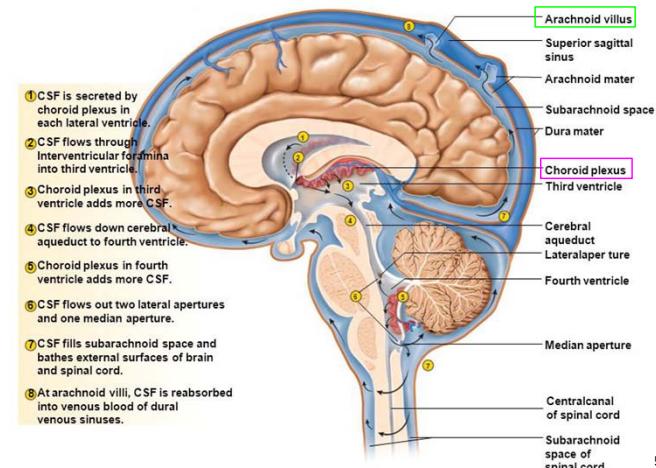
★**Reading**

**Chylous effusion becomes to be clear.**

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## Flow of Cerebrospinal Fluid



### Meninges: 3 layers

- ⊕ Dura mater
  - ⊕ *Dural sinus*
- ⊕ Arachnoid mater
  - ⊕ *Subarachnoid space*
- ⊕ Pia mater

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### Formation of CSF

**Rate:** 500 mL/day or 20 mL/hr

- ⊕ 75% from ventricular choroid plexuses
- ⊕ 25% from capillaries in the brain
  - ★ Ultrafiltration of plasma
  - ★ Active secretion or transport
- ⊕ *Arachnoid villi & granulation of dural sinuses (reabsorption)*
- ⊕ *Venous blood stream*

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## Functions of CSF

- ⊕ **Cushion**  
Brain (1300-1500 gm): 50 gm in CSF
- ⊕ **Protection:** mechanical buffer to prevent trauma
- ⊕ **Regulation of intracranial pressure**
- ⊕ **Nutrients and metabolic wastes**

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## Lumbar Puncture

- ⊕ **Indications**
  - ⊕ Suspected meningitis, encephalitis, subarachnoid hemorrhage, leukemia & malignancy involving the CNS
  - ⊕ Differential diagnosis of cerebral infarct vs. intracerebral hemorrhage
  - ⊕ Introduction of anesthetics, drugs etc.
  - ⊕ Treatment of marked intracranial hypertension

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## Cerebrospinal Fluid

### Brain-blood barrier (choroid plexus)

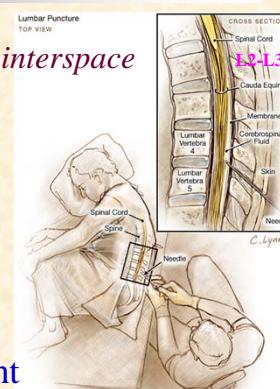
Constituent	CSF	Serum
Protein	15-45 mg/dL ↓↓	6-7.8 g/dL
Osmolality	280-295 mOsm/L	280-295 mOsm/L
Chloride	118-130 mEq/L ↑	96-104 mEq/L
pH	7.28-7.32	7.38-7.42 (artery)
Glucose	50-80 mg/dL ↓	70-110 mg/dL

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### Introduction

## Lumbar Puncture

- ⊕ **Position:** lumbar vertebral interspace
  - ⊕ L3-L4 or lower to avoid damage to spinal cord in adult
  - ⊕ L4-L5 or lower in small children or infant



## Routine Examination

- ⊕ Appearance
- ⊕ Protein
- ⊕ Glucose
- ⊕ Cell count
- ⊕ Differential count

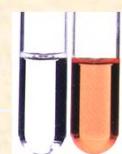
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## Protein

- ⊕ **Pandy Test**  
Globulin and albumin are precipitated by a saturated solution of phenol in water
- ⊕ **Nonne-Apelt Test**  
Globulin is precipitated by half saturated ammonium sulfate
- ★ Multiple sclerosis:  $\gamma$ -globulin increase in 75% CSF

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## Appearance



- ⊕ **Normal:** watery clear
- ⊕ **Turbidity:** microorganism, WBC, RBC etc.
- ⊕ **Xanthochromia**  
pale pink to orange or yellow color in supernatant of centrifuged CSF
- ⊕ **Causes:**
  - Subarachnoid hemorrhage (Hb),
  - Jaundice (Bilirubin), Protein,
  - Melanin & Carotenoid

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## Glucose Test

- ⊕ **Decrease:**  $< 40$  mg/dL
  - ⊕ Hypoglycemia
  - ⊕ Impaired active transport
  - ⊕ Increase utilization via CNS tissue, WBC, RBC
- ★ **Bacterial meningitis**

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## Cell Count

- ⊕ **Normal:** 0-5 cells/ $\mu\text{L}$  in adult  
0-30 cells/ $\mu\text{L}$  in neonate (<1 year)
- ⊕ **Procedure:**
  - Pipette Samson solution to WBC pipette marker 1
    - ⌚ Pipette CSF to mark 11
    - ⌚ Shake well & discard first 3-4 drops
    - ⌚ Charge counting chamber & stand for 5 min
    - ⌚ Count cells in 9 large squares
    - ⌚ Cell count = No. X **11/9** per  $\mu\text{L}$
  - ⌚ **Chamber differentiation:** Lym/Neu

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## Differential Count

- ⊕ **Lymphocyte increase**
  - ⊕ Viral meningitis
  - ⊕ Tuberculous/Cryptococcal meningitis
  - ⊕ Leukemia/lymphoma
- ⊕ **Neutrophil increase**
  - ⊕ Bacterial meningitis
  - ⊕ CNS hemorrhage
- ⊕ **Eosinophil increase**
  - ⊕ Parasitic infection
  - ⊕ Drug-induced CNS hypersensitivity

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## Differential Count

### Liu's or Wright's stains

Cell type	Adult (%)	Neonate (%)
Lymphocyte	<b>62 ± 34</b>	20 ± 18
Monocyte	<b>36 ± 20</b>	<b>72 ± 22</b>
Neutrophil	2 ± 5	3 ± 5
Histiocyte	rare	5 ± 4
Eosinophil	rare	rare
Ependymal cell	rare	rare

