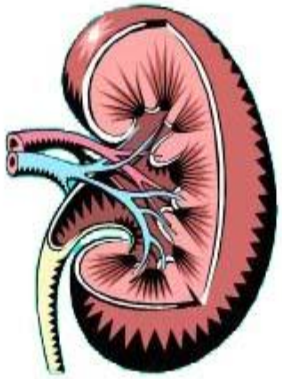
DIFFERENTIATION BETWEEN

TTP and HUS

TTP



HUS

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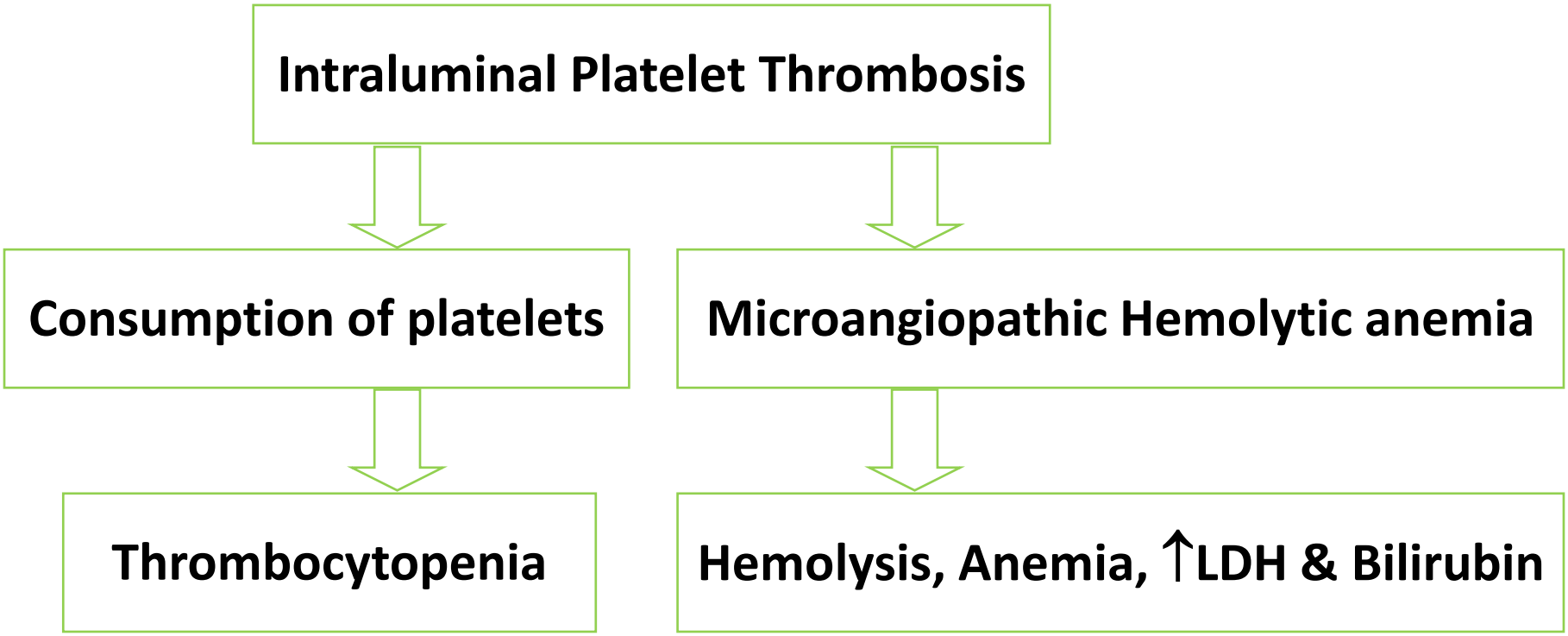
Chittagong Medical College.

What is meant by Thrombotic Microangiopathy (TMA)?

- Thrombotic Microangiopathy (TMA) is a group of disorders characterized by injured endothelial cells, microangiopathic hemolytic anemia (MAHA), with its typical features of thrombocytopenia and schistocytes.

- **Hemolytic Uremic Syndrome(HUS)** & **Thrombotic Thrombocytopenic Purpura (TTP)** are the prototypes for TMA

Mechanism of TMA in TTP-HUS?



