DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

TERM DEFINITION

A syndrome characterized by the systemic activation of blood coagulation, which generates intravascular fibrin, leading to thrombosis of small and medium-sized vessels, and eventually organ dysfunction.

TYPES OF DIC

ACCORDING TO PREDOMINANT CLINICAL PHENOTYPE

THROMBOTIC TYPE DIC	FIBRINOLYTIC TYPE DIC	PURPURA FULMINANS
Usually seen in patients with sepsis; characterized by multiorgan failure from widespread clotting	Typically seen in patients with trauma or acute leukemia; associated with excessive fibrinolysis and severe bleeding complications	Associated with characteristic skin lesions and particularly low protein C levels

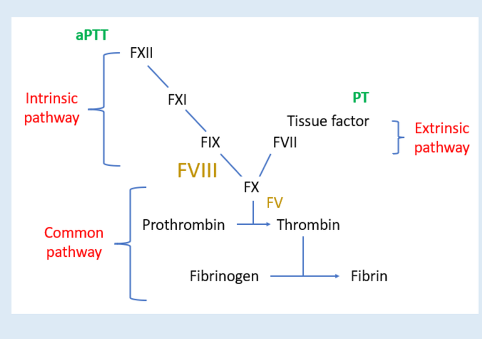
Other classifications include: Acute vs. chronic DIC | Overt vs. non-overt

CAUSES

- Infection (often chronic)
- Cancer
- Trauma
- Acute pancreatitis
- Liver failure
- Obstetrical disease

CLINICAL PEARLS

DIC is *not* a disease; it is a manifestation of other disorders



The PT/INR is more sensitive than the aPTT in diagnosing DIC, possibly because acute phase reactant FVIII (in the intrinsic pathway) is elevated

A low fibrinogen level is not very sensitive for diagnosing DIC because fibrinogen is an acute phase reactant (levels are low in only 30% of patients)

Some people consider DIC to be a type of **thrombotic microangiopathy** (TMA). Others seem to prefer excluding DIC from the TTP umbrella. In fact, DIC meets the definition for TMA, the major difference being that it involves activation of coagulation (the TMA conditions being platelet-mediated)

DIC is associated with the presence of **schistocytes** on the peripheral blood, but they are not nearly as numerous as in TTP, and they are not part of the clinical prediction scores for DIC

PRESENTATION

SIGNS & SYMPTOMS

Thrombotic-type DIC typically presents with multiple organ failure or skin lesions whereas **fibrinolytic type DIC** is characterized by oozing-type bleeding from multiple unrelated sites. **Purpura fulminans** presents with characteristic skin lesions.

LABS

HEMATOLOGICAL FINDINGS

- Thrombocytopenia (in 98% of cases)
- Anemia with schistocytes on peripheral smear

Other hematological findings associated with inflammation may include:

- Leukocytosis
- Left shift
- Reduced levels of clotting factor activity, though FVIII may be preserved because it is an acute phase reactant

OTHER LAB FINDINGS

Positive acute phase reactants associated with inflammation include elevated serum:

- C-reactive protein (CRP)
- Haptoglobin
- Ferritin

Negative acute phase reactants associated with inflammation include decreased serum:

- Albumin
- Total iron binding capacity

DIAGNOSIS

There is no single laboratory test specific for DIC

DIC is highly dynamic, so it is important to repeat testing over time

DIAGNOSTIC SCORING SYSTEMS

- **International Society of Thrombosis and Haemostasis (ISTH)***
- Japanese Association of Acute Medicine (JAAM)
- Japanese Ministry Health, Labour and Welfare (JMHLW)

** The ISTH score is most widely used in US*

ISTH DIAGNOSTIC SCORING SYSTEM

Note: *This scoring system is only appropriate for patients with an underlying disorder that can be associated with DIC*

PLATELET COUNT	POINTS
>100,000/ul	0
50-100,000/ul	1
< 50,000/ul	2

PT PROLONGATION	POINTS
3 seconds or less	0
> 3 seconds, < 1 second	1
> 6 seconds	2

