MANAGEMENT OF COMMON BLEEDING DISORDERS

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BLOOD CLOT:

PRIMARY HAEMOSTASIS (Platelets) + SECONDARY HAEMOSTASIS (Coagulation Factors)
## HAEMOSTATIC DISORDERS

### SCREENING TESTS

<table>
<thead>
<tr>
<th>PLATELET</th>
<th>BT*</th>
<th>PT</th>
<th>APTT</th>
<th>‘DIAGNOSIS’</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOW</td>
<td>P</td>
<td>N</td>
<td>N</td>
<td>THROMBOCYTOPAENIA</td>
</tr>
<tr>
<td>N</td>
<td>P</td>
<td>N</td>
<td>N</td>
<td>PLATELET DYSFUNC</td>
</tr>
<tr>
<td>N</td>
<td>P</td>
<td>N</td>
<td>P</td>
<td>VON WILLEBRANDS DIS</td>
</tr>
<tr>
<td>N</td>
<td>N</td>
<td>N</td>
<td>P</td>
<td>‘INTRINSIC’ PATH ABN</td>
</tr>
<tr>
<td>N</td>
<td>N</td>
<td>P</td>
<td>N</td>
<td>‘EXTRINSIC’ PATH ABN</td>
</tr>
<tr>
<td>N</td>
<td>N</td>
<td>P</td>
<td>P</td>
<td>‘COMMON’ PATH ABN</td>
</tr>
<tr>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>F XIII / OTHER ABN</td>
</tr>
</tbody>
</table>

*Not universally practiced

P=Prolonged; N=Nomal
HAEMOSTASIS FAILURE

INVESTIGATIONS

* COMPLETE BLOOD COUNTS, BLOOD PICTURE
  [To assess schistocytes / platelets]

* PROTHROMBIN TIME / ACTIVATED PARTIAL THROMBOPLASTIN TIME / THROMBIN TIME
  WITH 'CORRECTION' STUDIES USING 'CONTROL' PLASMA
  [To assess factor deficiency ± inhibitors]

* FIBRINOGEN LEVEL / D - DIMER / FDP
  [To evaluate consumptive coagulopathy
  DIC / Primary fibrinolysis]
# Clinical profile of hemophilia & outcome of treatment

<table>
<thead>
<tr>
<th>Frequent spontaneous bleeding</th>
<th>Occasional spontaneous bleeding</th>
<th>No spontaneous bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Haemophilia</td>
<td>Mod Haemophilia</td>
<td>Mild Haemophilia</td>
</tr>
<tr>
<td>FVIII:C – &lt;1%</td>
<td>FVIII:C – 1-5%</td>
<td>FVIII:C – 5-40%</td>
</tr>
</tbody>
</table>

**Clinical outcome**

- **Bleeding risks**
- **Clinical outcome**
- **Therapeutic interventions**
This study demonstrates the efficacy of prophylaxis with recombinant factor VIII in reducing the incidence of joint hemorrhages, life-threatening hemorrhages, and other hemorrhages and in lowering the risk of joint damage among young boys with severe factor VIII deficiency. However, the high cost of recombinant factor VIII (up to $300,000/yr) is a barrier to widespread acceptance of prophylaxis.
EPISODIC TREATMENT

SHORT-TERM PROPHYLAXIS

TERTIARY PROPHYLAXIS (after onset of joint disease)

SECONDARY PROPHYLAXIS (after second joint bleed)

PRIMARY PROPHYLAXIS (before second joint bleed)

Increasing intensity of factor replacement

Treatment of pain and serious bleeding

Improvement of target joints

Improves normal activities of daily life

Minimal musculoskeletal disease

Near normal musculoskeletal & psycho-social development

Treatment of pain and serious bleeding

Improvement of target joints

Improves normal activities of daily life

Minimal musculoskeletal disease

Near normal musculoskeletal & psycho-social development

Adapted from Blood Transfus 2008 Sep;6 Suppl 2:s4-11
SEVERE HEMOPHILIA – WITH EFFECTIVE TREATMENT!
FACTOR REPLACEMENT IN HEMOPHILIA

EPISODIC /“ON DEMAND” TREATMENT

*Factor infusion as when needed for bleeds
*Is the most common prevalent option of treatment
*Wide range of dosage reported from different parts of the world
*Total yearly dose : 100 - 2000 IU/kg/yr

*Results in reducing pain, crippling deformities & early mortality.

