# Chapter 1: Evidence-Based Guidelines on the Diagnosis and Treatment of Acquired Thrombotic Thrombocytopenic Purpura

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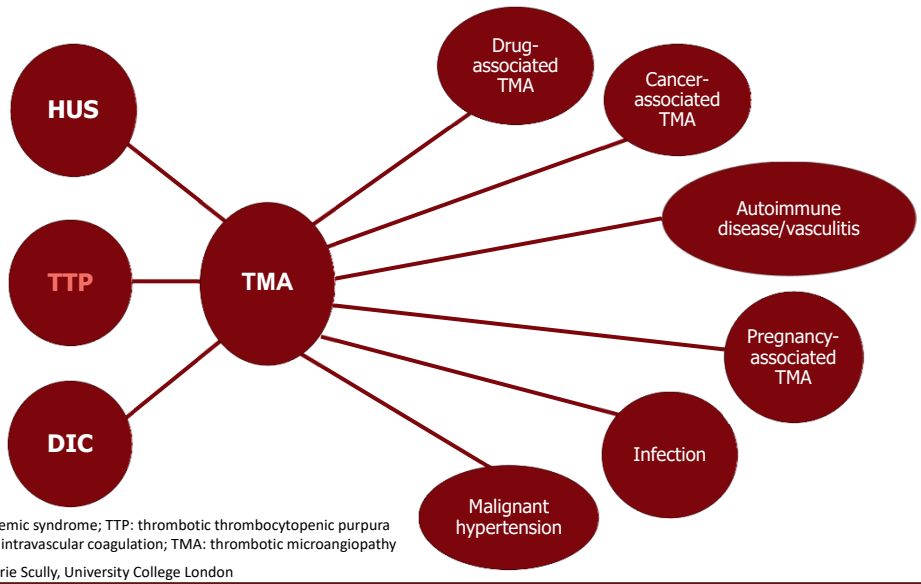
## Differential diagnosis of thrombotic microangiopathy (TMA)




HUS: hemolytic uremic syndrome; TTP: thrombotic thrombocytopenic purpura
DIC: disseminated intravascular coagulation; TMA: thrombotic microangiopathy

Courtesy of Dr Marie Scully, University College London

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# Thrombotic thrombocytopenic purpura: evolution of the pentad

| | 1925-1964 | 1964-1980 | 1982-1989 |
|---|---|---|---|
| **Thrombocytopenia** | 96% | 96% | 100% |
| **Hemolytic anemia** | 96% | 98% | 100% |
| **Neurologic symptoms** | 92% | 84% | 63% |
| **Renal disease** | 88% | 76% | 59% |
| **Fever** | 98% | 59% | 26% |
| **Death** | 90% | 54% | 22% |

Courtesy of Dr. James George, University of Oklahoma Health Sciences

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# Prediction of ADAMTS13 activity in acquired thrombotic microangiopathies

| Study | ADAMTS13 Threshold | ADAMTS13 Activity | | | |
|---|---|---|---|---|---|
| | | Deficient | | Non-Deficient | |
| | | Platelets (x $10^9$/L) | Creatinine (mg/dL) | Platelets (x $10^9$/L) | Creatinine (mg/dL) |
| **Raife et al, 2004[1]** | 15% | 13 | 1.2 | 44 | 2.7 |
| **Coppo et al, 2010[2]** | 18% | 17 | 1.3 | 67 | 5.1 |
| **Kremer Hovinga et al, 2010[3]** | 10% | 11 | 1.6 | 22 | 4.6 |
| **Bentley et al, 2010[4]** | 15% | 16 | 1.1 | 64 | 3.5 |
| **Cataland et al, 2012[5]** | 10% | 12 | 1.5 | 66 | 5.8 |

ADAMTS13: ADAM metallopeptidase with thrombospondin type 1 motif 13

1. Raife T, et al. *Transfusion.* 2004;44(2):146-150. 2. Coppo P, et al. *PLoS One.* 2010;5(4):e10208. 3. Kremer Hovinga JA, et al. *Blood.* 2010;115(8):1500-1511. 4. Bentley MJ, et al. *Transfusion.* 2010;50(8):1654-1664. 5. Cataland SR, et al. *Br J Haematol.* 2012;157(4):501-503.

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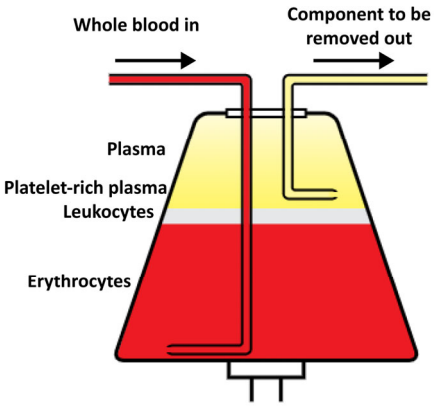
## Treatment of thrombotic thrombocytopenic purpura (TTP): *Goals of therapy*

- Clinical response of disease:
  - Plasma exchange (PEX) and immunosuppressive therapy
    - Normalization of platelet count
    - Surrogate for ongoing microvascular injury
  - End organ recovery
    - Short- and long-term
- Prevent exacerbations of TTP
  - Need to restart PEX within 30 days after stopping
    - 30-40% of cases[1,2]

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1. Peyvandi F, et al. *N Engl J Med*. 2016;374(6):511-522. 2. Scully M, et al. *N Engl J Med*. 2019;380(4):335-346.

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## Clinical issues in TTP: exacerbations

- Definition:
  - Recurrent thrombocytopenia <30 days after last PEX or anti-von Willebrand factor (anti-VWF) therapy
    - Differentiate between "new" event and continuation of prior event
  - Need to restart PEX therapy
    - Occurs in 30-40% of cases[1,2]
    - Most common in first 2 weeks
- <u>Significant clinical issue</u>
  - Readmission to hospital, line placement, restart PEX

1. Peyvandi F, et al. *N Engl J Med*. 2016;374(6):511-522. 2. Scully M, et al. *N Engl J Med*. 2019;380(4):335-346.

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## Treatment of TTP: immunosuppressive therapy

Corticosteroids:

- Suppress anti-ADAMTS13 antibody production
- Recovery of ADAMTS13 functional activity
- At least 2 weeks to see significant improvement in ADAMTS13 activity

✓Too late to help with exacerbations

Cataland SR, et al. *Blood Adv.* 2017;1(23):2075-2082.

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## Treatment of TTP: immunosuppressive therapy

- Rituximab
  - Anti-CD20 antibody
  - Suppresses production of anti-ADAMTS13 antibodies
  - Significant responses in ADAMTS13 activity begin after 2 weeks

✓Too late to help with exacerbations

Scully M, et al. *Blood.* 2011;118(7):1746-1753.

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# TITAN Study: caplacizumab for acquired TTP exacerbation, relapse status, and ADAMTS13 activity

**Caplacizumab treatment**:

- Median time to response was 3 days, significantly faster than for placebo (39% reduction in median time, *P* = 0.005)
- Fewer exacerbations than in placebo group (8% vs 28%)

| End Points | Caplacizumab (n = 36) | Placebo (n = 39) |
|---|---|---|
| **Primary end point: time to response** in patients with no plasma exchange before randomization *Days (95% CI)* | 3.0 (2.7-3.9) | 4.9 (3.2-6.6) |
| **Secondary end point: exacerbation of TTP** *Number of patients (%)* | 3 (8) | 11 (28) |

Peyvandi F, et al. *N Engl J Med.* 2016;374(6):511-522.

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