# *Disseminated Intravascular Coagulation (DIC)*

Moderators: Christian von Heymann

Monday, June 08, 2026

## 1. DISSEMINATED INTRAVASCULAR COAGULATION - BASIC

Ecaterina Scarlatescu

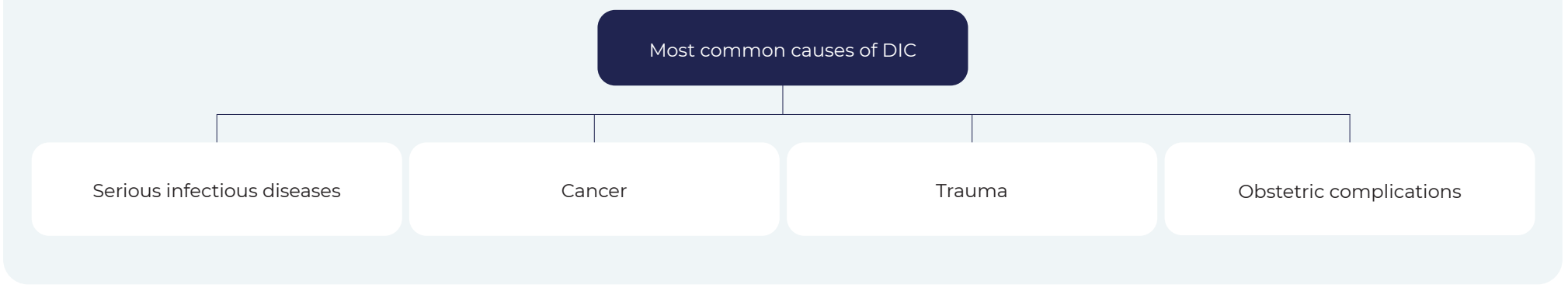
Disseminated Intravascular Coagulation (DIC) is an acquired syndrome characterized by intravascular activation of coagulation, with a loss of its physiological control, due to several causes; this causes damage to the microvasculature and, when severe, may lead to organ dysfunction[1]. This is a heterogeneous concept due to the various criteria used by physicians to determine the presence of DIC.

The DIC Subcommittee of the International Society on Thrombosis and Haemostasis (ISTH) updated the definition in 2025:

**DIC is an acquired, potentially-lethal disorder characterised by the systemic activation of coagulation, dysregulated fibrinolysis and endothelial damage, leading to the formation of microthrombi.**

Moreover, the ISTH stressed that, although clinical and laboratory manifestations of advanced DIC are similar regardless of the underlying cause, the phatophysiology of the early phase varies depending on the triggering disease, and that diagnosis and treatment in early stages must be adapted to the specific aetiology[2].

DIC always occurs as a consequence of an underlying condition. Sepsis is the most common cause, and roughly 30-50% of septic patients suffer from DIC[3].




DIC is a dynamic condition and behaves differently depending on whether it is compensated or decompensated.

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|---|---|
| **Compensated** | Coagulation is triggered with thrombin generation and platelet and white blood cell activation, but the regulatory mechanisms are still able to partially contain the process.<br>There are no clinical manifestations of bleeding or thrombosis.<br>There are no changes in coagulation tests. |
| **Decompensated** | When regulatory mechanisms are insufficient, established DIC develops.<br>Clinical manifestations are observed.<br>Abnormal values are observed in coagulation tests and the platelet count. |

The clinical expression of DIC depends on the balance between the activation of coagulation and fibrinolysis. The following patterns can be identified, and they can be distinguished using viscoelastic tests[4]:

- **Thrombotic**, characterised by the predominance of microvascular thrombosis.
- **Haemorrhagic**, characterised by the predominance of bleeding.
- **Asymptomatic**, with both systems activated and compensating for one another, with no obvious clinical manifestations and with normal viscoelastic tests.

Although the causes of DIC may vary, there is a common starting event: the increase and systemic spread of thrombin generation[5].

### PATHOPHYSIOLOGY OF DIC:

In sepsis, DIC has four distinct causes[6].