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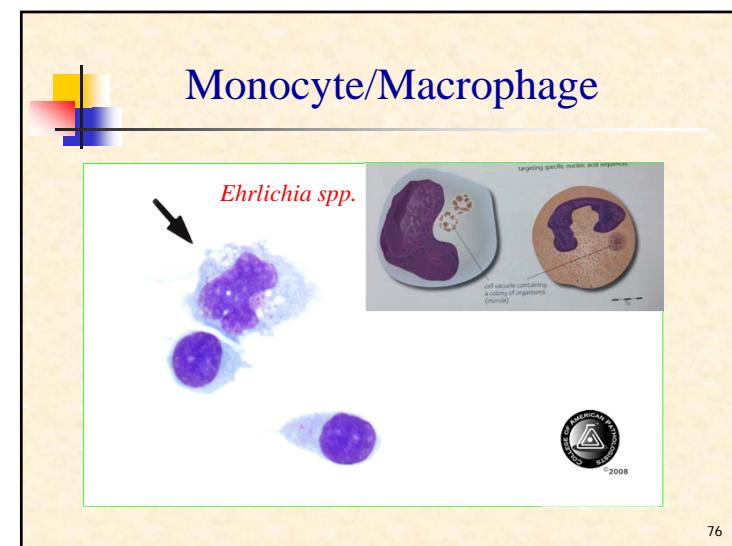
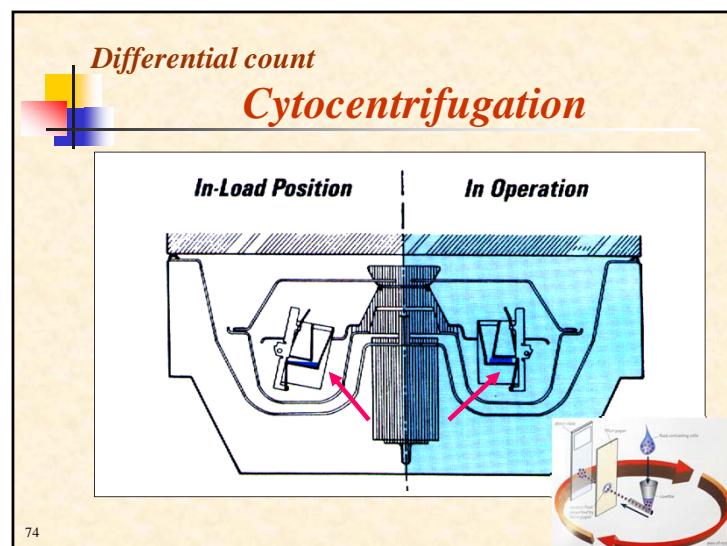
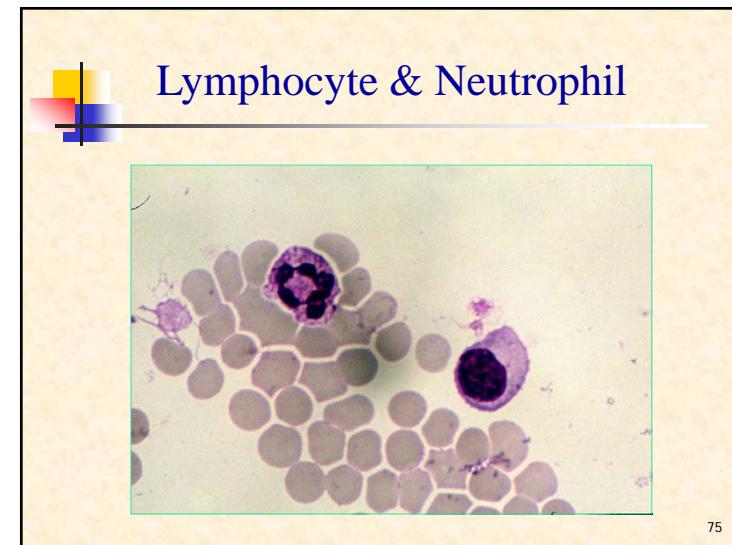
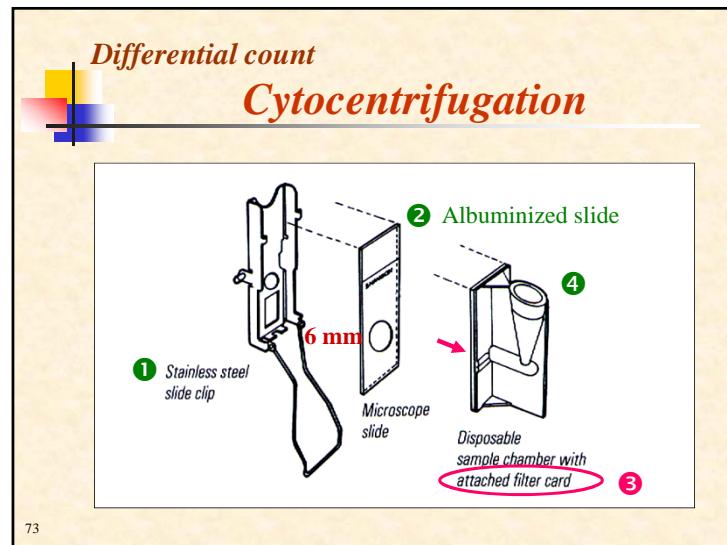
### CSF smear

## Cytocentrifugation

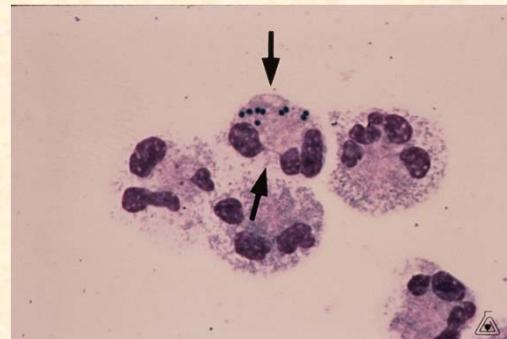


**Cytospin  
800 rpm  
5 min**

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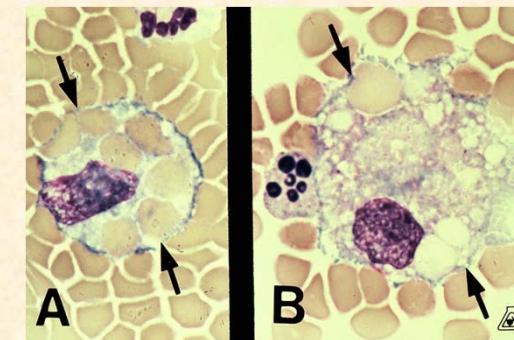


