Thrombotic Thrombocytopenic Purpura (TTP) Order Sets

Developed by Answering TTP Foundation, together with PatientOrderSets.com and an international panel of recognized TTP expert doctors, for use by medical professionals to help speed diagnosis and share best practice treatments for TTP.

1. *Suspected Thrombotic Thrombocytopenic Purpura (TTP) First Response – Initial Investigations Order.* This document is geared towards first responders to speed life-saving TTP treatment.
2. *First Response Treatment of Thrombotic Thrombocytopenic Purpura (TTP) Order Set.* This document consolidates best practices for the treatment of TTP.

- *Thrombotic Thrombocytopenic Purpura (TTP) Information (Discussion Document).* This document provides support information for order sets 1 & 2, as well as resources for complex TTP cases.

Download TTP Order Sets for FREE
at www.AnsweringTTP.org

For questions please email us at Contact@AnsweringTTP.org or call us at 1-888-506-5458.

Answering T.T.P.
Thrombotic Thrombocytopenic Purpura Foundation
www.AnsweringTTP.org

Document allergies on approved form and ensure medication reconciliation has been reviewed as per organizational process

Suspected Thrombotic Thrombocytopenic Purpura (TTP) First Response - Initial Investigations Order Set (Order Set # 1)

ACTION

*****TTP is Life Threatening; Urgent consultation with an MD with TTP specific expertise is required*****

Refer to Associated Document: Thrombotic Thrombocytopenic Purpura (TTP) Information

for first response treatment of suspected TTP, MD to refer to the First Response Treatment of Thrombotic Thrombocytopenic Purpura (TTP) Order Set (Order Set # 2)

Lab Investigations

Lab Investigations to be done to Screen for TTP

- ☑ CBC, including Platelet count, Smear
- ☑ Reticulocyte count
- ☑ Coagulation Screen: APTT, INR, Fibrinogen
- ☑ Direct Antiglobulin Test (DAT)
- ☑ Group + Screen
- ☑ Electrolytes ☑ Creatinine ☑ Glucose ☑ BUN ☑ LDH
- ☑ ALT, ALP, Bilirubin ☑ AST ☑ Albumin ☑ Ca ☑ Troponin
- ☑ If age of menstruation:
  - ☐ Serum β HCG **OR** ☐ Urine β HCG
- ☑ If patient has bloody diarrhea, Stool C+S and PCR for Shiga toxin

Other Lab Investigations to Consider

- ☐ Haptoglobin ☐ C-Reactive Protein ☐ ABG ☐ Lactic Acid ☐ Lipase
- ☐ Antiphospholipid Antibodies [Anticardiolipin Antibodies, Lupus Anticoagulant (ACLA)]
- ☐ Antinuclear Antibody (ANA) and Rheumatoid Factor (RF)
- ☐ Serum Drug Screen ☐ Other Drug Levels: _____
- ☐ Hepatitis B Serology (HBsAg/HBsAb/HBcAb)
- ☐ Hepatitis C Serology
- ☐ HIV Serology ☐ CMV PCR ☐ HSV PCR
- ☐ Blood C + S x 2 STAT
- ☑ Urine R + M ☐ Urine C + S ☐ Urine Drug Screen
- ☐ Additional Labs: _____
- ☐ Follow-up Labs: _____

Diagnostics

- ☐ CXR PA + Lateral Reason: _____
- ☑ ECG

CT/MRI brain scan may be considered to rule out hemorrhage or infarction, however, diagnostic testing should not delay initiation of therapy and can generally be arranged after plasma infusion/exchange has been initiated

- ☐ _____ Reason: _____

Consults

- ☑ Hematologist - **Urgent:** suspected TTP; requires plasma exchange
- ☐ Neurologist - _____
- ☐ Infectious Diseases MD - _____
- ☐ Obstetrician/Gynecologist - _____
- ☐ Nephrologist - **Urgent:** suspected TTP; requires plasma exchange
- ☐ Other - _____

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Practitioner: _____ (ID) _____ (PRINTED NAME) _____ (YYYY-MM-DD HH:MM) _____ (SIGNATURE)

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First Response Treatment of Thrombotic Thrombocytopenic Purpura (TTP) Order Set (Order Set # 2)