*Poor long-term musculoskeletal outcome even with significant doses

*May be worth developing lower dose prophylaxis protocols when regular supply of CFC is available at 500-1500iu/kg/yr
SEVERE HEMOPHILIA – WITH INADEQUATE TREATMENT
FACTOR REPLACEMENT FOR BLEEDING IN HEMOPHILIA

• TREAT EARLY - WITHIN 2 HOURS, IF POSSIBLE
  'HOME THERAPY'

• ‘IF IN DOUBT TREAT’ (?if possible)

• HANDLE VEINS WITH GREAT CARE
  - APPROPRIATE NEEDLE (21 - 23G)
  - PROPER TECHNIQUE
  - APPLY PRESSURE AFTER PROCEDURE
    FOR 10 - 15 MINUTES

• DOSE DEPENDENT ON SITE / SEVERITY OF BLEED

• AVOID DRUGS CAUSING PLATELET DYSFUNCTION
  FOR PAIN RELIEF  (ASPIRIN / NSAID)
TREATMENT OF BLEEDING IN HEMOPHILIA

*ADEQUATE FACTOR REPLACEMENT*

- HEMOSTATIC LEVELS *NOT* NORMAL LEVELS
- CLOTTING FACTOR CONCENTRATES
  PLASMA DERIVED / RECOMBINANT
- BLOOD BANK PRODUCTS: PLASMA / FFP / CRYO
  FVIII – 1 IU/KG WILL INCREASE PLASMA LEVEL BY 2%
  FIX – 1 IU/KG WILL INCREASE PLASMA LEVEL BY 1%

*GENERAL MEASURES*

- TO ADDRESS LOCAL FACTORS
- NON-SPECIFIC HEMOSTATIC AGENTS
<table>
<thead>
<tr>
<th>Type of hemorrhage</th>
<th>Desired level (IU dL(^{-1}))</th>
<th>Duration (days)</th>
<th>Desired level (IU dL(^{-1}))</th>
<th>Duration (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hemophilia A</td>
<td></td>
<td>Hemophilia B</td>
<td></td>
</tr>
<tr>
<td>Joint</td>
<td>40–60</td>
<td>1–2, may be longer if response is inadequate</td>
<td>40–60</td>
<td>1–2, may be longer if response is inadequate</td>
</tr>
<tr>
<td>Superficial muscle/no NV</td>
<td>40–60</td>
<td>2–3, sometimes longer if response is inadequate</td>
<td>40–60</td>
<td>2–3, sometimes longer if response is inadequate</td>
</tr>
<tr>
<td>compromise (except iliopsoas)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iliopsoas and deep muscle with NV injury, or substantial blood loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial</td>
<td>80–100</td>
<td>1–2</td>
<td>60–80</td>
<td>1–2</td>
</tr>
<tr>
<td>Maintenance</td>
<td>30–60</td>
<td>3–5, sometimes longer as secondary prophylaxis during physiotherapy</td>
<td>30–60</td>
<td>3–5, sometimes longer as secondary prophylaxis during physiotherapy</td>
</tr>
<tr>
<td>CNS/head</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial</td>
<td>80–100</td>
<td>1–7</td>
<td>60–80</td>
<td>1–7</td>
</tr>
<tr>
<td>Maintenance</td>
<td>50</td>
<td>8–21</td>
<td>30</td>
<td>8–21</td>
</tr>
<tr>
<td>Throat and neck</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial</td>
<td>80–100</td>
<td>1–7</td>
<td>60–80</td>
<td>1–7</td>
</tr>
<tr>
<td>Maintenance</td>
<td>50</td>
<td>8–14</td>
<td>30</td>
<td>8–14</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial</td>
<td>80–100</td>
<td>7–14</td>
<td>60–80</td>
<td>7–14</td>
</tr>
<tr>
<td>Maintenance</td>
<td>50</td>
<td></td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td>50</td>
<td>3–5</td>
<td>40</td>
<td>3–5</td>
</tr>
<tr>
<td>Deep laceration</td>
<td>50</td>
<td>5–7</td>
<td>40</td>
<td>5–7</td>
</tr>
<tr>
<td>Surgery (major)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-op</td>
<td>80–100</td>
<td>1–3</td>
<td>60–80</td>
<td>1–3</td>
</tr>
<tr>
<td>Post-op</td>
<td>60–80</td>
<td>4–6</td>
<td>40–60</td>
<td>4–6</td>
</tr>
<tr>
<td></td>
<td>40–60</td>
<td>7–14</td>
<td>30–50</td>
<td>7–14</td>
</tr>
<tr>
<td>Surgery (minor)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-op</td>
<td>50–80</td>
<td>1–5, depending on type of procedure</td>
<td>50–80</td>
<td>1–5, depending on type of procedure</td>
</tr>
<tr>
<td>Post-op</td>
<td>30–80</td>
<td></td>
<td>30–80</td>
<td></td>
</tr>
</tbody>
</table>

