

# HELLP

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Odense University Hospital  
Denmark  
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# Case History

- **26-year-old, GA 39 weeks**
- **Unwell last week, coughing**
- **Spontaneous vaginal delivery**
- **PPH 1 Liter, retained products removed after 1 hour**
- **Some hours later:**
  - **Chest pain and partial hemiparesis**
  - **Appeared confuse, BP 150/109, HR 109/min**
  - **Hb 3.8 mmol/L = (6.1 g/dL)**
  - **LDH 2226 U/L**
  - **AST 156 U/L**
  - **Platelets  $12 \times 10^9/L$**

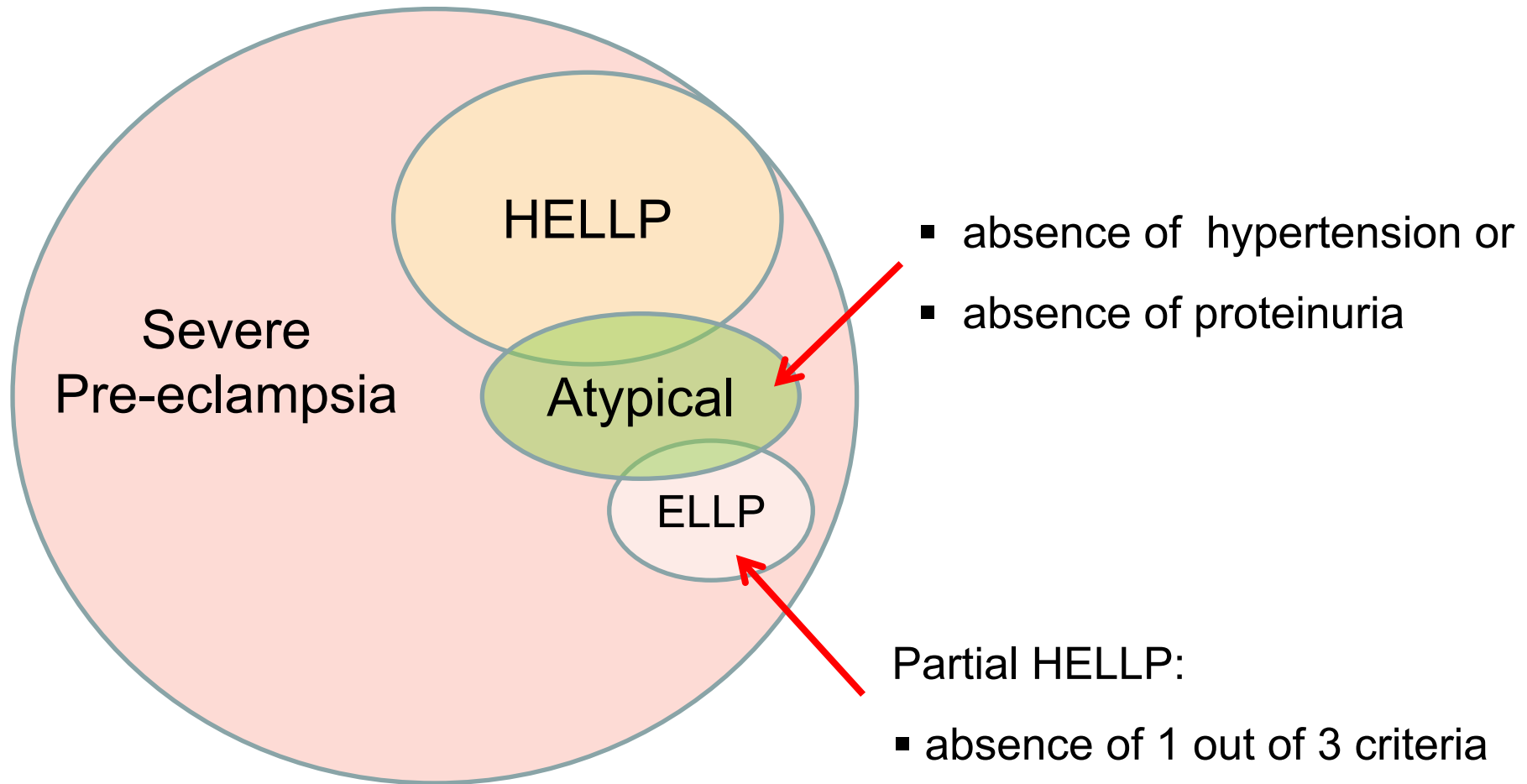


- **H**emolysis
- **E**levated **L**iver enzymes
- **L**ow **P**latelets

# Diagnostic Criteria

	Mississippi			Tennessee
<b>Hemolysis</b>	Microangiopathic hemolytic anemia: <ul style="list-style-type: none"> <li>➤ Fragmented red cells on blood smear</li> <li>➤ S-Bilirubin <math>\geq 1,2</math> mg/dL (<math>\geq 20.5</math> <math>\mu\text{mol/L}</math>)</li> <li>➤ S-Haptoglobin <math>\leq 25</math> mg/dL (<math>\leq 2,5</math> <math>\mu\text{mol/L}</math>)</li> </ul>			
	LDH $\geq 600$ U/L			
	Class 1	Class 2	Class 3	
<b>Elevated Liver Enzymes</b> AST (U/L)	$\geq 70$	$\geq 70$	$\geq 40$	$\geq 70$
<b>Low Platelets</b> ( $10^9/\text{L}$ )	$\leq 50$	51-100	100 - 150	$\leq 100$

