According to International Society of Thrombosis & Hemostasis

- Disseminated intravascular coagulation (DIC) is an acquired syndrome characterized by intravascular activation of coagulation with loss of localization arising from different causes.

- It can originate from and also cause damage to the microvasculature, which if sufficiently severe, can produce multi-organ dysfunction.
DIC occurs in 30 – 50% of patients with sepsis, with equal frequency in gram positive and gram negative bacterial infections.

It can occur in more than 50% patients with abruptio placentae, septic abortions and amniotic fluid embolism.

In about 30% patients with HELLP syndrome and severe pre eclampsia

In 10 -15% of Cancer patients with metastasis

50 -70% pts with neurotrauma
Summary Of Coagulation Pathways
Pathophysiology

Underlying Disease

Toxins, Proinflammatory cytokines

Activation of Monocytes & Endothelial Damage

Tissue Factor Release

Stimulation of Extrinsic Pathway

Uncontrolled Thrombin Release

Fibrin Deposits in the Microcirculation

Microvascular Thrombosis

Ischemic Organ Damage

Multi-organ Failure

Micro Angiopathic Hemolytic Anemia

Secondary Fibrinolysis

Bleeding & Fibrin Degradation Products Released

Consumption of Platelets and clotting Factors

Bleeding

Multi-organ Failure
Clinical Features of DIC

- Skin ecchymosis
- Bleeding from i/v sites, endotracheal tubes and urinary catheters.
- Gingival bleeding, epistaxis, malena
- Cough, dyspnoea
- Confusion, disorientation
- Fever

In addition, symptoms related to underlying disease
Common Clinical Causes Of DIC

Sepsis
- Bacterial: staphylococci, streptococci, pneumococci, meningococci, gram negative bacilli
- Viral
- Mycotic
- Parasitic
- Rickettsial

Trauma and tissue injury
- Brain injury, extensive burns, fat embolism, rhabdomyolysis
Common Clinical Causes Of DIC

Drugs

- Fibrinolytic agents, aprotinin, warfarin, prothrombin complex concentrates, amphetamine

Vascular disorders

- Giant hemangiomas, aortic aneurysms

Obstetrical complications

- Abruptio placentae, amniotic fluid embolism, septic abortion, dead fetus, HELLP syndrome, severe pre eclampsia

Cancer

- Adenocarcinoma of pancreas, prostrate, hematologic malignancies
Common Clinical Causes Of DIC

Immunologic disorders
- Acute hemolytic transfusion reaction, organ or tissue transplant rejection, Graft versus host disease

Envenomation
- Snake, insects

Liver disease
- Fulminant hepatic failure, cirrhosis, fatty liver of pregnancy

Miscellaneous
- Shock, acute respiratory distress syndrome, massive transfusion
Fibrinolytic System
Laboratory Studies

Screening assays
- Prothrombin time (PT)
- Activated partial thromboplastin time (APTT)
- Platelet count, RBC count and blood smear analysis
- Fibrinogen levels

Lab markers of thrombin generation
- D–dimer
- Protamine paracoagulation assay for fibrin monomer
- Ethanol gel assay for fibrin monomers
- Thrombin anti-thrombin complex

Ancillary tests
- Fibrin degradation products
- Antithrombin levels
- Anti plasmin levels
- Factor V levels
D-dimer test
- It is a very sensitive test for the diagnosis of DIC
- The test has a negative predictive value of > 90%
- Normal value is 0.2 – 0.5 mg/ml

False positive D-dimer test
- Recent surgery
- Trauma
- Renal, liver and cardiac failure
Fibrin degradation products

- FDPs are a measure of plasmin cleaved fibrinogen or fibrin
- FDPs do not distinguish between plasmin degradation by product of either fibrin or fibrinogen
- FDPs have a sensitivity of 85% & specificity 50%
- Normal value < 10 mg/ml
- A combination of FDP and D dimer has 100% specificity and sensitivity
## Diagnostic Criteria for DIC

**International Society for Thrombosis and Hemostasis**

**Disseminated Intravascular Coagulation Scoring System**

Use only in patients with an underlying condition known to be associated with DIC

<table>
<thead>
<tr>
<th><strong>Parameter</strong></th>
<th><strong>0</strong></th>
<th><strong>1</strong></th>
<th><strong>2</strong></th>
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<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>&gt; 100,000 /mm³</td>
<td>≤ 100,000 / mm³</td>
<td>≤ 50,000 / mm³</td>
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<tr>
<td>D-dimer</td>
<td>Normal</td>
<td>≤ 10 times ULN</td>
<td>≥ 10 times ULN</td>
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<tr>
<td>PT prolongation</td>
<td>&lt; 3 sec</td>
<td>3-6 sec</td>
<td>&gt; 6 sec</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>&gt; 100 mg/dl</td>
<td>≤ 100 mg/dl</td>
<td></td>
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</tbody>
</table>