### Cocci in Neutrophil



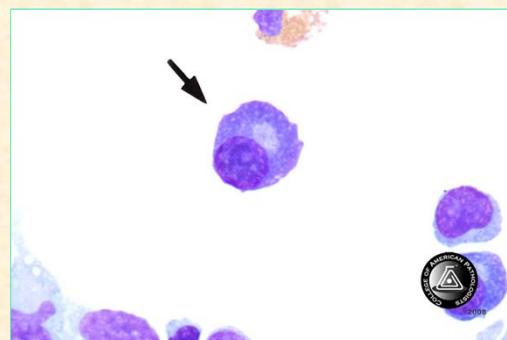
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### Erytrophage- CNS bleed



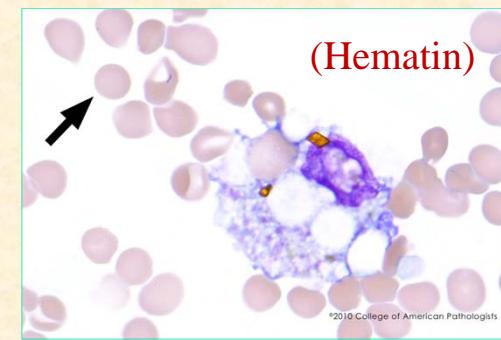
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### Plasma cell



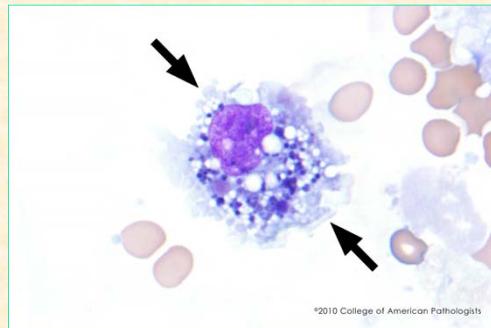
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### Erytrophage with hematoidin



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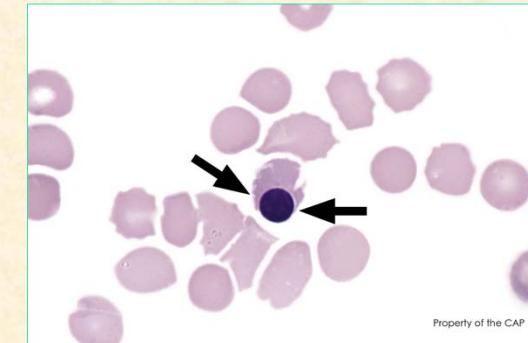
### Siderophage



★ Hemosiderin: Prussian blue stain

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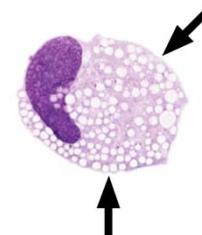
### Normoblast



Property of the CAP

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### Lipophage

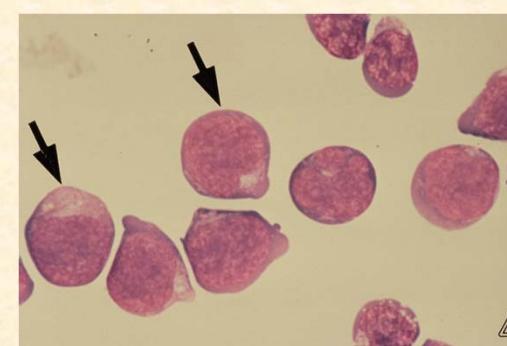


Property of the CAP

★ Tissue damage

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### Leukemic cells



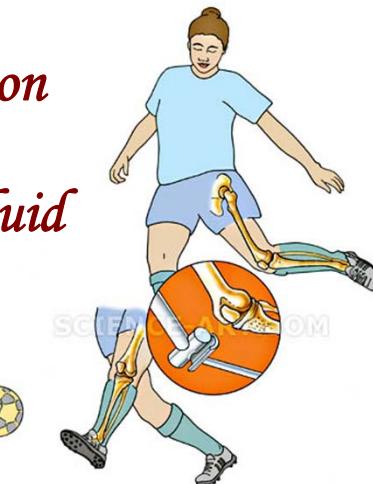
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## Microorganism Stains

- ⊕ Gram's or Loeffler's stains for bacterial observation
- ⊕ Acid-fast stain for tuberculous meningitis
- ⊕ India ink stain for *Cryptococcus neoformans* observation
- ⊕ 10% KOH for fungal observation

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## Examination of Synovial Fluid



SCIENCE

## *Cryptococcus neoformans*

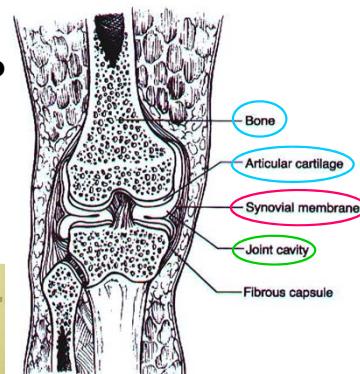
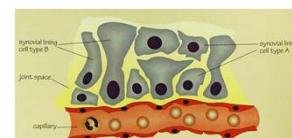
### India Ink Stain



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## Synovium

- Synoviocytes are arranged in one to three layers.
- A discontinuous surface with wide gaps



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## Synovial Fluid

- 0.1 ~ 2 (0.1 ~ 4) mL
  - Ultrafiltration of plasma across synovial membrane
  - Secretion of a **hyaluronate<sup>⊕</sup>-protein complex** (mucopolysaccharide, 5,000~10,000 kDa) by **synoviocytes (type B cells)**
    - ✿ Polymer of repeating **disaccharide** units (**glucuronic acid-glucosamine**) linked with about **2% protein**

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## Synovial Fluid

Constituents	Synovial Fluid	Plasma
Protein	1-3 g/dL	6-8 g/dL
Albumin	55-70%	50-65%
$\alpha_1$ -Globulin	6-8%	3-5%
$\alpha_2$ -Globulin	5-7%	7-13%
$\beta$ -Globulin	8-10%	8-14%
$\gamma$ -Globulin	10-14%	12-22%
Hyaluronate	0.3-0.4 g/dL	
Glucose	70-110 mg/dL	70-110 mg/dL
Uric acid	2-8 mg/dL	2-8 mg/dL

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## Synovial Fluid

- Functions
  - To lubricate joint space
  - To transport nutrients to articular cartilage
  - To transport waste and debris to synovium
    - ✿ Clean-up by phagocytosis