# A form of severe pre-eclampsia

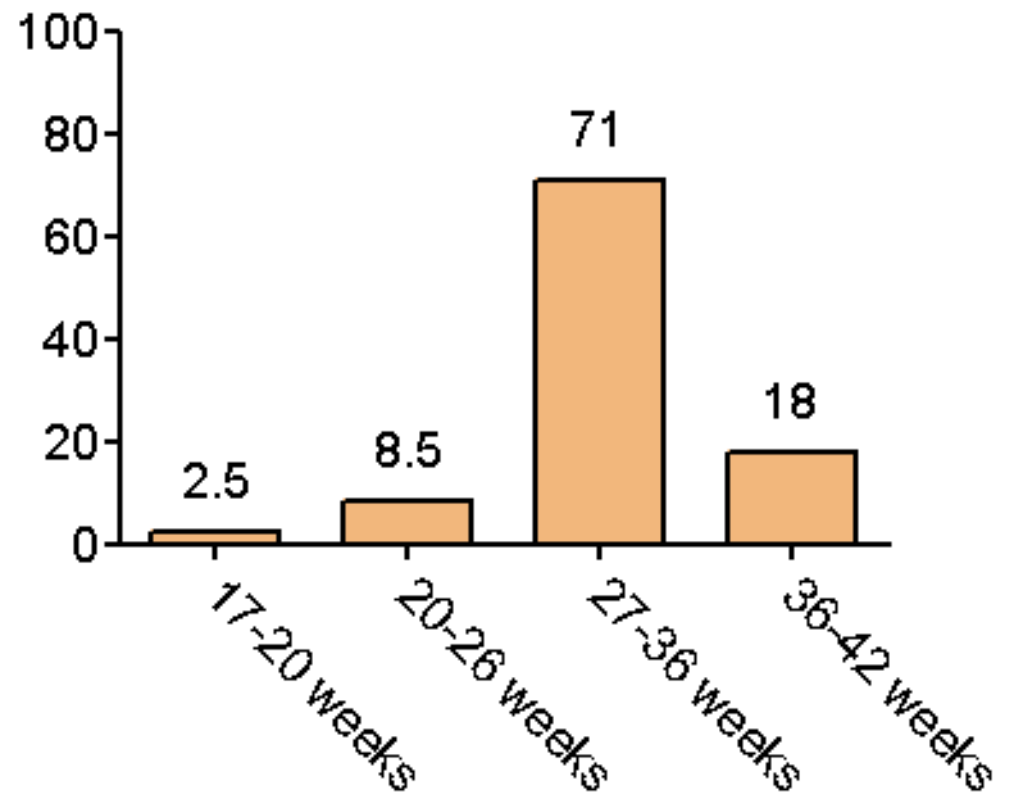
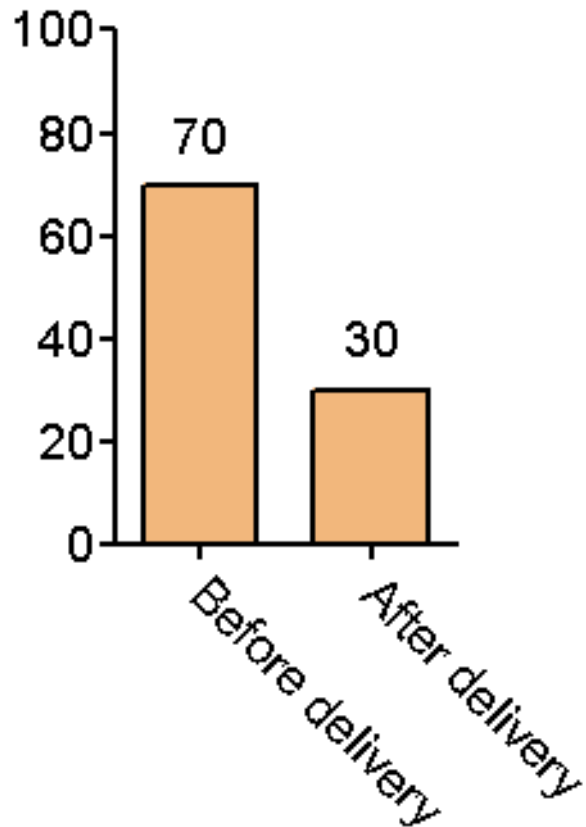