Overt DIC ≥ 5 points
Non overt DIC < 5 points
## Acute and Chronic DIC

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Acute (decompensated DIC)</th>
<th>Chronic (compensated DIC)</th>
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</thead>
<tbody>
<tr>
<td>Platelet count</td>
<td>Reduced</td>
<td>Variable</td>
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<tr>
<td>Prothrombin time</td>
<td>Prolonged</td>
<td>Normal</td>
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<tr>
<td>APTT</td>
<td>Prolonged</td>
<td>Normal</td>
</tr>
<tr>
<td>Thrombin time</td>
<td>Prolonged</td>
<td>Normal</td>
</tr>
<tr>
<td>Plasma fibrinogen</td>
<td>Reduced</td>
<td>Normal – elevated</td>
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<tr>
<td>Plasma factor 5</td>
<td>Reduced</td>
<td>Normal</td>
</tr>
<tr>
<td>Plasma factor 8</td>
<td>Reduced</td>
<td>Normal</td>
</tr>
<tr>
<td>Fibrin degradation products</td>
<td>Elevated</td>
<td>Elevated</td>
</tr>
<tr>
<td>D-dimer</td>
<td>Elevated</td>
<td>Elevated</td>
</tr>
</tbody>
</table>

Reference: Medicine Update 2015
Differential Diagnosis of DIC

- Advanced liver disease
- Thrombotic micro angiopathy
- Fibrinogenolysis
- Disorders of hemostasis (correctable factor deficiency, vit k deficiency)
- Thrombocytopenia
Management of DIC

- Management of DIC involves following three important steps, which should be initiated timely and sequentially.

  I. Vigorous therapy underlying disorder.
  II. Energetic treatment of life threatening complication e.g. shock, hypoxaemia, and acidosis.
  III. Therapy of DIC per se.

- When there is no bleeding or venous thromboembolism with only lab parameters deranged - observation without any replacement therapy
- Frequent monitoring of blood counts and clotting factors
- Monitoring the CVP, gas exchange and electrolyte balance
Prompt treatment of the underlying cause

- Optimal antibiotics in sepsis syndrome
- Uterine evacuation for abruptio placenta
- Restoration of hemodynamic stability for hypovolemic shock
- Anti snake venom for snake bite

ANTIBIOTICS

- Always i.v antibiotics are given
- started after taking blood cultures
- Outcomes are worse if the organism is insensitive to the initial regimen
COMPONENT SUPPORT

PLATELET TRANSFUSION

- Platelet count should be maintained around 20,000-30,000/mm$^3$ in a bleeding patient
- single donor platelet transfusion

CRYOPRECIPITATE

- Is rich in factor VIII, Fibrinogen and VWF
- 1-2 units/ 10 kg can be given
- Maintain fibrinogen level > 100 mg/dl
Management of DIC (Contd…)

FRESH FROZEN PLASMA
- Provides all clotting factors and corrects PT and APTT
- Dose 10-15ml/kg every 8-12 hrly
- Transfusion can be stopped once lab parameters improve

ANTITHROMBIN CONCENTRATES
- More effective in the presence of hepatic insufficiency

ACTIVATED PROTEIN C CONCENTRATES (Drotecogin alfa)

PROTHROMBIN COMPLEX CONCENTRATES
HEPARIN

- Is a naturally occurring anticoagulant
- In acute DIC heparin can aggravate bleeding
- To date use of heparin in acute DIC has no proven survival benefit

Indications of heparin in DIC

- Chronic DIC of malignancy
- Clinical thrombosis: dermal necrosis, purpura fulminans, acral ischemia, VTE
- Retained dead fetus with hypofibrinogrnemia
- AML M3 prior to conventional chemotherapy
SYNTHETIC INHIBITORS OF THROMBIN

- Hirudin, desirudin, bivalirudin, argatroban, melagatran, ximelgatran, dabigatran
- Can be used in heparin induced thrombocytopenia and when heparin is ineffective in the presence of antithrombin deficiency

FIBRINOLYSIS INHIBITORS

- They block the secondary fibrinolysis that accompanies DIC
  - Tranexamic acid and Epsilon Amino Caproic Acid (EACA) prevent fibrin degradation by plasmin and reduce bleeding episodes in patients with confirmed fibrinolysis
Prognosis depends on the underlying disorder
- If the condition is self-limiting, prognosis is good
- Appropriate and early initiation of antibiotic therapy has a positive impact on the outcome
- Prognosis is poor if there is
  - Failure to recognize the underlying etiology and in case of sepsis if the organism is insensitive to the initial empirical antibiotic regimen
References

- Harrison’s principles of internal medicine
- API Medicine update, VOLUME 25, 2015
- Furlong MA, Furlong BR. Disseminated intravascular coagulation. Jan 2009
- Disseminated intravascular coagulation in obstetric disorders and its acute hematological management, Jecko Thachil, School of Clinical Sciences, University of Liverpool, UK, 2009
Thank You !