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## Sample Collection

- Patient should be **fasting for 6 hr or longer for glucose test.**
- **1st tube:** 5-10 mL in sterile heparin<sup>⊖</sup> tube for microbiologic exam.
- **2nd tube:** 2-5 mL for microscopic exam.
  - ✿ **Anticoagulants:** sodium heparin or liquid EDTA
- **3rd tube:** 5 mL in plain tube for biochemical or immunological studies

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## Gross Examination - Viscosity

- Viscosity due to hyaluronic acid
- **Falling drop test:** forming a string when drop from a syringe without needle
  - Normal: 4-6 cm
  - Low: < 3 cm
    - Inflammatory or septic condition
    - Rapid effusion following trauma
- **Non-specific**



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## Appearance & Color

- **Grossly bloody fluid:**
  - Fracture through joint surface
  - Tumor involving joint
  - Hemophilic arthritis
  - **Traumatic tap (streaks of blood)**
- **Grossly purulent (yellow-green) fluid:**
  - Severe bacterial infection

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## Appearance & Color

- **Normal:** crystal clear & colorless or pale yellow (*uncooked egg white*)
- **Turbidity:**
  - Leukocytosis (most common)
  - Massive number of crystal
  - Droplets of fat (fracture)
  - Clumps of degenerating synovial cells

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## Appearance & Color

- **Milky or pseudochylous fluid:**
  - Tuberculosis arthritis
  - Chronic rheumatoid arthritis
  - Acute gouty arthritis
- **Greenish-tinged fluid:**
  - *Haemophilus influenzae* septic arthritis
  - Chronic rheumatoid arthritis
  - Acute synovitis due to gout or pseudogout

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**Microscopic Examination**

- Total cell count performed immediately
  - SF ↳ Undiluted
  - ↳ Diluted with saline (0.9%) or 0.1N HCl (or 0.3% saline) to lyse RBC
- ✿ Pre-treat with 0.05% hyaluronidase in PBS (37 °C, 5 min)
  - Normal: 13-300 (< 200)/μL
  - Septic arthritis: > 20,000/μL
    - ✿ Acute urate gout
    - ✿ Rheumatoid arthritis

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**Microscopic Examination**

- ✿ Neutrophil > 80%
  - ▶ Bacterial arthritis
  - ▶ Urate gout
  - ▶ Rheumatoid arthritis
- ✿ Eosinophil > 2%
  - ▶ Metastatic carcinoma
  - ▶ Rheumatoid arthritis
  - ▶ Parasite infestation (Dracunculus medinensis, Guinea worm)

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**Microscopic Examination**

- Differential count performed within 1 hr
  - Smear prepared by spreading or Cytospin (200~1000 rpm for 5~10 min)
- Normal: 65% mononuclear phagocyte (monocyte & histiocyte)  
15-25% lymphocyte  
10-20% (<25%) neutrophil

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**Microscopic Examination**

- ✿ Ragocytes (RA cells)
  - ▶ PMN with cytoplasmic granules containing rheumatoid factor and IgG complex
  - ▶ Staining with 0.2% brilliant cresyl blue, Sternheimer-Malbin stain, oil red O

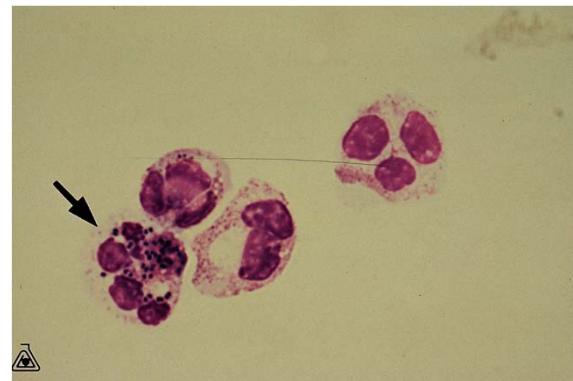
100

 **Microscopic Examination**

- ✿ **Reiter's cells**
  - ♦ Macrophages containing degenerating neutrophils (Neutrophage)
- ✿ **LE (lupus erythematosus) cells**
  - ♦ Neutrophil or monocyte with degenerated nucleus