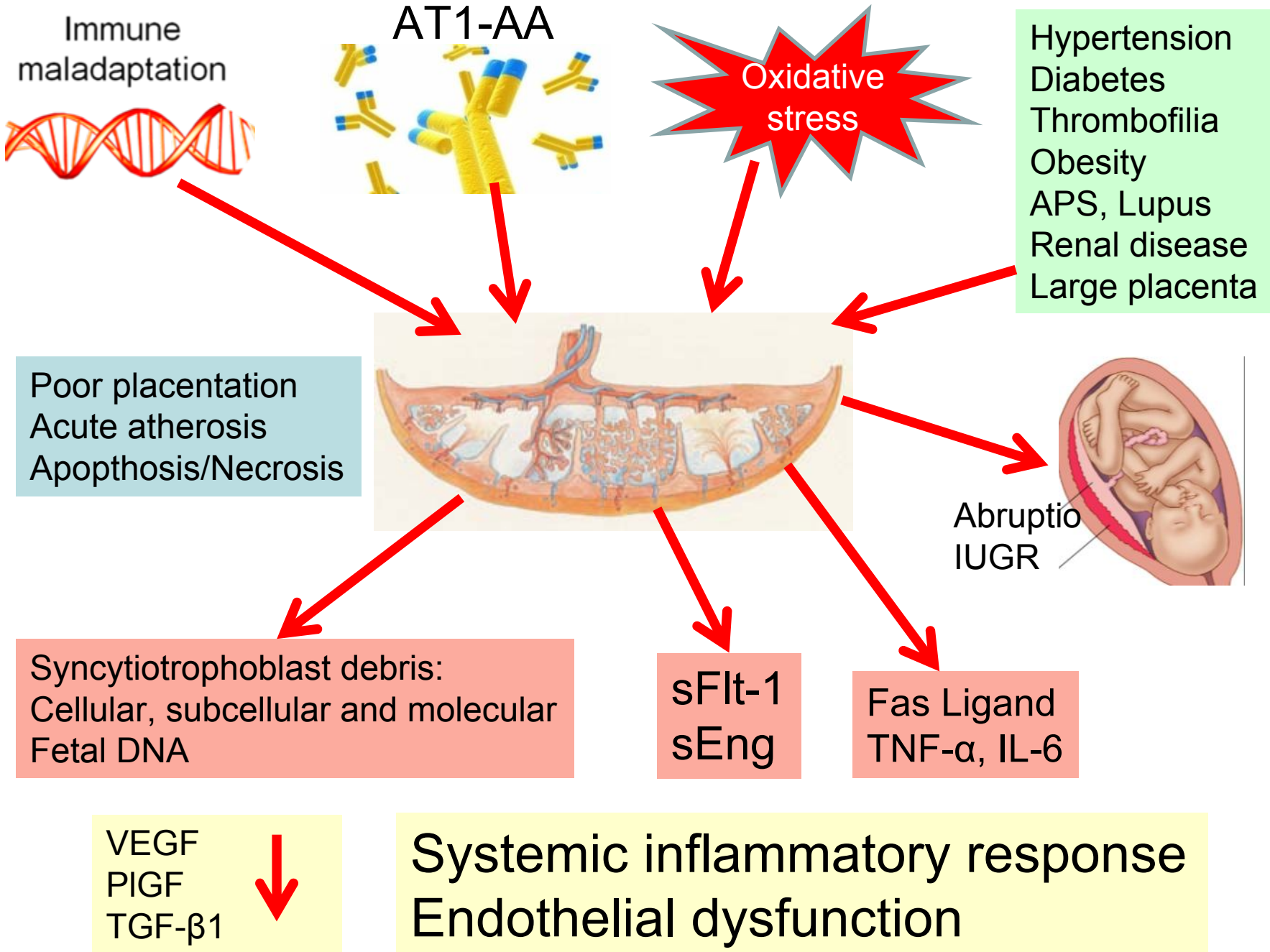
# Signs & Symptoms

Hypertension and proteinuria	80-85%
Right upper quadrant/epigastric pain	40-90%
Nausea /Vomiting	29-84%
Headache	33-61%
Visual changes	10-20%
Jaundice	5%

# Onset

Percentage of women (%)