FIBRIN MARKERS*	POINTS
No change	0
Moderate rise	1
Strong rise	2

FIBRINOGEN LEVEL	POINTS
> 1 g/L	0
< 1 g/L	1

*Fibrin degradation products or D-dimers

0-4 POINTS, NO OVERT DIC | 5-8 POINTS DIC PROBABLE

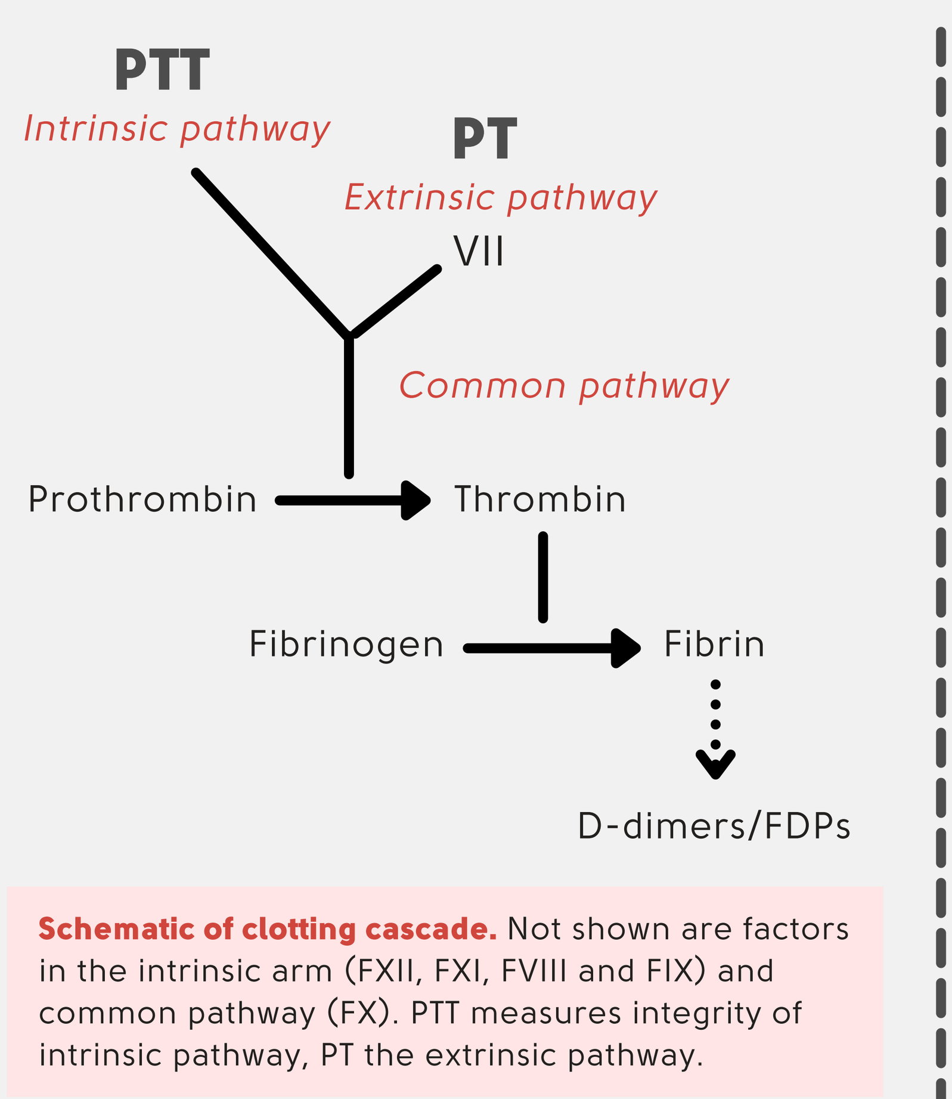
THERAPEUTIC PRINCIPLES

1. Treat underlying condition causing DIC
2. Replace depleted clotting factors, typically with **fresh frozen plasma** and **cryoprecipitate**, and platelets with **platelet transfusions**, if patient is actively bleeding or at high risk of bleeding (for example, with procedures). *Do not* treat the numbers!
3. Provide prophylactic anticoagulation in all non-bleeding patients with DIC. Consider therapeutic **heparin** in patients with thrombotic-type DIC and multiorgan failure.