Case Senario 1

- A 35-year-old woman presented with an epileptic seizure five days after having a baby by Caesarean section. There was no previous history of epilepsy. She had been well throughout her pregnancy. She had two normal pregnancies without any complication.

  On examination her heart rate was 90 beats/min and regular and her temperature was 100.2^0F. The blood pressure was 180/102 mmHg. She had a Glasgow coma score of 13/15. There was no evidence of a focal neurological deficit. Investigations are shown:

Hb	**10 g/dl**	**Sodium**	**137 mmol/l**
WCC	**11×10^9/l**	**potassium**	**4.6 mmol/l**
Platelets	**45×10^9/l**	**Urea**	**10 mmol/l**
Blood film	**Normochromic normocytic anaemia**	**Creatinine**	**1.9 mg/dl**
	Fragmented red cells;	**Bilirubin**	**1 mg/dl**
	microspherocytes	**AST**	**34 iu/l**
PT	**14 s (control 14 s)**	**LDH**	**1530iu/l(NR 252-525iu/l)**
APTT	**45 s (control 44 s)**	**Alkaline phosphatase**	**80 iu/l**
Factor V level	**Normal**	**Albumin**	**30 g/l**
Factor VII level	**Normal**	**Urinalysis**	**Protein ++**
		CT scan brain	**Normal**

What is the immediate management ?

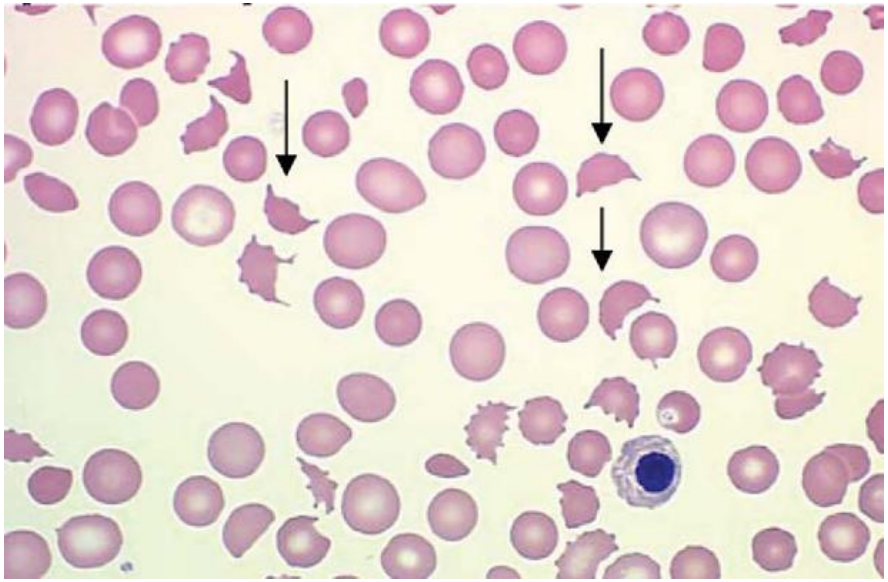
a. **Intravenous high-dose steroids.**
b. **Platelet transfusion.**
c. **Vitamin K.**
d. **Plasma exchange with fresh-frozen plasma.**
e. **Warfarin.**

Case Senario 2

- A 5-year-old male was admitted with a two-day history of blood-stained diarrhea. Three days after, he felt nauseous and generally unwell. On examination he had periorbital oedema and a blood pressure of 150/95mmHg.

Investigations are shown

Hb	**8 g/dl**
WCC	**13×10^9/l**
Platelets	**63×10^9/l**
PT	**13 s (control 13 s)**
APTT	**34 s (Control 36 s)**
Blood film	
Sodium	**138 mmol/l**
Potassium	**5.9 mmol/l**
Creatinine	**130µmol/l**
Urea	**11mmol/l**



What is the diagnosis?

a. Nephrotic syndrome secondary to minimal Change glomerulonephritis.
b. IgA nephritis.
c. Haemolytic uraemic syndrome.
d. Thrombotic thrombocytopenic purpura.
e. Chronic pyelonephritis.