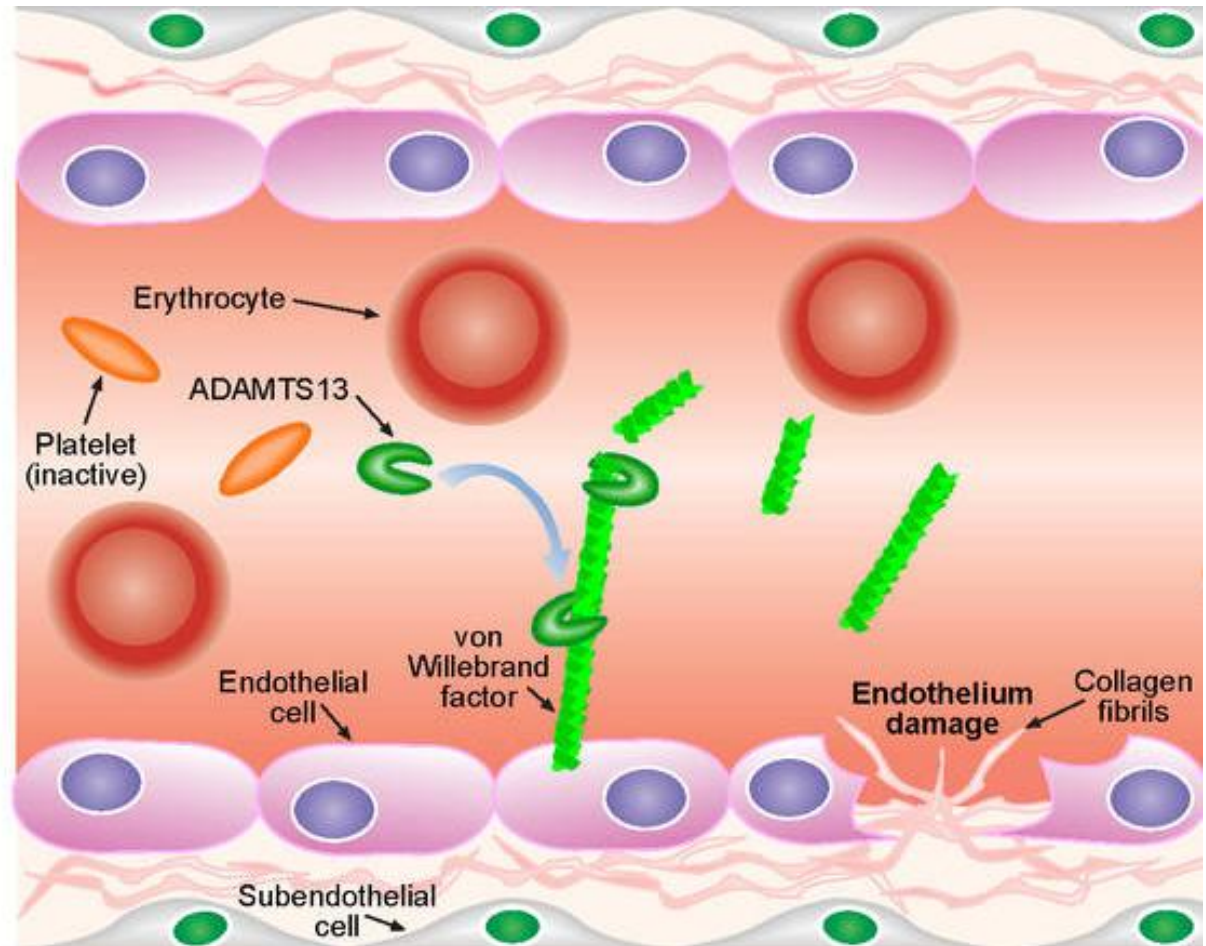






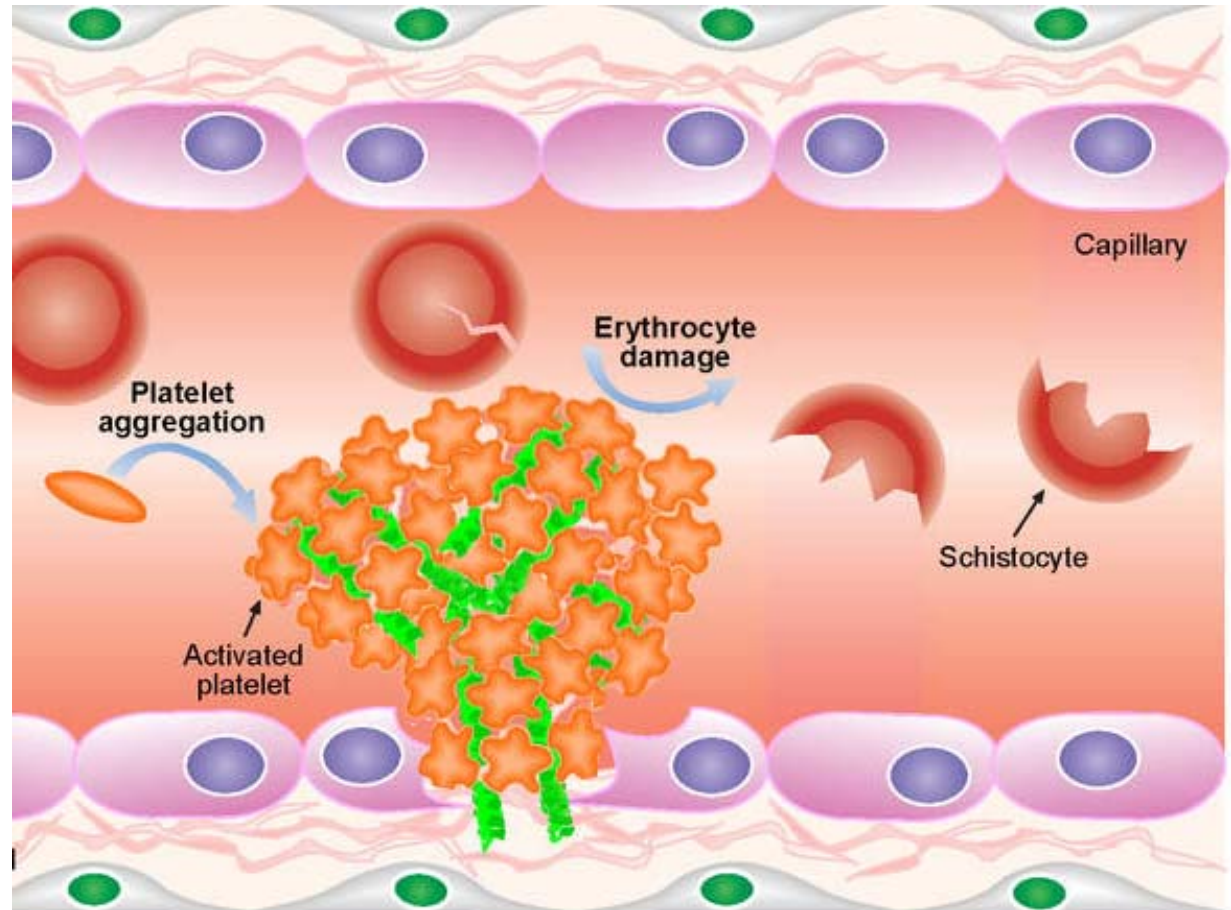
# Patophysiology

- Endothelial damage
- Platelet activation
- vWf ↑↑↑



# Patophysiology

- Reduced ADAM-TS13 activity
- Thrombotic micro-angiopathy
- Schistocytes

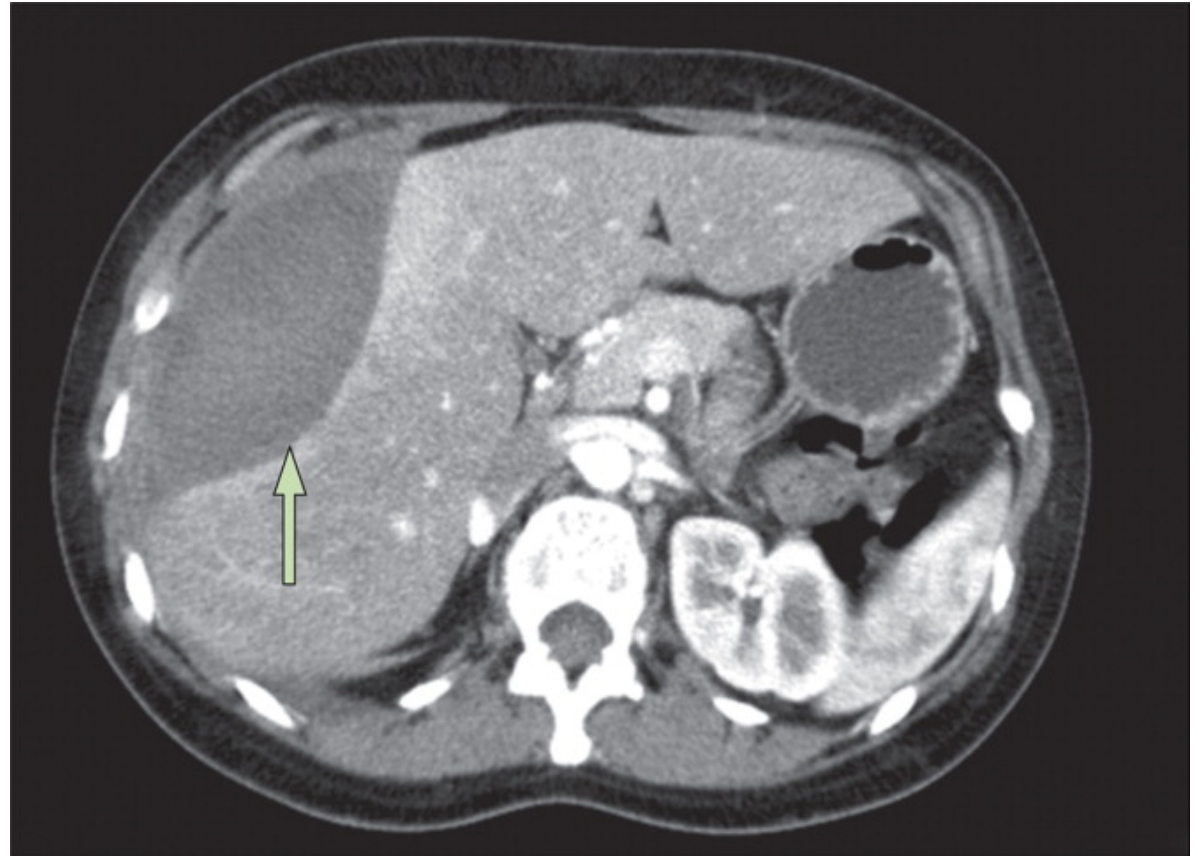


# Liver affection in HELLP

Periportal  
necrosis, &  
hemorrhage

Hematoma -1%

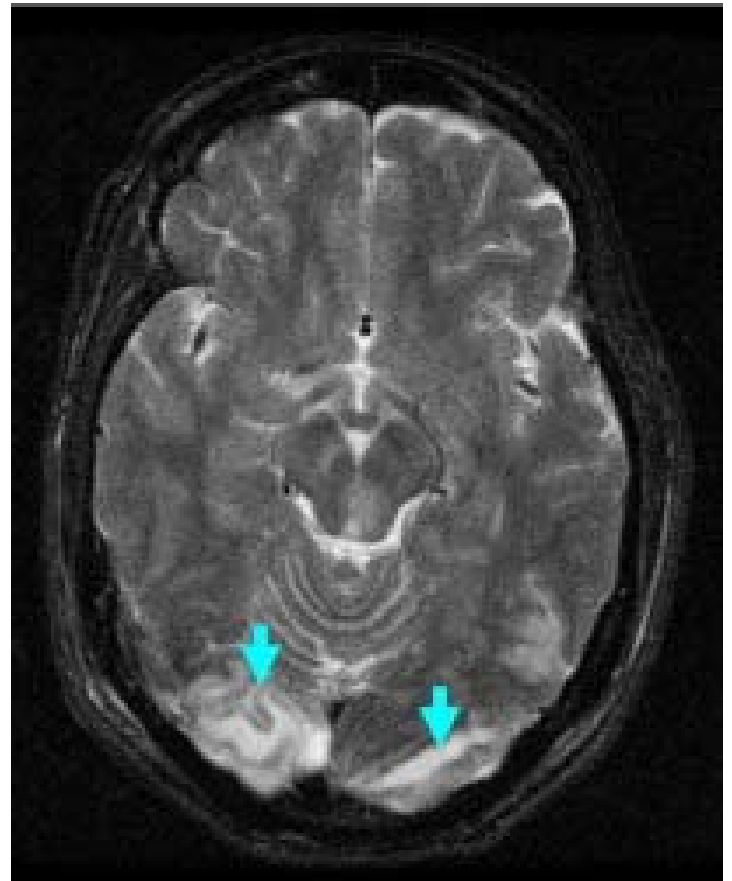
Rupture



# PRES

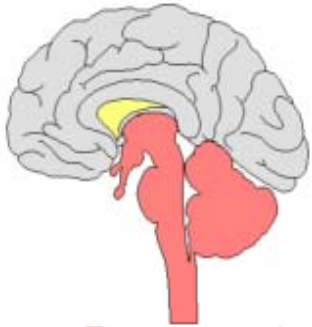
## Posterior Reversible Encephalopathy Syndrome

- Cerebral vasogenic edema
- Headache
- Altered consciousness