COMPARATIVE PHYSIOLOGY

DIC has been described in a variety of clinical settings and in various experimental conditions. It was first reported in 1889 in rabbits subjected to burns. In 1961, intravascular thrombosis was reported as a result of intravascular hemoconcentration in porcine edema disease. Since then, DIC has been widely reported in pigs with porcine erysipelas, calves with septicemia, especially colibacillosis; and in death due to shock, especially in canine species. A quick perusal of PubMed also yields descriptions of DIC in **minks**, dolphins, and horses. There is widespread appreciation in the comparative literature that DIC is not a primary disease, but rather reflects a complication of an underlying condition such as neoplasm or infection.

PROXIMATE MECHANISMS

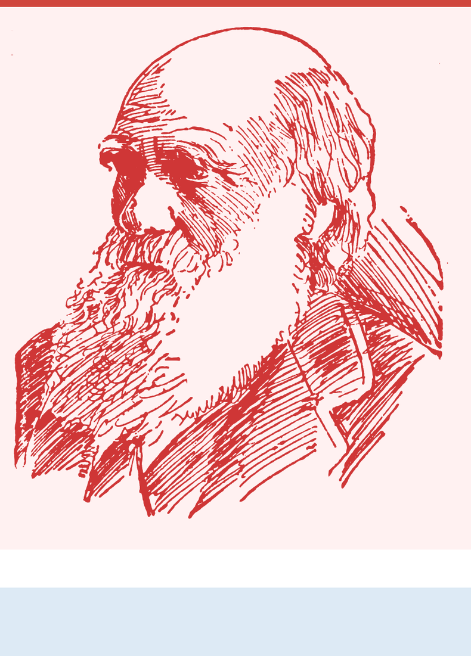


Schematic of clotting cascade. Not shown are factors in the intrinsic arm (FXII, FXI, FVIII and FIX) and common pathway (FX). PTT measures integrity of intrinsic pathway, PT the extrinsic pathway.

In DIC, there is **overwhelming activation of the clotting cascade** via tissue factor-mediated activation of factor VII. This leads to **deficiency of virtually all clotting factors**, since the liver, which produces all clotting factors except FVIII, can't keep up with factor consumption. As factors are depleted, the PT and to lesser extent the PTT increase. One reason for the poor sensitivity of a prolonged PTT is that FVIII (intrinsic arm) is an acute phase reactant and does not become as depleted as the other factors. As long as there is enough substrate (fibrinogen), **fibrin is formed, leading to microvascular occlusion**. Platelets become trapped and consumed in the clot, leading to thrombocytopenia. The fibrin is degraded into D-dimers/FDPs. Eventually, with sufficient loss of clotting factors, or with hyper-activation of fibrinolysis, **the phenotype may switch from thrombotic to bleeding**.

EVOLUTIONARY MECHANISMS

The closed circulation evolved in the ancestral vertebrate. It is accompanied by high blood pressures to ensure sufficient oxygen delivery to the tissues. High pressures mean increased susceptibility to wear and tear in the circulation, and this was most certainly the prime selective pressure for the appearance of a highly complex clotting system to stem the loss of blood. In DIC, the clotting mechanism turns on its bearer. This may represent a trade-off for having such a responsive repair system.



HISTORY OF MEDICINE

As late as 1967, authors were noting that: "[DIC] is a new concept in the etiology disease". More aptly, another paper from the same year noted that "behind every clotting episode [referring to DIC] there lies an etiological factor that triggers the clotting" and that the best prevention and treatment of intravascular coagulation lies in the prevention and treatment of the underlying disease. In some respects, little has changed!

NOTES

ATTRIBUTIONS

Written by Dr. William Aird

Input from Dr. Stephen Stearns *(Evolutionary Medicine)*
Dr. John Harvey *(Comparative Physiology)*
Dr. Jane Maienschein & Dr. Kate McCord *(History of Medicine)*

The Blood Project
ENCYCLOPEDIA OF BLOOD