Thrombotic Thrombocytopenic Purpura (TTP)

- Traditionally, TTP is characterized by the pentad:
- MAHA,
- Thrombocytopenia,
- Neurologic symptoms,
- fever, and
- renal failure.
- The pathophysiology of TTP involves the accumulation of utra-large multimers of von Willebrand factors as result of decreased activity of the plasma protease **ADAMTS13**

  (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13)

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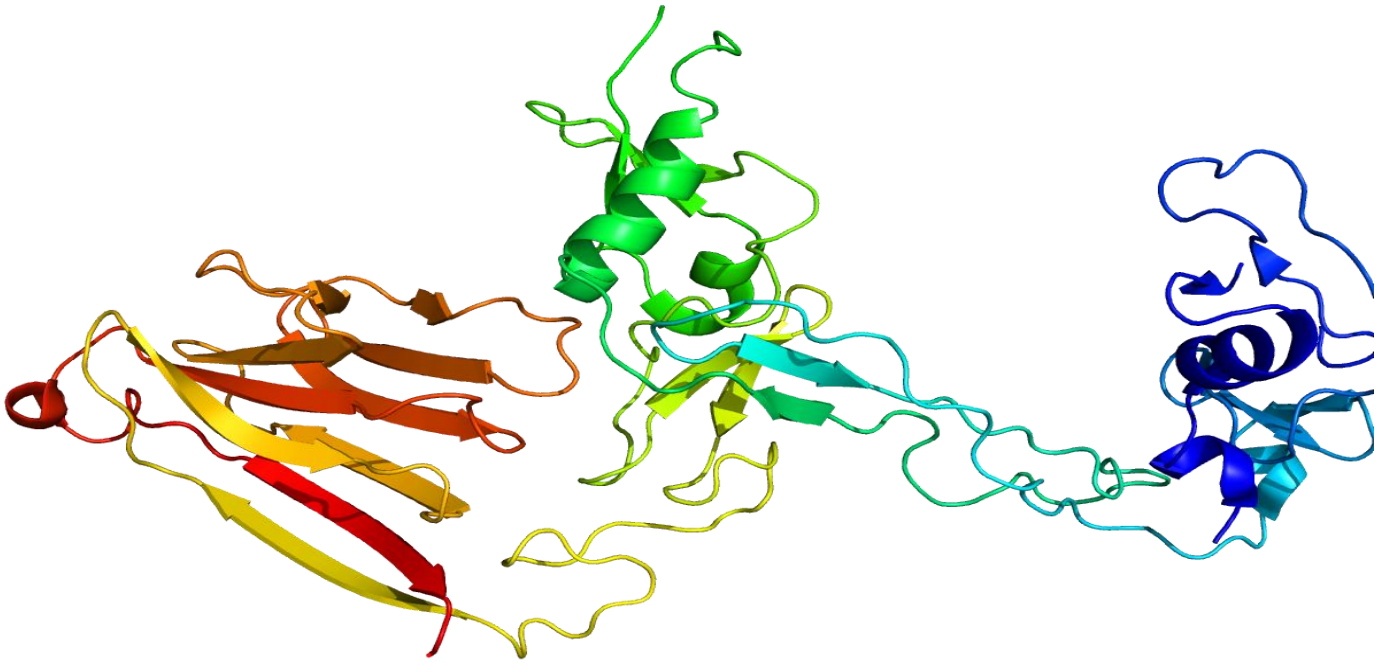
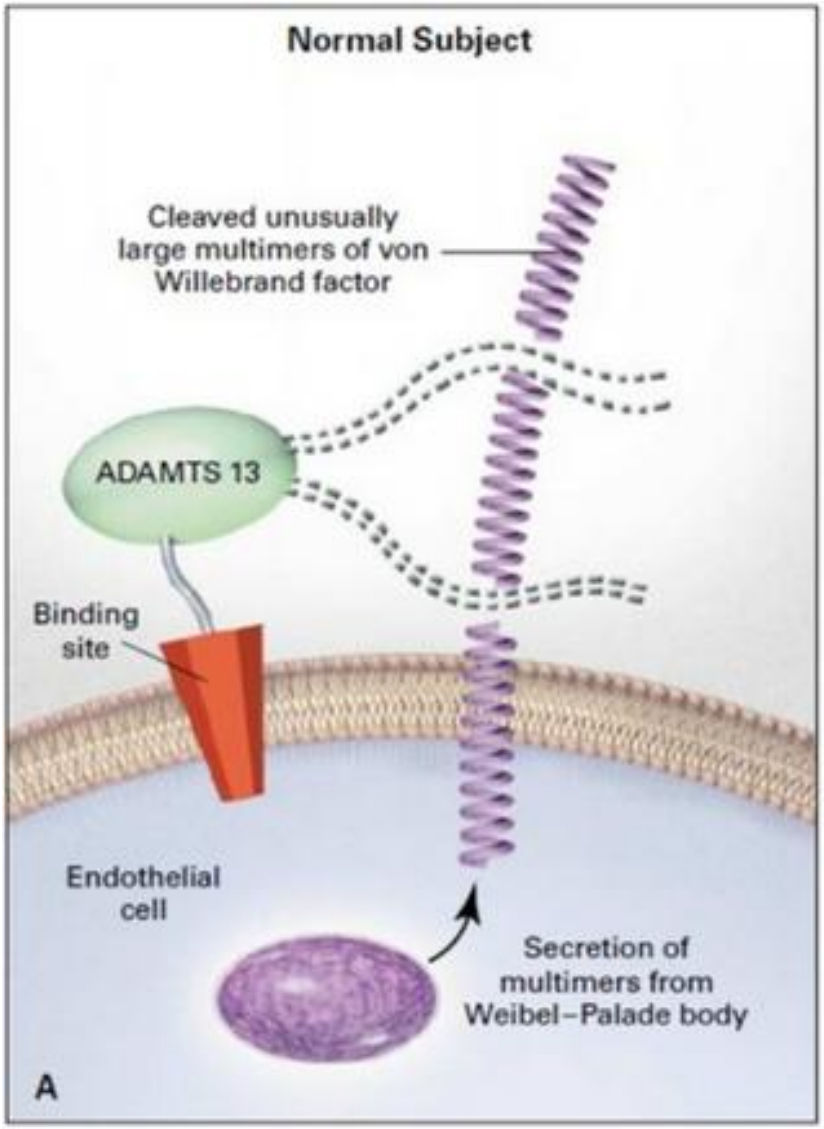
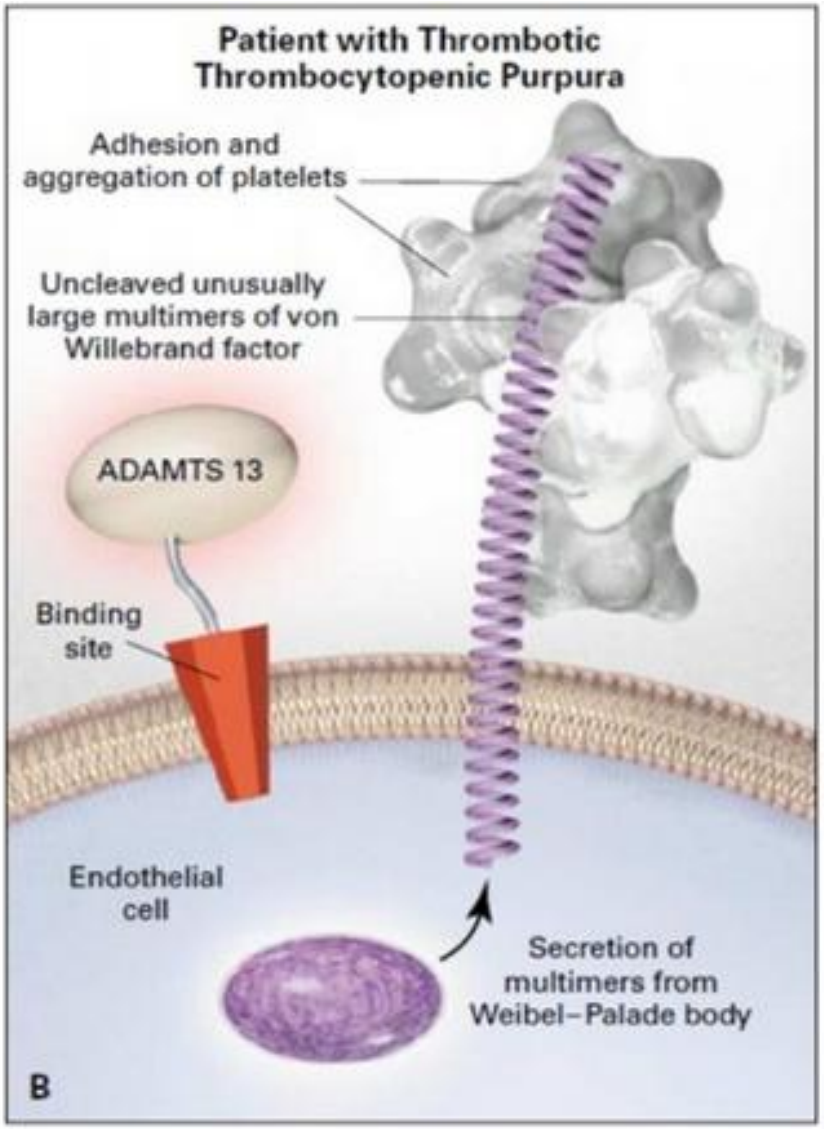
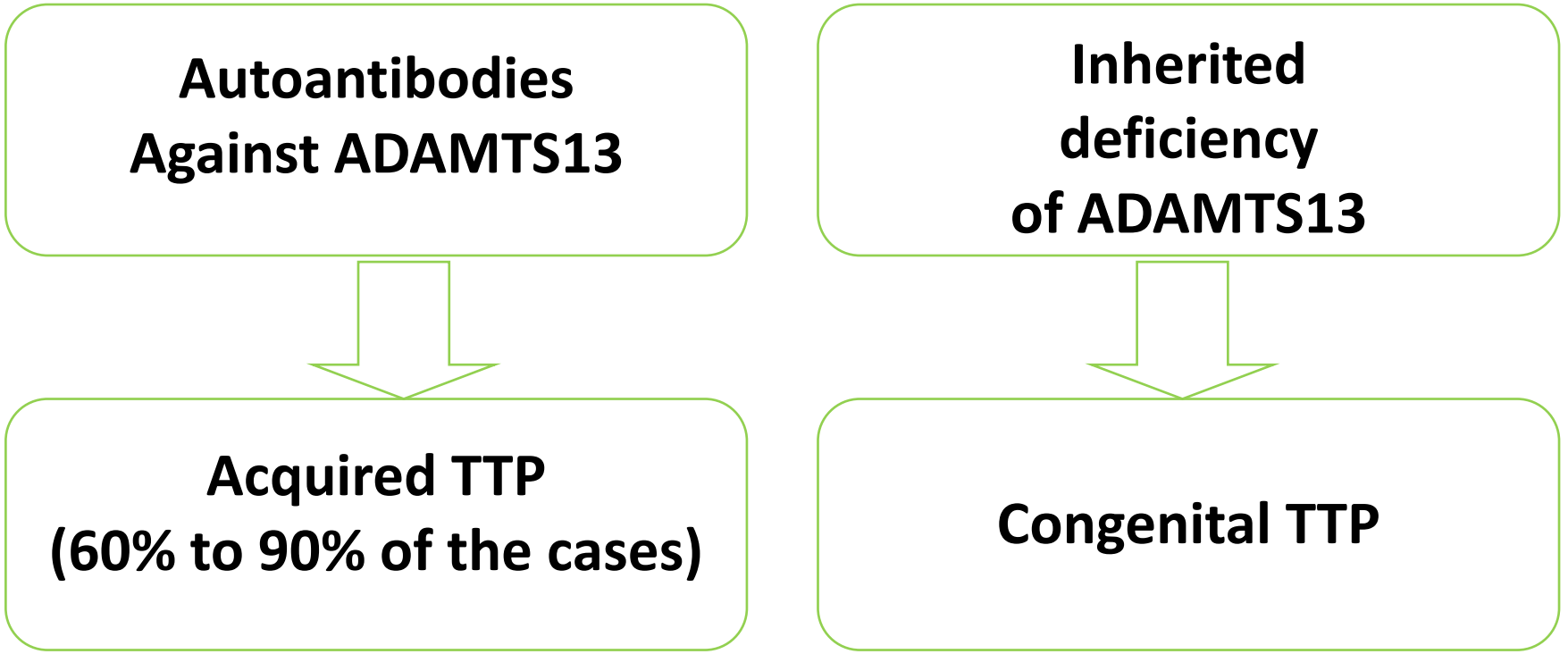