- Visual abnormalities
  - Blurred vision
  - **Cortical Blindness**
- Seizures (Eclampsia)



T2-weighted MRI

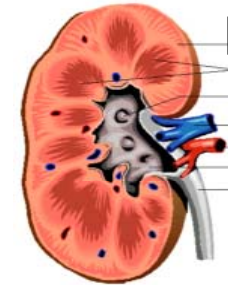
# Other Complications



Hemorrhage  
Infarction



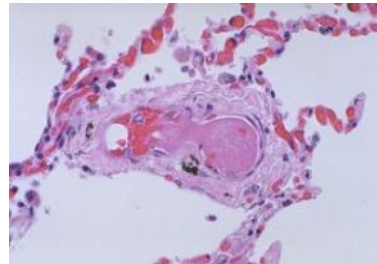
Detach-  
ment



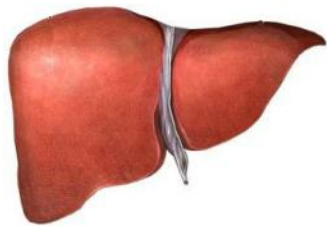
Failure - 8%



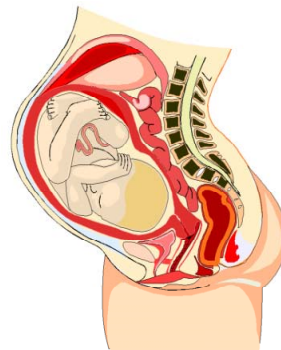
Edema - 6%  
ARDS - 1%  
Effusion - 6%



DIC - 21%  
MOF



Failure  
Ascites - 8%



Abruptio - 16%  
Fetal death  
Hemorrhage

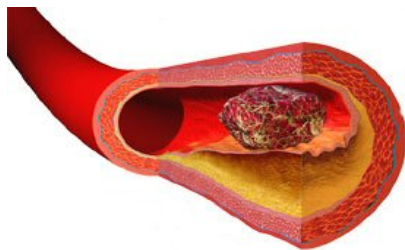
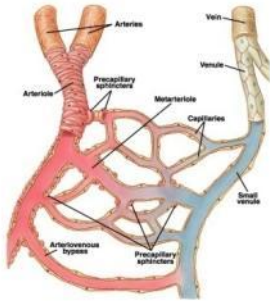
# Management