NV, neurovascular.
<table>
<thead>
<tr>
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<td>1–3</td>
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<td>Throat and neck</td>
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<tr>
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<td>30–50</td>
<td>1–3</td>
</tr>
<tr>
<td>Renal</td>
<td>20–40</td>
<td>3–5</td>
</tr>
<tr>
<td>Deep laceration</td>
<td>20–40</td>
<td>5–7</td>
</tr>
<tr>
<td>Surgery (major)</td>
<td>Pre-op</td>
<td>60–80</td>
</tr>
<tr>
<td></td>
<td>Post-op</td>
<td>30–40</td>
</tr>
<tr>
<td></td>
<td>20–30</td>
<td>1–3</td>
</tr>
<tr>
<td></td>
<td>10–20</td>
<td>7–14</td>
</tr>
<tr>
<td>Surgery (minor)</td>
<td>Pre-op</td>
<td>40–80</td>
</tr>
<tr>
<td></td>
<td>Post-op</td>
<td>20–50</td>
</tr>
</tbody>
</table>

NV, neurovascular.
Definition of disseminated intravascular coagulation

DIC is an acquired syndrome characterized by the intravascular activation of coagulation with loss of localization arising from different causes. It can originate from and cause damage to the microvasculature, which if sufficiently severe, can produce organ dysfunction.

ISTH’s Scientific Subcommittee on DIC, July 2001
Considerations in practical diagnostic approach to DIC

- Presence of an underlying disorder
- The severity of haemostatic changes
  - Decompensated haemostatic system: Overt DIC
  - Compensated haemostatic system: Non-overt DIC
- The duration of activation
  - Temporary: e.g. Abruptio placentae, transfusion reaction
  - Prolonged: e.g. Sepsis, malignancy, polytrauma
- Laboratory tests
  - Global tests / Molecular markers
  - Diagnostic value / Prognostic value
- Use of scoring systems
  - DIC scoring system
  - Other scoring systems

ISTH’s Scientific Subcommittee on DIC, July 2001
Clinical Conditions Associated with DIC

1. Sepsis / severe infection (any micro-organism)
2. Trauma (polytrauma, neurotrauma, fat embolism)
3. Organ destruction (severe pancreatitis)
4. Malignancy - solid tumours, myelo/lymphoproliferative disorders
5. Obstetric calamities - amniotic fluid embolism, abruptio placentae
6. Vascular abnormalities - Kasaback-Merrit syndrome, Large vascular malformation
7. Severe hepatic failure -
8. Severe toxic / immunologic reactions - snake bites, recreational drugs, transfusion reactions, transplant rejection
ACTIVATION OF COAGULATION

EVENTS LEADING TO THROMBOSIS
- Thrombotic occlusion of microcirculation of all organs
- Fibrinolysis in the microcirculation

EVENTS LEADING TO BLEEDING
- Circulating fibrin degradation products
- Consumption of platelets and coagulation factors

Signs of microvascular thrombosis
- Neurologic: focal deficit, coma
- Skin: gangrene
- Renal: oliguria, azotemia
- Pulmonary: ARDS
- Gastrointestinal: ulceration