Pathophysiology of TTP





TTP - Classification



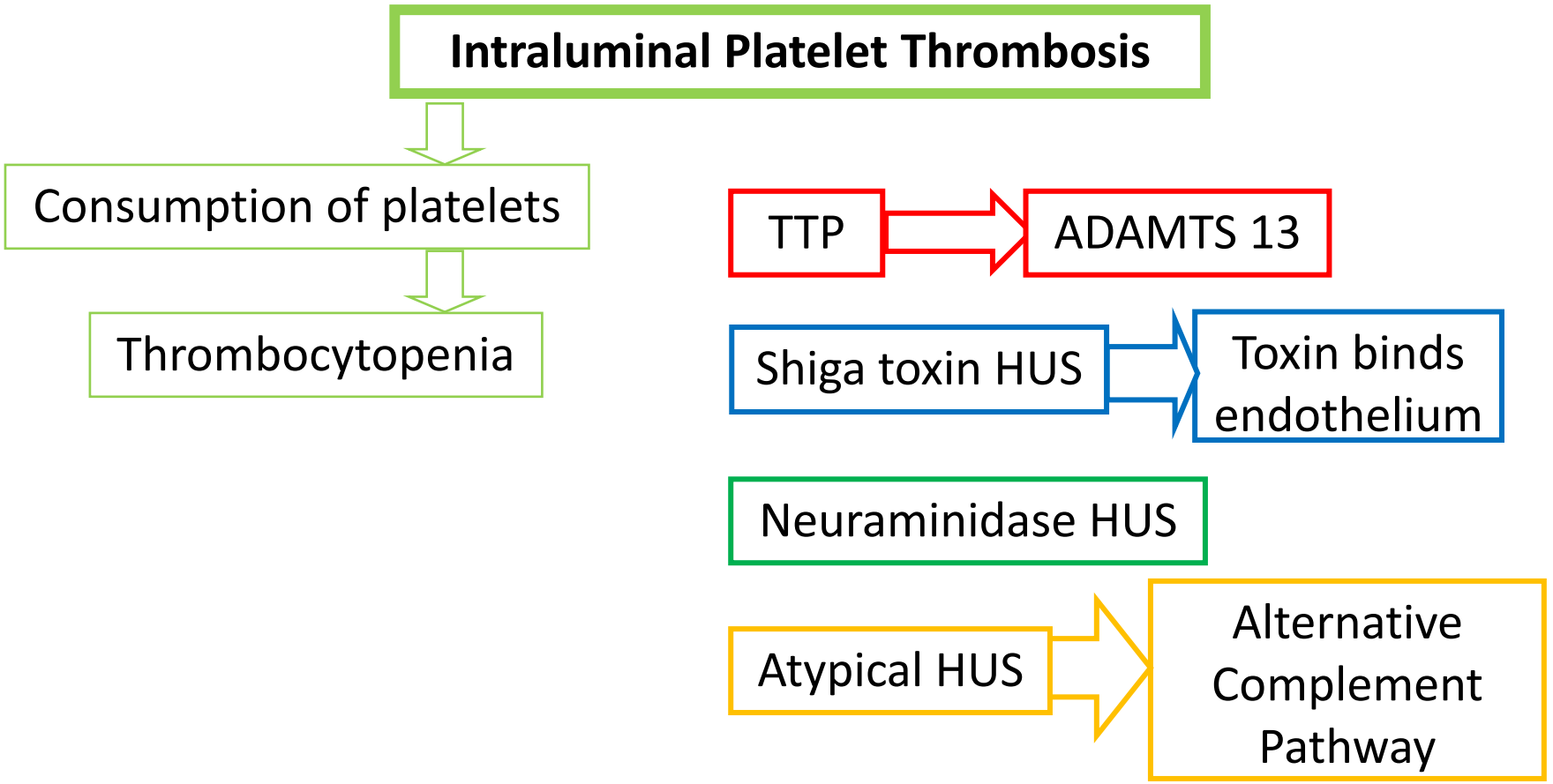
Hemolytic Uremic Syndrome(HUS)