Timing of delivery	<ul style="list-style-type: none"><li>▪ Prompt delivery: GA &gt;34 weeks, non-reassuring fetal status, severe maternal disease</li><li>▪ Expectant management may be considered at GA 24-34 weeks.</li></ul>
BP	Aim: Systolic < 150, Diastolic 80-100 mmHg
MgSO <sub>4</sub>	During the stabilization period and 24-48 h after delivery
Platelets	Transfusion trigger: <ul style="list-style-type: none"><li>• &lt; 20 x 10<sup>9</sup>/L</li><li>• &lt; 50 x 10<sup>9</sup>/L if rapidly falling or coagulopathy</li></ul>
Fluid therapy	Restrictive
Corticosteroids	On fetal indication
Plasma exchange	Progressive HELLP unresponsive to traditional therapy

# Expectant management before 34 weeks gestation

	Visser (n=128)	van Pampus (n=41)
Intervention	Vasodil + Volume No corticosteroids	Magnesium + Corticosteroids on fetal indication
Median prolongation (d)	15 (in 106 pts.)	3 (in 27 pts.)
Complete reversal of laboratory abnormalities	43%	37%
Fetal deaths	9%	24%

# MgSO<sub>4</sub>

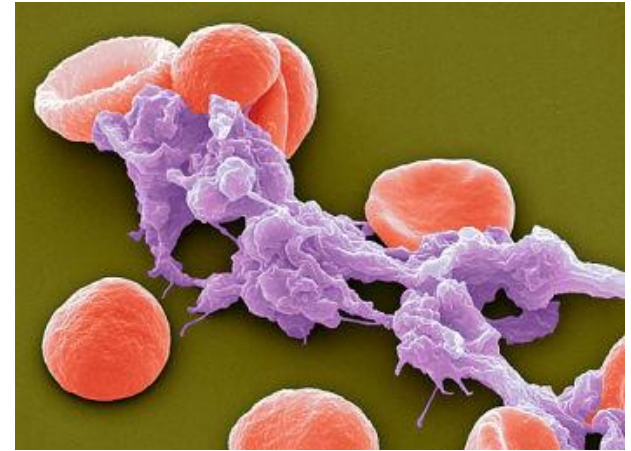


- CNS
  - Anticonvulsive
- Endothelium
  - Vasodilating
  - ❖ Up-regulates proteolysis of vWf
  - ❖ Reduces platelet aggregation
  - ❖ Increases placental VEGF



# Platelet transfusion trigger

- Platelet count  $< 40 \times 10^9/L$  → PPH ↑↑
- Transfusion trigger:
  - $50 \times 10^9/L$  → Delayed recovery
  - $40 \times 10^9/L$  → No effect on PPH incidence
- Prophylactic transfusion :
  - $< 20 \times 10^9/L$
  - $< 50 \times 10^9/L$  and rapidly falling or coagulopathy



# Fluid Therapy

- Limit iv fluids to 80 ml/h  
+ abnormal losses
  - Level 3 evidence


	<b>Restrictive (n=472)</b>	<b>Liberal (n=408)</b>
Pulm. edema	0	19
Renal failure	2	1



# The Dexamethasone Controversy



BM Sibai - Cincinnati  
Remains experimental



JN Martin Jr. - Mississippi

Ante-partum: 10 mg iv. every 12 h  
Post-partum: 10+10+5+5 mg

# Plasma Exchange

- No RCT's.
- 1 Retrospective study with historic control.
- Shorter stay at ICU.
- Lower mortality.
- Quicker recovery of platelets, LDH and AST.
- May be considered in pt.'s not responding to supportive therapy.
  - Level III evidence

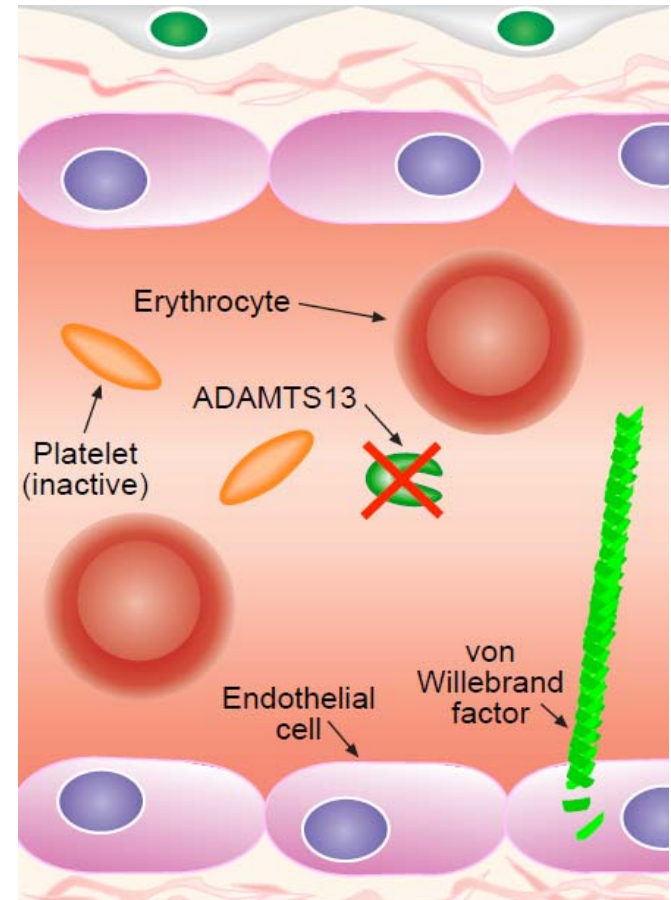


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# TTP

- ADAMTS13 activity ↓ ↓
- Multiorgan thromboses
  - Ischemic sequelae
    - CNS 70-80%
    - Heart – pain, failure
    - Intestines - pain
    - Renal impairment - usually mild
- Petechiae - hemorrhages
- Fever
- Mortality 90% - if untreated