ACTION

This order set is intended for treatment of the patient with suspected TTP on first presentation

treatment beyond first response should be managed by an MD with a specific expertise in TTP

Refer to Associated Document: Thrombotic Thrombocytopenic Purpura (TTP) Information

Lab Investigations

Lab Investigations if not already done

☑ ADAMTS13

☐ ADAMTS13 Activity Assay ☐ ADAMTS13 Antibody Inhibitor Titre

☑ Draw ordered ADAMTS13 blood before plasma infusion/exchange begins/before transfusion of blood product begins

Start ordered plasma infusion/exchange pending results

☐ Haptoglobin ☐ Thrombin-anti-thrombin complex (TAT)

☐ Group + Screen for _____ units red blood cells

☐ Antiphospholipid Antibodies [Anticardiolipin Antibodies, Lupus Anticoagulant (ACLA)]

☐ Antinuclear Antibody (ANA) and Rheumatoid Factor (RF)

☐ Hepatitis B Serology (including HBsAg/HBsAb/HBcAb) ☐ Hepatitis C Serology

☐ HIV Serology ☐ CMV PCR ☐ HSV PCR

☐ Additional Labs: _____

☐ Follow-up Labs: _____

Diagnostics

CT/MRI brain scan may be considered to rule out hemorrhage or infarction, however, diagnostic testing should not delay initiation of therapy and can generally be arranged after plasma infusion/exchange has been initiated

☐ _____ Reason: _____

IV Therapy

☐ 0.9% NaCl at _____ mL/h ☐ _____

Blood Product Transfusion: Reaction Prophylaxis and Reaction Management

if patient has had a previous transfusion reaction, MD to consider the following*

Prior Blood Product Allergic Reaction: Pre Blood Product Transfusion Medications

☐ acetaminophen _____ mg PO/PR 30 minutes prior to transfusion (325 – 650 mg)

☐ diphenhydr**AMINE** _____ mg PO/IV 30 minutes prior to transfusion (25 – 50 mg)

☐ hydrocortisone 100 mg IV for 1 dose prior to transfusion

Allergic Reaction to Blood Product Medication Management

☐ In the event of an allergic reaction to a blood product follow hospital policy/procedure and administer the following:

- ☐ acetaminophen 650 mg PO/PR q4h PRN
- ☐ diphenhydr**AMINE** 50 mg IV for 1 dose, notify MD and request further orders
- ☐ hydrocortisone 100 mg IV for 1 dose

☐ _____

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First Response Treatment of Thrombotic Thrombocytopenic Purpura (TTP) Order Set (Order Set # 2)

ACTION

Plasma Exchange or Plasma Infusion

Refer to plasma exchange/infusion hospital policy/procedure

plasma exchange is the preferred treatment (with Solvent/Detergent treated Fresh Frozen Plasma (S/D FFP) where available). Recommendation is to start plasma exchange (PEX) as soon as possible

Plasma Exchange

☐ Plasma exchange using: ☐ Cryosupernatant Plasma ☐ Fresh Frozen Plasma ☐ _____
☐ Solvent/Detergent treated Fresh Frozen Plasma (S/D FFP)

Plasma exchange volume: _____ Plasma exchange frequency: _____

☐ _____

☐ furosemide _____ mg IV to be given _____

Plasma Infusion

if delay in arranging plasma exchange or it is not available at the hospital, large volume plasma infusions are indicated

☐ Plasma infusion using: ☐ Cryosupernatant Plasma ☐ Fresh Frozen Plasma ☐ _____
☐ Solvent/Detergent treated Fresh Frozen Plasma (S/D FFP)

Plasma infusion _____ mL infusion over _____ until plasma exchange arranged

☐ _____

☐ furosemide _____ mg IV to be given _____

Red Blood Cell Transfusion

Refer to red blood cell transfusion hospital policy/procedure

☐ Transfuse _____ units of red blood cells, each over _____ Reason for transfusion: _____

☐ furosemide _____ mg IV to be given _____

Post Transfusion Lab Investigations

☐ _____

Adjunct Management

recommendations are to initiate a systemic corticosteroid and a gastric protection agent e.g. pantoprazole, ranitidine

methylPREDNISolone may be the preferred corticosteroid if patient is already on prednisone