Signs of haemorrhagic diathesis
- Neurologic: intracerebral bleed
- Skin: purpura
- Renal: haematuria
- Mucous membrane: epistaxis, gum bleeding
- Gastrointestinal: massive bleeding
Common Haemostatic Defects in DIC

1. Platelet count decreased
2. Blood picture - schistocytes
3. PT / APTT / TT prolonged
4. Fibrinogen decreased
5. D-dimer / FDP elevated
6. ATIII / PC decreased
7. TAT complexes increased
SCANNING ELECTRON MICROSCOPE IMAGE OF RED BLOOD CELL BEING CUT BY FIBRIN STRANDS
PERIPHERAL BLOOD SMEAR IN DIC

MICROSPHEROCYTE

SCHISTOCYTE
Scoring system for overt DIC

- Underlying disorder known to be associated with overt DIC
  - YES
  - NO

- Platelet count
  - (>100=0, <100=1, <50=2) ........................................
  - NO
  - YES

- Soluble fibrin/D-dimer
  - (normal=0, ↑=2, ↑↑=3) ........................................
  - NO
  - YES

- Prolongation of PT
  - (<3s=0, 3-6s=1, >6s=2) ..................................
  - NO
  - YES

- Fibrinogen
  - (>1g/l=0, <1g/l=1) ........................................
  - NO
  - YES

- Calculate sum .....................................................
  - NO
  - YES

ISTH’s Scientific Subcommittee on DIC, July 2001
## Scoring system for overt DIC

### - Example -

- **Underlying disorder known to be associated with overt DIC**
  - YES
  - NO

<table>
<thead>
<tr>
<th>SEPSIS</th>
<th>SEPSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count</td>
<td></td>
</tr>
<tr>
<td>- (&gt;100=0, &lt;100=1, &lt;50=2)</td>
<td>85</td>
</tr>
<tr>
<td>Soluble fibrin/D-dimer</td>
<td></td>
</tr>
<tr>
<td>- (normal=0, ↑=2, ↑↑=3)</td>
<td>8</td>
</tr>
<tr>
<td>Prolongation of PT</td>
<td></td>
</tr>
<tr>
<td>- (&lt;3s=0, 3-6s=1, &gt;6s=2)</td>
<td>+3</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td></td>
</tr>
<tr>
<td>- (&gt;1g/l=0, &lt;1g/l=1)</td>
<td>2,2</td>
</tr>
</tbody>
</table>

- **Calculate sum**
  - 5

*ISTH’s Scientific Subcommittee on DIC, July 2001*
Scoring system for overt DIC

- If the calculated score is
  - $\geq 5$: compatible with overt DIC repeat scoring daily
  - $< 5$: suggestive (not affirmative) for non-overt DIC repeat next 1-2 days.

ISTH’s Scientific Subcommittee on DIC, July 2001
Management of DIC

• TREAT THE CAUSE
  • ANTIBIOTICS FOR INFECTION
  • REMOVE THE DEAD FOETUS

• SUPPLY THE DEPLETED HAEMOSTATIC FACTORS
  • PLATELETS
  • FFP
  • CRYOPRECIPITATE

• Do not forget to transfuse Packed Red cell to maintain adequate Hb%
PLATELETS – 4 – 6 bags if bleeding

FFP – 15 – 20 ml / kg

Cryoppt – 1-2 bags / 10 kg body weight.

Do monitor at 4- 6 hourly - clinically and looking at the lab parameters. If still active bleed and lab parameters are worsening; continue the same support.