**1. Activation of coagulation:** Infection and inflammation activate coagulation through mechanisms specific to the innate immune system. The activation of coagulation during sepsis does not depend on a single mechanism, but rather on the interaction of multiple components.

| | | | |
|---|---|---|---|
| **Tissue factor** | **Extracellular vesicles** | **Platelets** | **Von Willebrand factor** |
| **Extracellular neutrophil traps (ENTs)** | **Pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs)** | **Polyphosphates** | **Complement** |

**2. Alteration of anticoagulant mechanisms:** Sepsis leads to a progressive loss of the physiological mechanisms limiting coagulation.

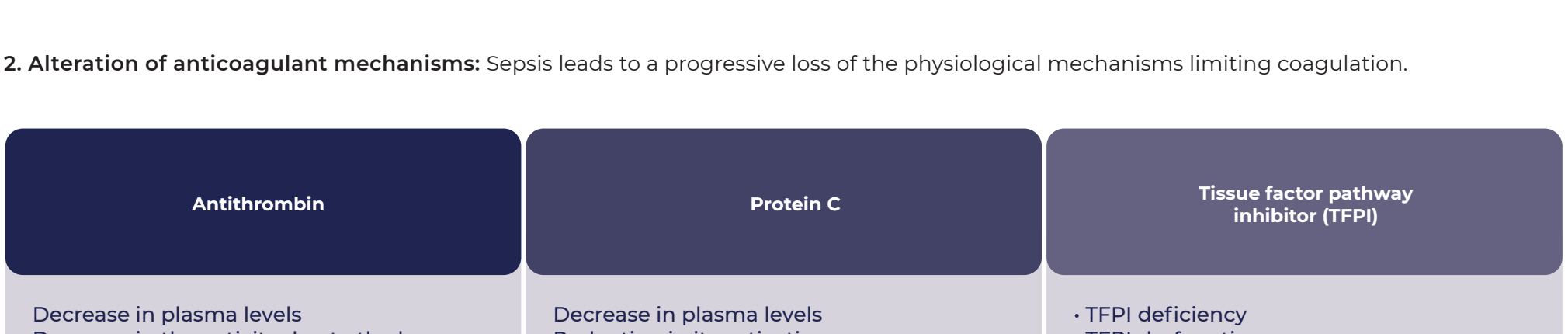
| **Antithrombin** | **Protein C** | **Tissue factor pathway inhibitor (TFPI)** |
|---|---|---|
| Decrease in plasma levels<br>Decrease in the activity due to the loss of cofactors | Decrease in plasma levels<br>Reduction in its activation | • TFPI deficiency<br>• TFPI dysfunction |

**3. Alteration of fibrinolysis:** The fibrinolytic response can vary depending on the clinical context and the pattern observed:

- Phenotype I: Inhibited fibrinolysis.
- Phenotype II: Increased fibrinolysis.
- Phenotype III: Balanced fibrinolysis, which is usually asymptomatic until the physiological balance is disrupted.

**4. Endothelial damage:** Endothelial damage: Endothelial damage is the fourth pillar of the pathophysiology of DIC[7]. In sepsis, the glycocalyx is destroyed from the very early stages, which promotes the adhesion of white blood cells and the formation of thrombi.

Organically, a vicious circle develops between hypoxia and the activation of coagulation: microvascular thrombosis leads to tissue hypoxia. This hypoxia stabilises HIF-1α, which increases the expression of the tissue factor and PAI-1, and reduces that of certain anticoagulant proteins, further promoting thrombosis[8].




Last, it is important to note that immunothrombosis is initially a protective mechanism against pathogens, but when it becomes dysregulated, it leads to the development of DIC and multiorgan failure. In this regard, the link between coagulation and the activation of the immune system offers an opportunity to develop treatment strategies based on anticoagulation in sepsis[9].

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## 2. DISSEMINATED INTRAVASCULAR COAGULATION - ADVANCED

Marcella Muller

DIC is a dynamic process, the identification of which remains a clinical challenge. Its diagnosis is still based primarily on conventional coagulation tests.

A survey conducted by the ISTH found that platelet count, prothrombin time (PT/INR), activated partial thromboplastin time (aPTT), fibrinogen and D-dimer are the most widely used parameters in clinical practice. Other necessary biomarkers are not universally available, which makes it difficult to consistently apply the diagnostic criteria[10].