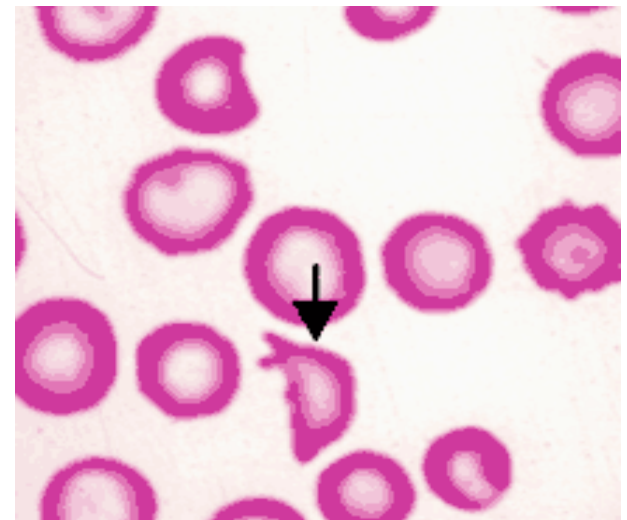


# Case history - Final Outcome

- TTP treated with plasma exchange
  - ADAM-TS 13 <5% of normal
  - No auto-antibodies
- Chronic cardiac failure, EF 50%
  - Normal Coronary angiography
  - ACE inhibitor,  $\alpha$ - and  $\beta$ -receptor blocking agent, aldosteron antagonist and diuretic
- Neurologic sequelae
  - Slight problems with motor function in left hand

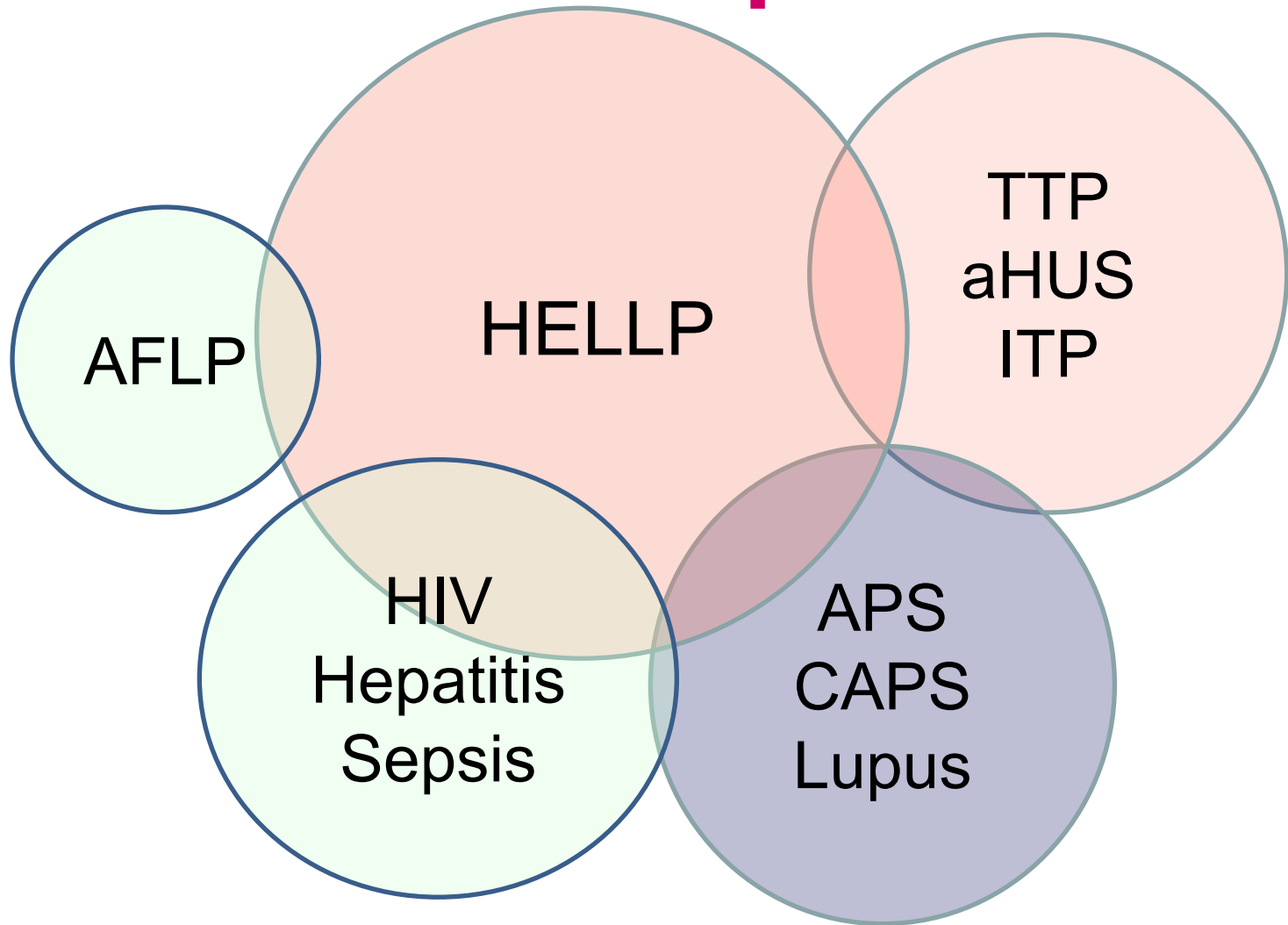
# Suspect TTP

- Platelets  $< 20 \times 10^9/L$
- Schistocytes  $> 1\%$
- Hemoglobin  $< 100 \text{ g/l} \approx$   
 $< 6 \text{ mmol/l}$
- LDH : AST Ratio  $> 25 : 1$
- Troponin ( $\uparrow$  in 50% of pts.)