Role of Heparin controversial.
The Vicious Cycle of Inflammation and Coagulation
ROLE OF LIVER IN COAGULATION

*SYNTHESIS OF FACTORS THAT CONTROL COAGULATION
(EXCEPT VWF)

1. PROMOTERS OF COAGULATION

   I, II, V, VII, VIII, IX, X, XI, XII, XIII, PK, HMWK

2. INHIBITORS OF COAGULATION

   AT III, PROTEIN C, PROTEIN S,

3. PROMOTERS OF FIBRINOLYSIS

   PLASMINOGEN

4. INHIBITORS OF FIBRINOLYSIS

   ALPHA - 2 ANTIPLASMIN, PAI-1, TAFI

*CLEARANCE OF ACTIVATED COAGULATION FACTORS
HAEMOSTASIS IN ACUTE LIVER FAILURE

CAUSES OF DYSFUNCTION

*LIVER CELL DYSFUNCTION
*ENDOTHELIAL CELL ACTIVATION
*VITAMIN K DEFICIENCY
*HYPERSPLENISM
*PERITONEAL - VENOUS SHUNTING
*SEPSIS
HAEMOSTASIS DEFECTS - ACUTE LIVER FAILURE

TYPES OF DEFECTS

*DEFICIENCY OF COAGULANT FACTORS: PROLONGED PT, APTT, COMPLETE CORRECTION WITH 'CONTROL' PLASMA

*HYPERFIBRINOLYSIS: PROLONGED PT, APTT, TT, PARTIAL CORRECTION ONLY WITH 'CONTROL' PLASMA, SHORTENED ELT, REDUCED FIBRINOGEN, INCREASED FDP, D-DIMER *NOT* ELEVATED

*DIC: AS FOR HYPERFIBRINOLYSIS WITH SCHISTOCYTES, DECREASED PLATELETS, INCREASED D-DIMER
HAEMOSTATIC DEFECTS – ACUTE LIVER FAILURE

MANAGEMENT DEPENDS UPON

* SEVERITY AND PROFILE OF THE ABNORMALITIES
  DEFICIENCY OF COAGULATION FACTORS
  HYPER-FIBRINOLYSIS
  DIC

*CLINICAL CONTEXT OF THE INTERVENTION
  PROPHYLACTIC – TO PREVENT BLEEDING
  CONTROL OF HAEMORRHAGE
  LIVER BIOPSY
HAEMOSTATIC DEFECTS – ACUTE LIVER FAILURE

AIMS OF THERAPEUTIC INTERVENTION

* 'NORMALIZE' COAGULATION TIMES (PT, APTT, TT) – FFP – 15-20ml/kg + Cryoprecipitate – 1-2bags/10kg

* MAINTAIN PLATELET COUNT ~ 20,000/cu mm
  (>50,000/cu mm, IN CASE OF BLEEDING /
  ~80,000/cu mm FOR BIOPSY)

* MAINTAIN A 'SAFE' LEVEL OF HAEMOGLOBIN (8 – 10g%)
DRUG THERAPY FOR HAEMOSTASIS IN LIVER FAILURE

*VITAMIN K1 : 2.5-10mg SC / IM / slow IV (SINGLE DOSE)

*TRANEXAMIC ACID: Derivative of lysine

- Blocks conversion of plasminogen to plasmin
- 20-40mg/kg IN 3-4 div doses / day
- Avoid in DIC / presence of hematuria

*Novoseven - rFVIIa : One dose of 90 ug/kg can normalize PT for 12 hrs
Very expensive but often very effective
ANTICOAGULATION RELATED BLEED

**HASHTI**
1. **H**old further doses of anticoagulant
2. Consider **A**ntidote
3. **S**upportive treatment: volume resuscitation, inotropes as needed
4. Local or surgical **H**emostatic measures: topical agents (aminocaproic acid, tranexamic acid)
5. **T**ransfusion (red cells, platelets, FFP as indicated)
6. **I**nvestigate for bleeding source

### 1. Reversal of Warfarin (Coumadin®, Jantoven®)

<table>
<thead>
<tr>
<th>Non-Urgent</th>
<th>Urgent (Not Bleeding)</th>
<th>Urgent (Bleeding)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stop 5 days prior to procedure</td>
<td>• If procedure can be delayed 6-24 hours, vitamin K 5-10 mg PO/IV; otherwise • FFP or PCC prior to procedure. Repeat in 6-12 hours if INR high and • Vitamin K 5-10 mg PO/IV if sustained reversal is desired</td>
<td>• <strong>HASHTI</strong> • Vitamin K 5-10 mg IV; repeat every 12 hours as needed • PCC or FFP; repeat every 6 hours as needed</td>
</tr>
<tr>
<td>• Check INR 1-2 days prior</td>
<td>• If INR &gt;1.5 administer vitamin K 1-2 mg PO</td>
<td></td>
</tr>
<tr>
<td>• If INR &gt;1.5 administer vitamin K 1-2 mg PO</td>
<td>• repeat every 12 hours as needed</td>
<td></td>
</tr>
</tbody>
</table>
2. **Reversal of Low-Molecular-Weight Heparins (Enoxaparin/ Lovenox®, Dalteparin/ Fragmin®, Tinzaparin/ Innohep®) and Fondaparinux¹ (Arixtra®)**