☐ methyl**PREDNIS**olone 1 g IV daily for 3 days, then MD to reassess

☐ predni**SONE** _____ mg PO daily (1 mg/kg/day)

Gastric Protection Agent

☐ _____

Disposition (to Unit Specializing in Management of TTP)

transfer should be arranged and accomplished as rapidly as possible

☐ Arrange transfer to tertiary centre _____ Date/Time of transfer _____

☐ Admit to _____ Date/Time of transfer _____

☐ _____

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Thrombotic Thrombocytopenic Purpura (TTP) Information

Key source: Scully, M., Hunt, B. J., Benjamin, S., Liesner, R., Rose, P., Peyvandi, F…Machin, S. J., and on behalf of British Committee for Standards in Haematology. (2012). Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies. *British Journal of Haematology, 158(3),* 323-335. doi:10.1111/j.1365-2141.2012.09167.x (referred to as Scully, M., et al 2012 within this document). Retrieved from: http://www.bcshguidelines.com/documents/BJH_TTP_Guideline_0512.pdf

*****Rapid treatment is required; emergent transfer must be arranged to a center with expertise in management of TTP*****

If TTP is suspected, use the following order sets:

- Suspected Thrombotic Thrombocytopenic Purpura (TTP) First Response - Initial Investigations Order Set (Order Set # 1)
- First Response Treatment of Thrombotic Thrombocytopenic Purpura (TTP) Order Set (Order Set # 2)

AND

Refer urgently to an MD with TTP specific expertise (usually a hematologist or nephrologist) for guidance/further management

NOTE: The following 'points of interest/statements of opinions ' serve as general information and are NOT to be interpreted as complete or as orders. Medications listed on the order sets will/may be adjusted by hospitals according to their drug formularies and policies/procedures

Suspected Thrombotic Thrombocytopenic Purpura (TTP)

See Tables I, II and IV (Scully, M., et al 2012)

- Suspect Idiopathic TTP if patient has, microangiopathic hemolytic anemia (MAHA) and thrombocytopenia in absence of other identifiable cause
- The diagnosis of TTP should be treated as a medical emergency. The initial diagnosis of TTP should be made on clinical history, examination and routine laboratory parameters of the patient, including blood film review
- Start treatment immediately if TTP is suspected. **Refer urgently for TTP specialist advice and Plasma Exchange (PEX)**
- The diagnosis of congenital TTP should be considered with unexplained thrombocytopenia or for patient presenting with severe jaundice
- The diagnosis of congenital TTP is confirmed by ADAMTS13 activity < 5%, absence of antibody and confirmation of homozygous or compound heterozygous defects of the ADAMTS13 gene

Investigations

See Table II and III (in Scully, M., et al.)

- Serological tests for HIV, hepatitis B virus and hepatitis C virus, autoantibody screen and when appropriate, a pregnancy test, should be performed at presentation
- Other investigations should be performed promptly, but can be delayed until after starting PEX: urinalysis, stool culture (if diarrhea), echocardiogram, CT brain (if neurological signs), and CT chest/abdomen/pelvis to check for underlying malignancy (if indicated)

Urgent Treatment

- In view of the high risk of preventable, early deaths in TTP, treatment with plasma exchange (PEX) should be initiated as soon as possible regardless of the time of day at presentation
- Plasma replacing ADAMTS 13 is required. Viral inactivation products e.g. Solvent detergent-treated (S/D) fresh frozen plasma (S/D FFP) is preferred. Use standard FFP or Cryosupernatant plasma if S/D is not available
- If any delay in starting PEX, initiate FFP or Cryosupernatant plasma infusion. Watch for fluid overload.
- PEX should be started with 1·5 Plasma Volume (PV) exchanges
  - Usually 1·5 plasma volumes x 3 days, then 1 plasma volume/day with stabilization of condition
  - More intensive exchange therapy such as twice daily PEX may be deemed necessary by the MD with a specific expertise in TTP for resistant cases, especially if there is new symptomology, such as neurological or cardiac events
- Daily PEX is generally continued for a minimum of 2 treatments over 2 days after the platelet count has been >150 x 10^9/L, and then stopped
- Transfuse red cells when necessary to correct anemia
- Platelet transfusions are contraindicated unless bleeding is life-threatening