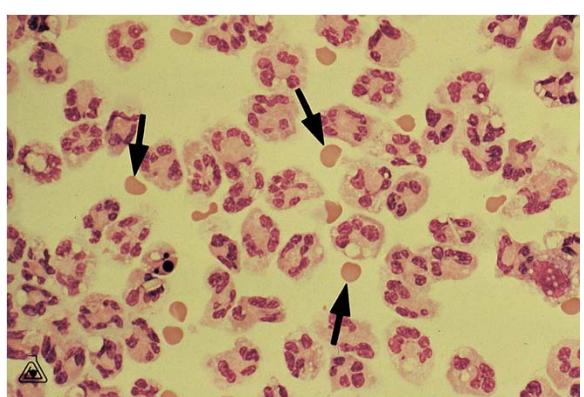
101

 **Neutrophil with Bacteria**



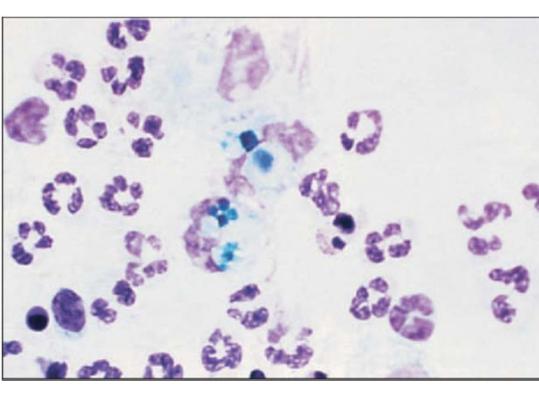
103

 **RBC & Neutrophil**



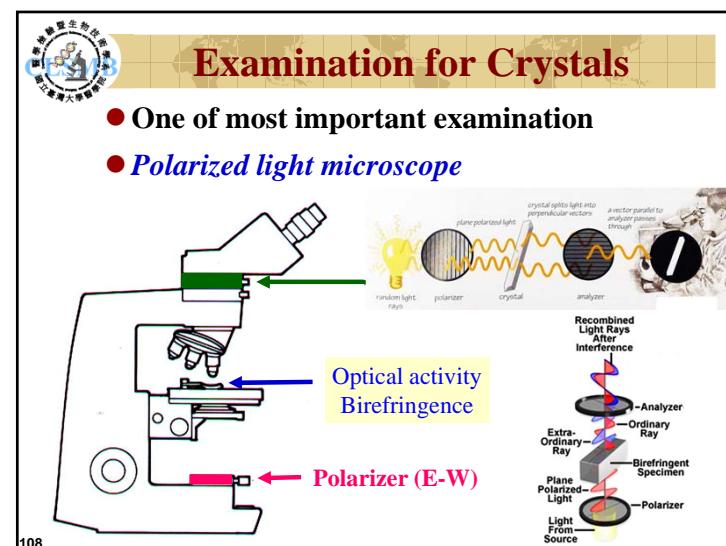
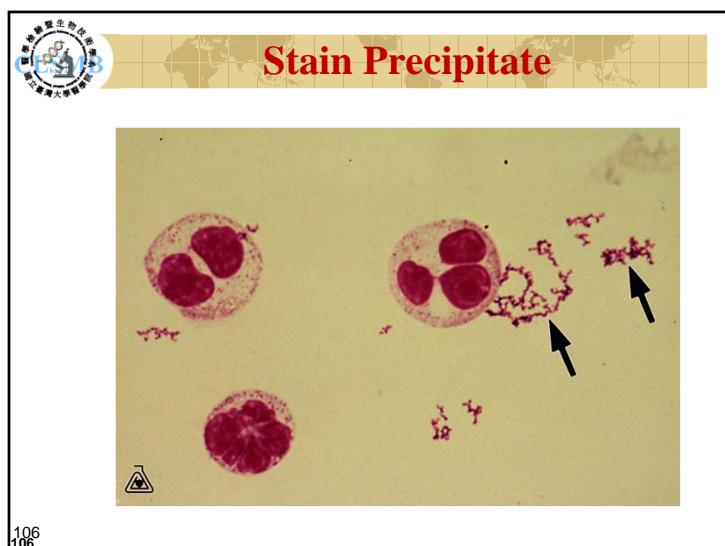
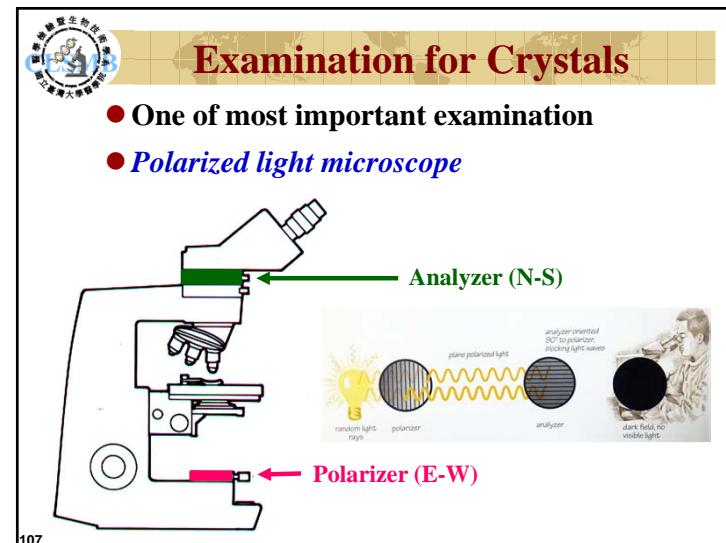
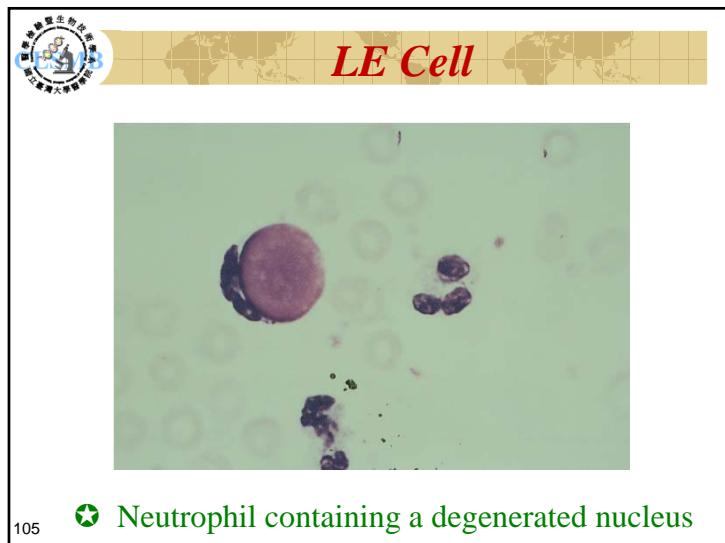
102

 **Reiter's Cell (Neutrophage)**



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✿ Acute phase of reactive arthritis



**CEMB** Examination for Crystals

- One of most important examination
- Polarized light microscope

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**CEMB** Gout by Endogenous Crystals

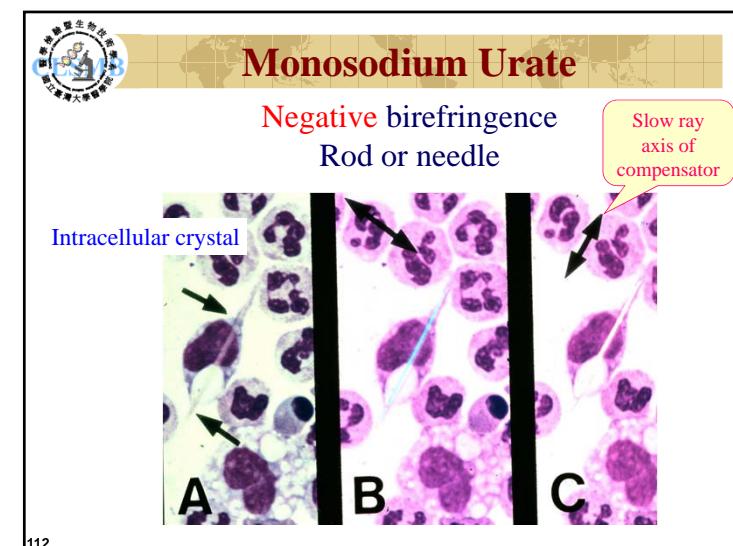
Clinical condition	Crystal
Urate gout*	Monosodium urate monohydrate
Pyrophosphate gout*	Calcium pyrophosphate dihydrate
Apatite gout	Basic calcium phosphate
Lipid gout	Lipid
Oxalate gout	Calcium oxalate monohydrate
	Calcium oxalate dihydrate