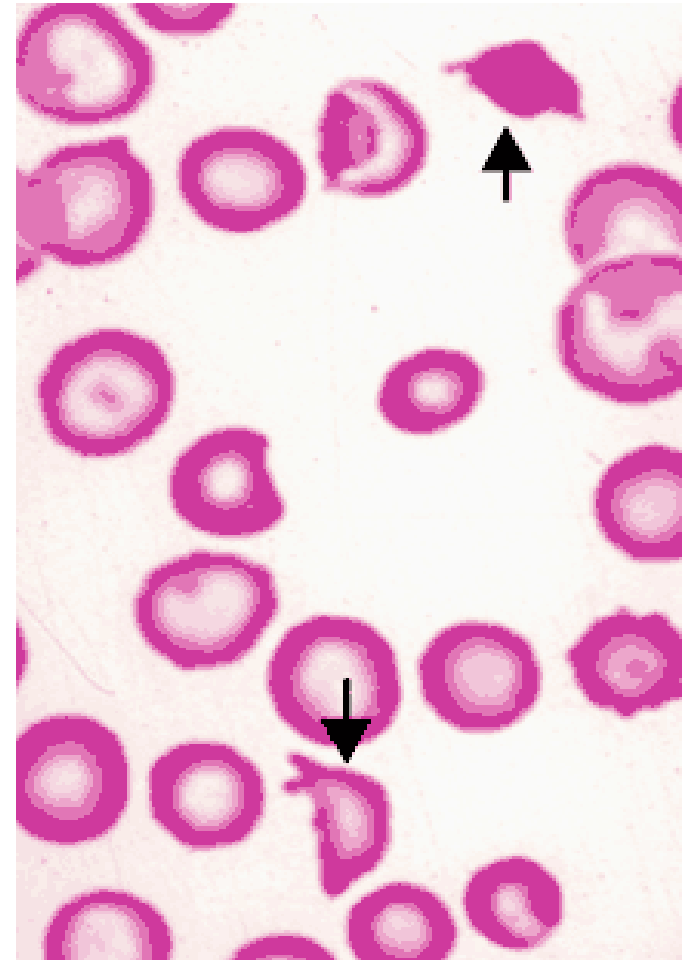


# Differential diagnosis and overlap



# aHUS

- Complement dysregulation
- Triad:
  - Acute renal failure
  - Thrombocytopenia
  - Microangiopathic hemolytic anemia (Coomb negative)



# aPL positive - APS vs. CAPS

Autoimmune disorder, may be associated with SLE and RA

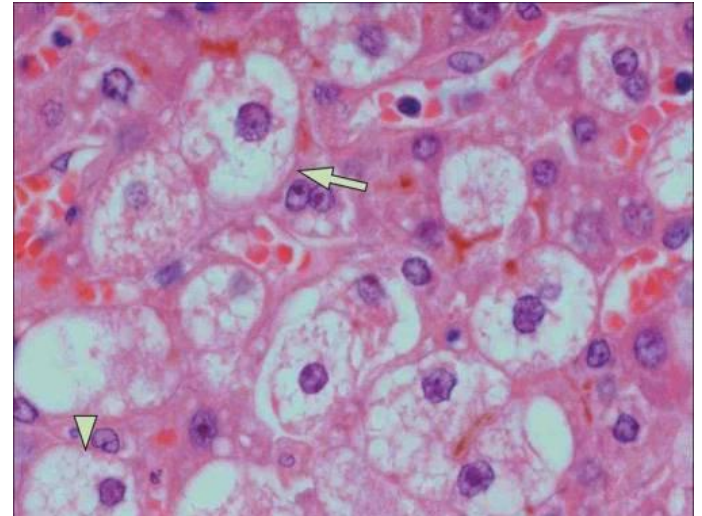
APS Antiphospholipid Syndrome	CAPS Catastrophic APS
Venous and/or arterial thromboses	Microvascular thromboses
Recurrent abortions, foetal deaths Early onset Pre-eclampsia & HELLP	Thrombotic microangiopathy Trombocytopenia
Sporadic often a single site	Simultaneously in multiple sites
Pregnant pts. with Hepatic infarcts are usually aPL positive	Multiple organ failure Mortality rate 50% ARDS (34%), Stroke (44%)

# SLE flare during Pregnancy

- Rash, arthritis, fever, pleuritis, lymphopenia
- Hemolytic anemia – Coombs positive
- Thrombocytopenia
- Lupus Nephritis
  - Proteinuria
  - Hypertension
- Rising DNA antibodies
- >25% drop in complement levels

# Acute Fatty Liver of Pregnancy

- AFLP
  - Nausea/vomiting
  - Abdominal Pain
  - Jaundice
  - INR and APTT ↑
  - Fibrinogen and P-glucose ↓



# PTMS = Postpartum Thrombotic Microangiopathic Syndrome

- Postpartum progressive HELLP/partial HELLP like presentation unresponsive to traditional therapy
- Thrombotic microangiopathy/DIC with multiorgan injury
- Criteria for TTP, HUS, ITP not fulfilled
- Often responsive to plasma exchange

# Acute Management

HELLP	MgSO <sub>4</sub> , Antihypertensives, Fluid restriction
TTP	FFP, Plasma Exchange, Corticosteroids, MgSO <sub>4</sub> ,
aHUS	Plasma Exchange, Complement C5 inhibitor
CAPS	Plasma Exchange, Corticosteroids, LMWH, ASA, IV Immunoglobulins, Cyclophosphamide, Rituximab
AFLP	FFP, Glucose infusion, Prompt delivery
Sepsis	Meropenem 1 g x 3 + Metronidazole 0,5 g x 3
Lupus flare	Corticosteroids, Asathioprine, Cyclosporine , IV Immunoglobulins
PTMS	Plasma Exchange

# Key Messages

1. Diagnosis and management of HELLP remain controversial
2. Many conditions share a range of signs, symptoms and laboratory tests with HELLP
3. Rapid diagnosis and close consultation with an interdisciplinary team is crucial



Thank you!





# Differential Diagnosis

	MAHA*	Plate-lets. ↓	Coag ↓	BP ↑	Abd	Renal	CNS
HELLP	+	++	+/-	+	+++	+	+
TTP	++	+++	-	+/-	+	++	+++
HUS	+	++	+/-	++	+	+++	+/-
AFLP		+	+++++	+	+++	++	+
SLE	+	+	+/-	+	+/-	++	+
CAPS	+	++	+/-	+/-	+/-	+/-	+/-

MAHA\* **Micro-Angiopathic Haemolytic Anemia**