- HUS is loosely defined by the presence of MAHA and renal impairment.
- Most cases involve children <5 years of age, but adults also are susceptible.
- Diarrhea, often bloody, precedes MAHA within 1 week in majority of cases.
- Abdominal pain, cramping, and vomiting are frequent.
- Fever is typically absent.
- Neurologic involvement might occur.

Types of HUS

- **Shiga Toxin Associated HUS**
  - STEC HUS (Shiga Toxin Producing E.coli e,g O157:H7)
  - Shigella Dysenteriae.
- **Neuraminidase Associated HUS**
  - S. pneumoniae
- **Atypical HUS**
  - Factor H deficiency leads to alternative complement pathway activation with↓C3, normalC4,
  - Autoimmune variant

Pathophysiology of TTP-HUS



HUS Versus TTP

HUS	VS	TTP
Usually Children <5 years		Usually Adult
Tetrad		**Pentad**
• MAHA		• MAHA
• Marked renal dysfunction		• Mild renal dysfunction
• Mild to moderate thrombocytopenia		• Marked thrombocytopenia
• Mild CNS dysfunction		• Severe CNS dysfunction
• Fever usually absent		• Fever
History of diarrhea or dysentery present		No history of diarrhea or dysentery

HUS Versus TTP

HUS	VS	TTP
Cause: • Shiga toxin producing E.coli and Shigella dysenteriae. • Neuraminidase producing S. pneumoniae. • Atypical HUS (Complement dysregulation)		**Cause:** • Congenital deficiency or auto anti body to metalloproteinase ADAMTS13.

HUS Versus TTP

Management:

- STEC HUS (Shiga toxin associated): supportive eg, fluid balance, dialysis, blood transfusion,
- Neuraminidase-HUS:
  - Antibiotics and washed red cells.
- Atypical HUS:
  - Eculizumab (A monoclonal ab to C5)
  - Autoimmune variant: Plasmapheresis

Management:

- Plasma exchange or plasmapheresis

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Answer

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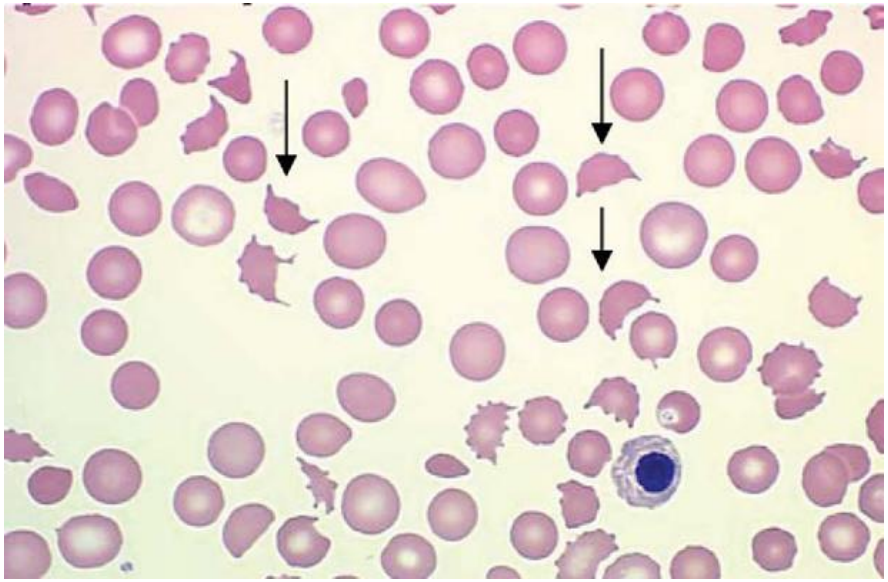

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THANK
YOU