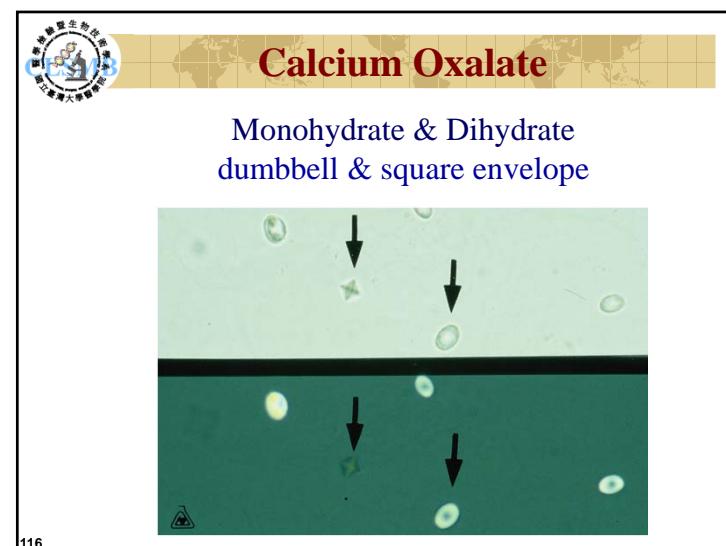
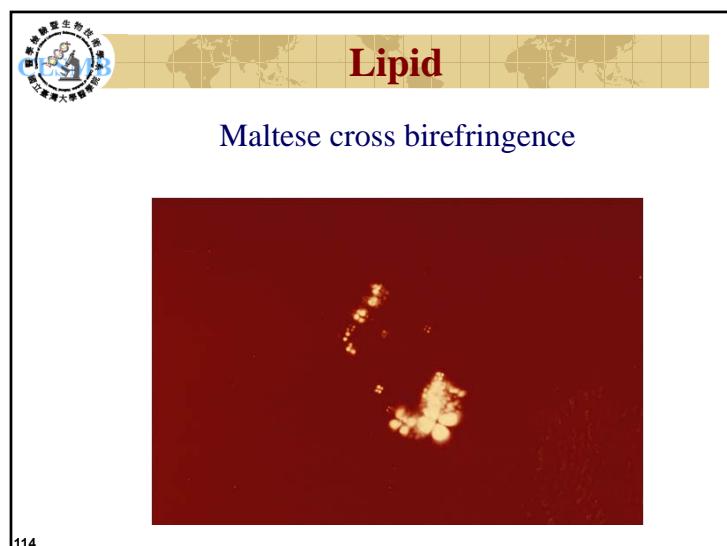
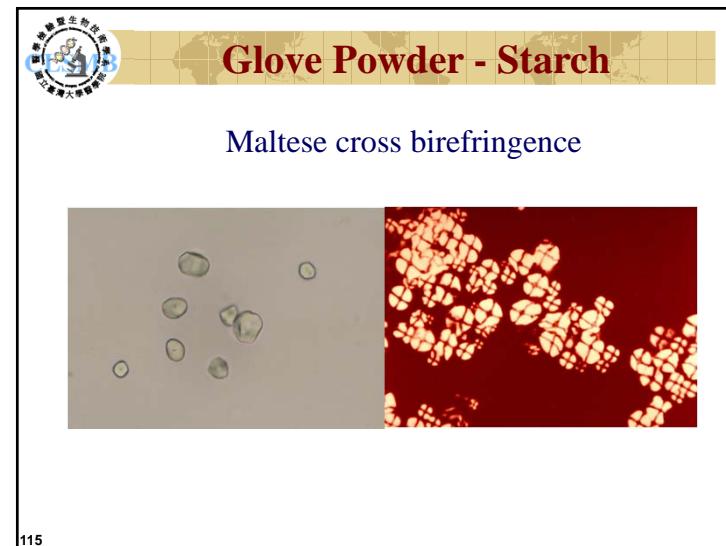
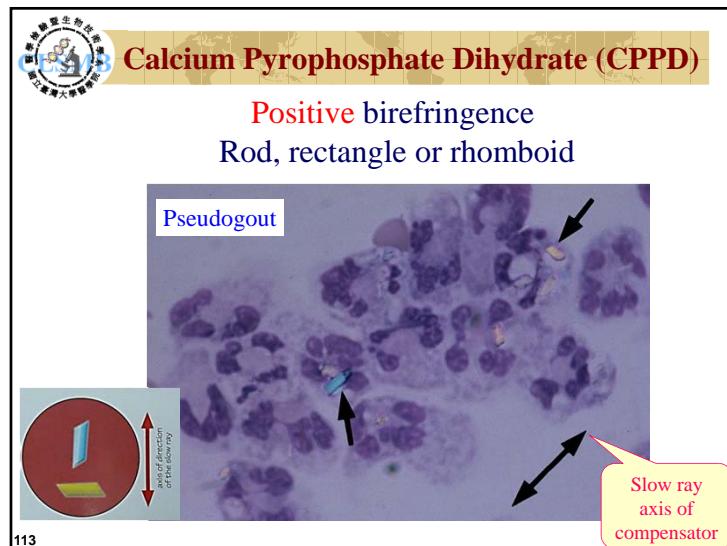
111

**CEMB** Crystals in Synovial Fluid

- Exogenous
  - Glove powder
  - Corticosteroid preparation
- Endogenous
  - Monosodium urate (MSU)
  - Calcium pyrophosphate dihydrate (CPPD)
  - Cholesterol
  - Lipid

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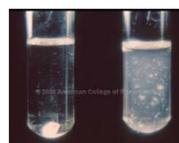
 **Hydroxyapatite**

- **Endogenous crystal**
  - Basic calcium phosphate
  - $$[(\text{Ca})_{10}(\text{PO}_4)_6(\text{OH})_2]$$
  - Non-birefringent
  - Clump as spherical microaggregate

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 **Chemical Analysis**

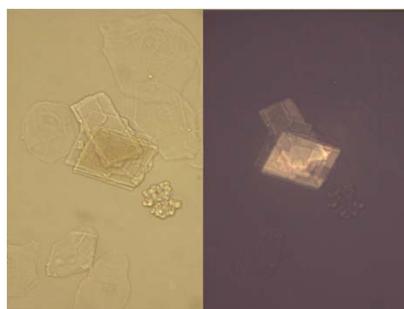
- **Mucin clot test or Ropes test**
  - Several drops of SF
  - Add into 20 mL 5% acetic acid
  - Mucin clot forming within 1 min
  - Shake to determine friability
  - Report: good, fair, poor

