

## Guidelines to Management of Immune Thrombocytopenic Purpura (ITP)

### Background:

ITP is the most common cause of isolated thrombocytopenia causing clinically significant bleeding. There is no single diagnostic study that can confirm the diagnosis. ITP can be assumed if other diagnosis such as thrombotic thrombocytopenic purpura, pseudothrombocytopenia (platelet clumping), hereditary macrothrombocytopenia and myelodysplasia are excluded. Less than 3% of ITP is drug induced. The most common medications associated with immune platelet destruction include quinidine/quinine, bactrim, rifampin, penicillin and cephalosporins. Underlying diseases associated with ITP include lymphoproliferative disorders, SLE and other autoimmune disorders, HIV, Hepatitis C, H. Pylori and chronic inflammatory bowel disease.

### Treatment:

1. **Steroids:** Patients with ITP and a platelet count of <20,000 should be treated. Patients with platelets less than 10,000 and bleeding are probably best managed initially in the hospital. Steroids are the backbone of therapy. Traditionally prednisone at 1-1.5 mg/kg in divided doses has been the standard treatment but a recent studies suggest that high dose decadron at 40 mg/day for 4 days leads to more durable responses and I believe is the treatment of choice in uncomplicated patients without significant co-morbidities.
2. **Intravenous gamma globulin(IVIG), WinRho:** Patients with significant bleeding or a platelet count of <5000 with wet purpura (nose, gum or mucosal bleeding) require a more urgent rise in platelet count – IVIG at 1gm/kg over 24 hours x 2 days or WinRho 75µgm/kg over 5-10 minutes both will reliably increase platelet counts within 24 to 36 hours. WinRho can only be used if patients are Rh(+) and have not had a splenectomy. There is an average drop of 1.5 gms of hemoglobin in patients given WinRho so it is not an optimal choice in patients with significant anemia.
3. **Platelet Transfusion:** Platelet transfusion should only be used in patients with significant bleeding. The platelet count will not rise significantly but bleeding is controlled in the majority of patients. Patients without bleeding should not be transfused with platelets no matter how low the platelet count is. Platelet transfusions in patients with thrombotic thrombocytopenia purpura and heparin induced thrombocytopenia are contraindicated, so careful consideration to exclude these diagnoses is mandatory prior to transfusion.

4. **Platelet growth factors:** The majority of patients with ITP have defective platelet production. Romiplostim and eltrombopag are small molecules which directly activate the MPL receptor on megakaryocyte membranes causing increased platelet production and release. Although not used in initial therapy these drugs are extremely helpful in the long term management of patients with ITP.

## **Guidelines For The Management of Thrombotic Thrombocytopenic Purpura (TTP)**

**Background:** TTP is a rapidly fatal disorder characterized by microvascular destruction of multiple organs by complexes of high molecular vonWillebrands factor(vWF) and platelets. Clinically this is manifested by microangiopathic hemolytic anemia and destructive thrombocytopenia. Symptoms include fever, abdominal pain, musculoskeletal discomfort and headaches. A Coombs test is negative and the d-dimer is <2000. PT and PTT are usually normal and LDH is always significantly elevated at 3-10 times normal. If this disease cannot be excluded at initial evaluation the patient must be treated urgently for TTP.

TTP is an autoimmune disease with antibody to vonWillebrand factor cleaving enzyme. Please draw a vWF cleaving enzyme level prior to starting therapy. Drugs associated with TTP include clopidogrel, ticlopidine, cyclosporin, quinine and chemotherapy agents (mitomycin C and cisplatin).

### **Treatment:**

1. Contact the renal service for emergency plasma exchange (i.e. to start within a few hours).
2. In the interim give 3 units of fresh frozen plasma every 3-4 hours until exchange started – continue exchange daily until remission.
3. Begin solumedrol 1.5 mg/kg IV in divided doses.
4. Do not use cryoprecipitate or platelet transfusion except with a life threatening CNS bleed.
5. Transfuse leukodepleted packed red blood cells as indicated clinically.
6. Plasma exchange should be done daily until LDH and platelets are in the normal range than tapered over 5-7 days.

**Outcome:** Before the use of plasma exchange this disorder had a mortality rate of 85-90%. With this present aggressive approach to treatment the mortality rate has dropped to less than 20%.

## **Guidelines for Management of Heparin Induced Thrombocytopenia (HIT)**

**Background:** Antibodies to platelet factor4/heparin complexes interact with platelet receptors causing platelet activation, microparticle release and thrombophilia. Any patient exposed to heparin who develops clot or dropping platelet count after the 5<sup>th</sup> day of heparin therapy should be suspected of having HIT. Failure to recognize this syndrome will lead to a thrombotic diathesis and high mortality rates. Be aware that an increasing percentage of patients have been reported with delayed onset of HIT presenting 15-20 days after exposure.

### **Treatment:**

1. If HIT is suspected stop all forms of heparin and draw anti-heparin antibody studies.
2. Even if the patient does not have a clot they must be treated with systemic anticoagulation (risk of clot >50% in next 30 days).
3. Begin a direct thrombin inhibitor (DTI) IV; lepirudin (avoid in renal insufficiency) – bolus dose 0.4 mg/kg IVP over 15-20 seconds then continuous infusion at 0.15 mg/kg/hr OR argatroban (avoid with liver disease) – 2 µgm/kg/minute adjust dose to a PTT 1.5-3.0 times baseline. DO NOT EXCEED 10µgm/kg/minute.
4. Do not use coumadin alone.
5. May begin conversion to coumadin once platelet count >100,000.
6. Do not rechallenge patient with heparin for at least 3 months – if heparin necessary (i.e. CABG) and no detectable antibody after 3 months, it is safe to use.
7. Direct thrombin inhibitors have no specific antidote – use FFP for bleeding. Activated recombinant Factor 7 can be considered for unresponsive life threatening bleeding
8. Fondaparinux (a pentasaccharide Factor 10a inhibitor) does not cause HIT and has been safely used in patients unable to tolerate direct thrombin inhibitors.