A number of diagnostic scoring systems have been developed in the last few years. The *Japanese Association for Acute Medicine* (JAAM) and the ISTH updated their diagnostic criteria in 2024 and 2025, respectively, to include the following parameters: platelet count, PT/INR, fibrin degradation products (FDP) and fibrinogen[11].

All systems share significant limitations:

- They use non-universally available parameters.
- They basically detect established DIC rather than compensated DIC.
- They do not estimate the risk of haemorrhage or thrombosis.
- The validation of JAAM and SIC scores has been carried out primarily in patients with sepsis.

Despite these limitations and the fact that their clinical use remains limited, scoring systems continue to be necessary tools to objectively identify patients with DIC.

Other alternative markers may be used, but they are not always available.

| Endogenous anticoagulants | Endothelial makers | Nuclear materials | Other relevant markers | Comprehensive haemostasis tests |
|---|---|---|---|---|
| • Antithrombin<br>• Protein C<br>• Thrombomodulin<br>• TFPI | • Von Willebrand factor<br>• ADAMTS-13 | • HMGB1<br>• Nucleosomes<br>• Histones<br>• Circulating free DNA | • Complement<br>• Presepsin | • ROTEM<br>• TEG<br>• Quantra<br>• ClotPro |

As for viscoelastic tests, they help detect states of hypocoagulability and hypercoagulability. However, presently, they are not sufficiently standardised to detect DIC.

## COMPLICATIONS

DIC is associated with both thrombotic and haemorrhagic complications.

- In a large European multicentre cohort of over 1,000 patients at risk of DIC, 5 out of every 100 developed a major haemorrhagic episode (Taha et al. ESICM 2025).
- Thrombotic complications also occur more frequently in patients with DIC, not only microthrombosis and immunothrombosis, but also major thrombotic events (unpublished data from Muller and Juffermans).

Treatment decisions aimed at correcting analytical abnormalities prior to invasive procedures remain a subject of debate. A randomised trial in patients with thrombocytopenia undergoing central venous catheter insertion showed that the discontinuation of prophylactic platelet transfusion increases the risk of procedure-related bleeding[12]. However, the optimal transfusion threshold must be defined. Furthermore, the prophylactic administration of fresh frozen plasma has not been shown to reduce the risk of bleeding in critical patients with coagulopathy[13].

## TREATMENT

The treatment of DIC should be based on three fundamental principles:

1. **Treating the triggering condition**
2. **Inhibiting the activation of coagulation where indicated**
3. **Adapting the management of the predominant clinical phenotype, taking into account the triggering condition**

If we focus on the management of patients with fibrinolytic phenotype, the use of tranexamic acid may be considered. In patients with a thrombotic phenotype, anticoagulation is a potential strategy, but there is not enough high-quality evidence on this matter[2].

### Heparin

Although clinical trials with heparin in patients with sepsis have not shown a consistent benefit in terms of survival, in patients with sepsis-associated pre-CID, low-dose heparin is suggested to improve hypercoagulability and multi-organ dysfunction[2,14].

Consequently, the ISTH recommendations state that heparin may be considered in patients with coagulopathy before the development of a established DIC, with the aim of preventing its progression[2].

### Antithrombin

Clinical trials with antithrombin in patients with severe sepsis have not shown a reduction in mortality, but have shown an increased risk of haemorrhage[15], particularly when administered alongside heparin[16].

### Thrombomodulin

The SCARLET trial assessed thrombomodulin in patients with sepsis-associated coagulopathy and did not show a significant reduction in mortality, except for the subgroup of patients with baseline INR > 1.4 and baseline platelet count > 30[17].

## FUTURE PROSPECTS

Main needs identified to improve the management of DIC:

- **Developing tools for the early identification of DIC and distinguishing phenotypes at the beside.**
- **Improving the determination of haemorrhagic and thrombotic risk.**
- **Establishing optimal thresholds to correct coagulopathy.**
- **Developing clinical trials of personalised treatment strategies based on the phenotype and the stage of the disease.**

In this context, a number of studies are currently under way to evaluate new diagnostic and treatment approaches, including the use of ROTEM in critical patients at risk of DIC, the determination of the optimal threshold for platelet transfusion, and the role of heparin in sepsis-induced DIC, among others.

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