④ *Depolymerization of hyaluronic acid in inflammatory arthritis* 

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 **Cholesterol**

- Plate with notched corner
- Birefringence
- \**Old chronic effusion*



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 **Chemical Analysis**

- **Glucose**
  - Test within 1 hr or add NaF
  - 0-10 mg/dL lower than plasma glucose
  - Correlates inversely with cell count
  - Decrease:
    - Glucose < 40 mg/dL
    - >10 mg/dL lower than plasma glucose

④ *Bacterial, rheumatoid or gout arthritis (non-specific)*

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## Chemical Analysis

- Protein

- 1~3 g/dL (1/4 ~ 1/2 of serum)
- 55~70% albumin
- Inflammation
  - Increased vascular permeability
- Immunoglobulin synthesis

⌚ Rheumatoid, gout or septic arthritis

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## Immunological Studies

- Lyme disease: antibodies against *Borrelia spp.*
- Immunoglobulin
- Rheumatoid factor
- Antinuclear antibody
- Complement measurement
- ⌚ Rheumatoid arthritis, SLE



## Chemical Analysis

- Lactate

- Increased in septic arthritis or due to anaerobic glycolysis
- Associated with severe inflammatory diseases

⌚ Rheumatoid arthritis

- Uric acid

- Gout

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## Microbiologic Studies

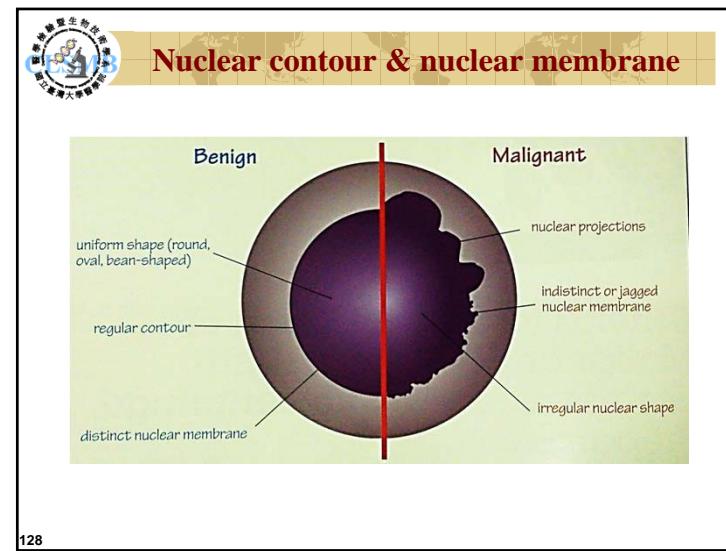
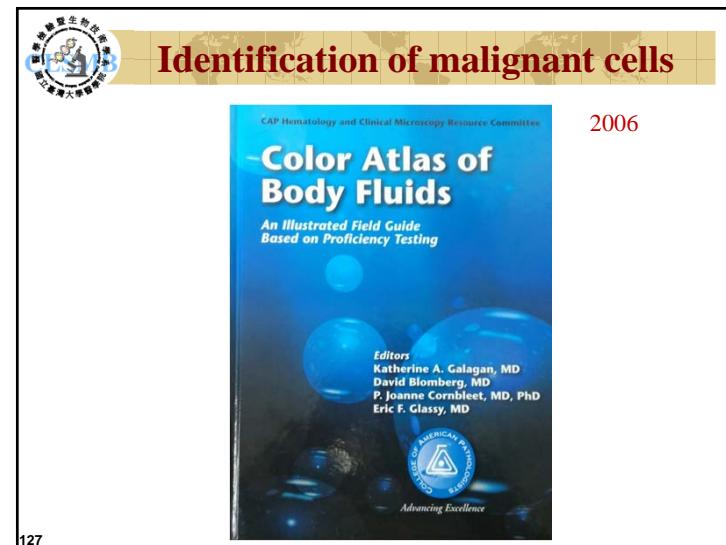
- Gram stain
- Acid fast stain
- SF culture: aerobic & anaerobic
  - *Gonococcus*
  - *Staphylococcus*
  - Tuberculosis
- ⌚ From blood stream