<table>
<thead>
<tr>
<th>Non-Urgent</th>
<th>Urgent (Not Bleeding)</th>
<th>Urgent (Bleeding)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hold day of procedure</td>
<td>• Wait 12-24 hours if possible</td>
<td>• HASHTI</td>
</tr>
<tr>
<td>• Once-daily regimens</td>
<td>• Consider protamine sulfate if delay not possible for high bleeding risk procedure</td>
<td>• Protamine sulfate</td>
</tr>
<tr>
<td>◦ ½ dose day prior</td>
<td></td>
<td>• Consider rVIIa</td>
</tr>
<tr>
<td>• Twice-daily regimens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>◦ Hold evening dose day prior</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹Fondaparinux has no specific antidote
<table>
<thead>
<tr>
<th>Condition</th>
<th>Incidence (%)</th>
<th>Timing of Onset</th>
<th>Degree of Thrombocytopenia</th>
<th>Microangiopathic Chemolytic Anemia</th>
<th>Hypertension</th>
<th>Coagulopathy</th>
<th>Liver Disease</th>
<th>Renal Disease</th>
<th>CNS Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITP</td>
<td>3–4</td>
<td>Most common in first trimester, anytime</td>
<td>Mild to severe</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Gestational/incidental thrombocytopenia</td>
<td>75–80</td>
<td>Second–third trimester</td>
<td>Mild</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>15–20</td>
<td>Late second to third trimester</td>
<td>Mild to moderate</td>
<td>Mild</td>
<td>Moderate to severe</td>
<td>None to mild</td>
<td>None</td>
<td>Proteinuria</td>
<td>Seizures with preeclampsia</td>
</tr>
<tr>
<td>HELPP</td>
<td>—</td>
<td>Late second to third trimester</td>
<td>Moderate to severe</td>
<td>None</td>
<td>Absent to mild</td>
<td>Moderate to severe</td>
<td>None to moderate</td>
<td>None to moderate</td>
<td>None to moderate</td>
</tr>
<tr>
<td>DIC</td>
<td>Rare</td>
<td>Anytime</td>
<td>Moderate to severe</td>
<td>Mild</td>
<td>None</td>
<td>Mild to moderate</td>
<td>Variable</td>
<td>Variable</td>
<td>None</td>
</tr>
<tr>
<td>AFLP</td>
<td>Rare</td>
<td>Third trimester</td>
<td>Mild</td>
<td>None</td>
<td>None to mild</td>
<td>Severe</td>
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<td>None to mild</td>
<td>None</td>
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<tr>
<td>TTP</td>
<td>Rare</td>
<td>Second to third trimester</td>
<td>Severe</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None to moderate</td>
<td>None to severe</td>
</tr>
<tr>
<td>HUS</td>
<td>Rare</td>
<td>After birth</td>
<td>Moderate to severe</td>
<td>None</td>
<td>None to mild</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Moderate to severe</td>
</tr>
</tbody>
</table>

THROMBOTIC MICROANGIOPATHY

- Plasmapheresis: First-line therapy – removes platelet-aggregating substances. Rx 90% successful with TTP but is less with HUS.
- Plasma infusion daily (FFP)
- Steroids not very useful (response rates 25%).
- Avoid Platelet transfusions – can cause clinical deterioration. Use only for uncontrolled or intracranial bleeding.
- Other drugs – IS agents (Vincristine, CSA, azathioprine), antiplatelet drugs for TTP, and hemodialysis for HUS.
- No indication for premature termination of pregnancy unless no response to other Rx.