Adjunctive Management

- Either IV methylprednisolone (1 g/day for 3 days) or oral prednisolone (e.g. 1 mg/kg/day) with gastric protection e.g. an oral proton pump inhibitor or H2 blocker
- Oral folic acid 5 mg daily
- Prevent Thrombosis: When platelet count > 50 x 10^9/L, MD may consider LMWH thromboprophylaxis and daily low dose aspirin

Adjunctive Management Continued…

Special Cases See Section 3.7.2 (Scully et al)

- If HIV-positive, start HAART immediately
- If neurological or cardiac involvement, the MD with TTP expertise may consider further immunosuppressive therapy e.g. rituximab

For Ongoing Treatment and Complex Cases

*****patients with TTP must be under the care of an MD with TTP specific expertise*****

- For information on progressive symptoms, refractory, relapsing disease and supportive therapies refer to Scully et al 2012 Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies. *British Journal of Haematology*
- In cases of poor responses/refractory cases to PEX, ADAMTS13 biomarkers should be repeated (Cataland, S.)
- Evaluations of kidney function, serum Creatinine (Cataland, S.) and LDH should continue
- If normal/measureable (>10%) ADAMT13 at presentation, repeat testing if: (Cataland. S.)
  - poor response to PEX with worsening renal function
  - hematologic improvement but with worsening kidney function
- Increased frequency of PEX and further immunosuppressant therapy e.g. rituximab may be considered in refractory or relapsing disease

Discharge Planning and Follow-up

- Once discharged, Complete Blood Count, Platelet Count, Smear and LDH are recommended weekly x 4 weeks, then on a patient by patient basis to assess for sustained remission
- After achieving sustained remission (normal platelet count, LDH, independent of PEX for 30 days), regular follow-up will be arranged: (practice at Ohio State is to see patients approximately every 3 months)
  - Regular ADAMTS13 activity testing at these visits to monitor and predict risk of relapse
  - If patient is pregnant, ADAMTS13 every 3 months or more often as indicated by an MD with TTP expertise
- Careful follow-up is essential:
  - to ensure prompt diagnosis and treatment of a relapsed episode of TTP
  - to assess for long-term complications of previous TTP episodes and initiate early intervention if required
  - to prevent complications and to ensure proper management of the patient's physical and mental health (for neurocognitive assessments, depression/mood disorder assessments and monitoring for hypertension

General Follow-up Information

- Caution should be used in patients requiring estrogen- containing medications and other medications associated with the precipitation of TTP
- ADAMTS13 activity and future pregnancies: Risk of relapse meditated by ADAMTS13 deficiency during pregnancy (Cataland, S., et al, Scully, M.) (retrospective and opinion). Follow-up should be by an MD with TTP expertise

Patient Information and Medical Professional Information

- Answering T.T.P. Foundation www.AnsweringTTP.org
  - Educational Brochures
    - Thrombotic Thrombocytopenic Purpura Information for Patients & Supporters
    - Information about Solvent Detergent Plasma (SDP) and other pathogen inactivation technologies for the use in the treatment of TTP
  - International Support Programs listing http://www.answeringttp.org/support-programs
  - Information for Medical Professionals http://www.answeringttp.org/Medical-Professionals
- UK ttpnetwork: http://www.ttpnetwork.org.uk/
- USA, Oklahoma: http://www.ouhsc.edu/platelets/ttp.html
- Italy: Dr. Pier Mannucci: http://www.ttpdatabase.org/en/contact.htm
- Australia: Dr. Louise Philips: http://www.torc.org.au/node/4
- Switzerland: Dr. Johanna Kremer Hovinga: http://www.ttpregistry.net/

PatientOrderSets.com and Answering T.T.P. acknowledge and thank Dr. Marie Scully (UK), Dr. Katerina Pavenski (Toronto, Canada), Dr. Spero Cataland (Ohio, USA), and Dr. James N. George (Oklahoma, USA) for their dedication to making a difference to the lives of people with TTP and for the significant contributions towards the development of the TTP order sets and this information document.