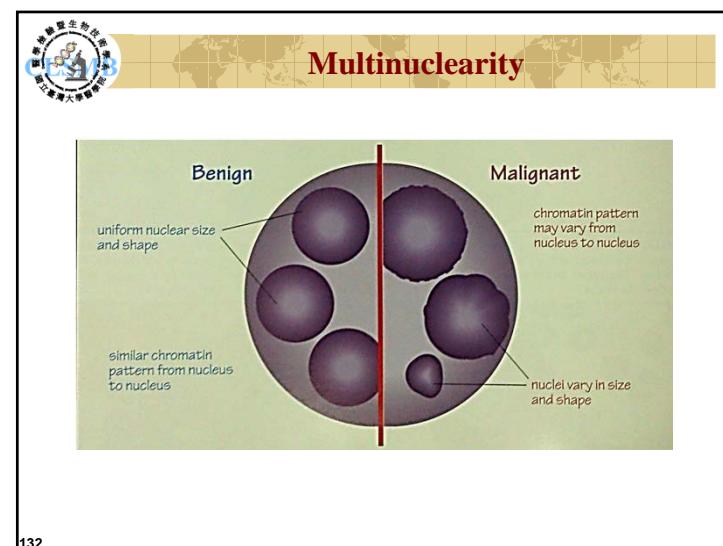
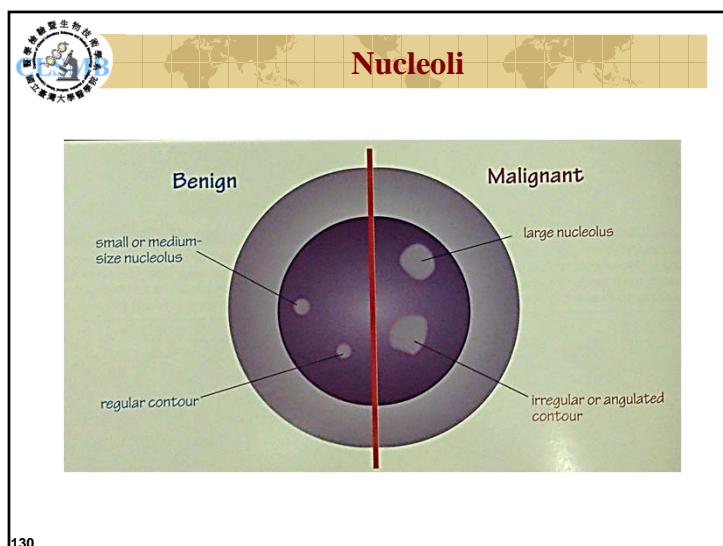
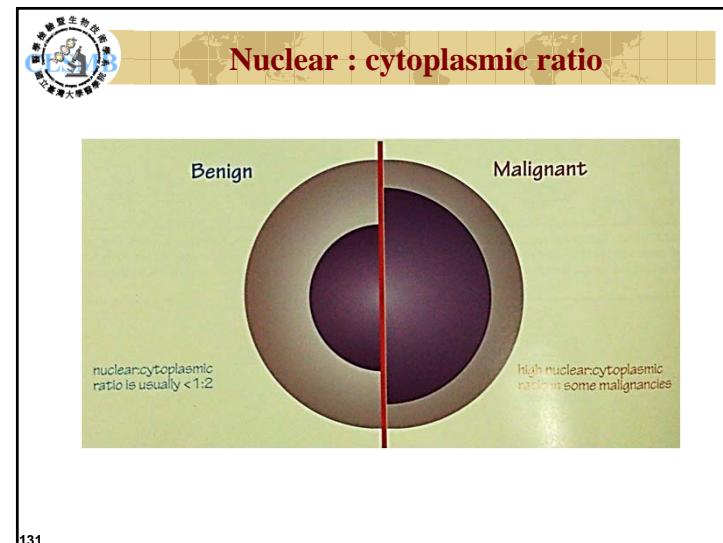
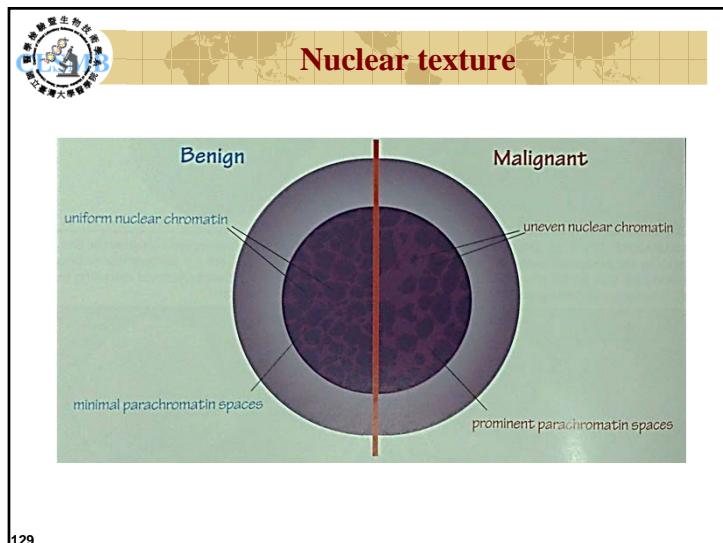
124

 Reference Intervals

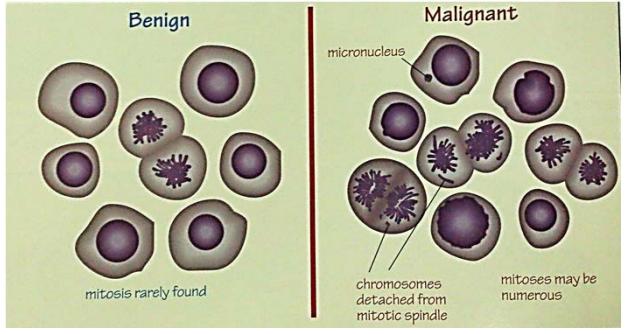
Component	Values
Volume	< 3.5 mL
Viscosity	High
Fibrin clot	Absent
Mucin clot	Abundant
WBC	< 200 cells/ $\mu$ L
Differential cell count	Granulocytes < 25%
Serum-SF glucose difference	< 10 mg/dL

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 **Mitotic cells**

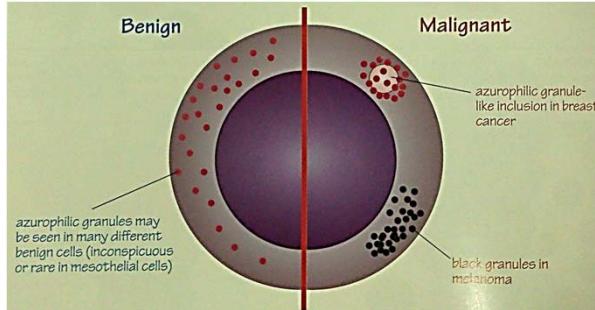


**Benign**  
mitosis rarely found

**Malignant**  
micronucleus  
chromosomes detached from mitotic spindle  
mitoses may be numerous

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 **Cytoplasmic granules**

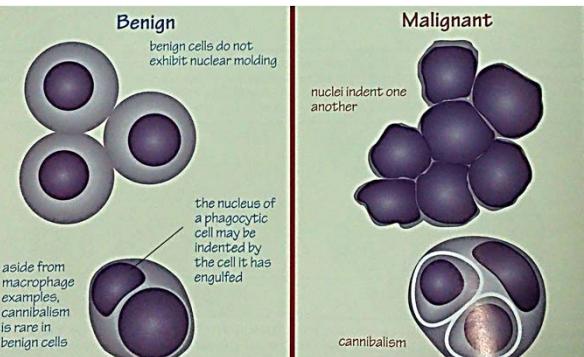


**Benign**  
azurophilic granules may be seen in many different benign cells (inconspicuous or rare in mesothelial cells)

**Malignant**  
azurophilic granule-like inclusion in breast cancer  
black granules in melanoma

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 **Nuclear molding and cannibalism**

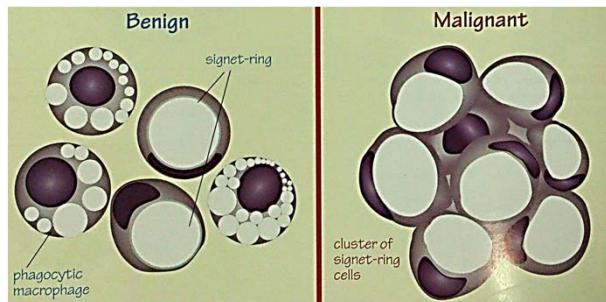


**Benign**  
benign cells do not exhibit nuclear molding

**Malignant**  
nuclei indent one another  
cannibalism  
the nucleus of a phagocytic cell may be indented by the cell it has engulfed  
aside from macrophage examples, cannibalism is rare in benign cells

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 **Signet-ring cells**



**Benign**  
signet-ring  
phagocytic macrophage

**Malignant**  
cluster of signet-ring cells

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