Disseminated Intravascular

Coagulation (DIC)

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Disseminated Intravascular Coagulation (DIC)

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Latest Update

First Edition

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First Edition 2020

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Intended Learning Outcomes

Disseminated Intravascular Coagulation (DIC)

1. Describe the clinical syndrome of disseminated intravascular coagulation (DIC)
2. Understand clinical consequences of DIC including the risk for bleeding and thrombosis
3. Describe the pathophysiology of DIC
4. Recognize the patient at risk for DIC
5. Interpret laboratory findings in DIC
6. Determine the likelihood of DIC with the use of scoring systems
7. List differential diagnoses of DIC
8. Describe supportive care for DIC
9. Describe transfusion strategies for DIC
10. Describe current and future anticoagulant strategies for DIC
11. Understand the prognosis and clinical outcomes of DIC

eModule Information

Relevant competencies from CoBaTrICE

Disseminated Intravascular Coagulation (DIC)

- **2.1** Obtains a history and performs an accurate clinical examination
- **2.2** Undertakes timely and appropriate investigations
- **2.10** Integrates clinical findings with laboratory investigations to form a differential diagnosis
- **3.1** Manages the care of the critically ill patient with specific acute medical conditions
- **4.1** Prescribes drugs and therapies safely
- **5.10** Performs arterial catheterisation
- **6.1** Manages the pre- and post-operative care of the high risk surgical patient

Faculty Disclosures:

The authors of this module have not reported any disclosures.

1. Introduction

Disseminated intravascular coagulation (DIC) is a syndrome characterised by systemic intravascular activation of coagulation, leading to the widespread deposition of fibrin, with formation of widespread microvascular thrombosis. These microthrombi impair organ perfusion and thus contribute to organ failure. During the coagulation process, consumption of coagulation factors and aggregation of platelets occur resulting in reduced levels of both procoagulant and anticoagulant clotting proteins. Therefore patients with DIC may have both thromboembolic events and hemorrhage.

The Subcommittee on DIC of the International Society on Thrombosis and Haemostasis has suggested the following definition for DIC: "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 and produce organ dysfunction".

Patients with DIC can have renal, hepatic and respiratory organ failure, as well as central nervous system (CNS) and cutaneous/skin sequelae. Thromboembolic complications can include both venous and arterial thrombosis. Venous embolism include deep venous thrombosis and pulmonary embolism, which may be asymptomatic. Arterial thrombosis includes acute limb ischemia and intraabdominal thromboses. Bleeding may present as petechiae/ecchymoses (Figure 1) or oozing from wounds, sites of intravascular access, mucosal surfaces and the gastrointestinal tract. Bleeding and thromboembolic events may occur simultanously.

Figure 1: Skin lesions in DIC.

2. Etiology of DIC

DIC never occurs by itself but is always secondary to an underlying disorder. DIC is associated with a number of clinical conditions that generally involve activation of systemic inflammation except for snake envenomations. These are listed in Table 1.

Table 1: Clinical conditions associated with DIC
Severe infection and sepsis
Solid tumors
Hematologic malignancies
Obstetrical complications (HELLP, fluid embolism, eclampsia)
Acute pancreatitis
Trauma
Severe transfusion reactions
Snake venom or other severe toxic reactions
Heat stroke and hyperthermia

Severe infection and sepsis induce DIC through the release of proinflammatory cytokines, such as TNF-α and intraleukin (IL)-6.

In sepsis, the cytokine release is induced by microbial membrane components which cause a strong immune response. An increase in expression of tissue factor (TF) on immune cells probably triggers a procoagulant response. Also, severe infection and sepsis result in activation of the endothelium, which then also expresses tissue fator and sheds high quantities of von Willeband factor, which initiates platelet aggregation. Both Gram negative and Gram positive microorganisms have been associated with DIC, as have viral and fungal pathogens.

Additionally, the cytokines released during sterile systemic inflammation, eg. in severe acute pancreatitis, can lead to endothelial cell activation and coagulation dysfunction.

Malignancies may be complicated by DIC through an increased expression of tissue factor, microparticles and cancer specific procoagulants by tumor cells. Usually thrombotic events appear more frequently than hemorrhage in DIC resulting from cancer.

Obstetric complications causing DIC consist of abruptio placentae, amniotic fluid embolism and pre-eclampsia. In patients with abruptio placentae, the cause of the activation of the coagulation system is most likely the leakage of TF from the placental system into the maternal circulation. In the case of amniotic fluid embolism, the release of procoagulant phosphatidylserine and tissue factor exposing extracellular vesicles may be of importance in the development of DIC.

Trauma patients also develop heightened activation of the coagulation system and accelerated fibrinolysis due to an inflammatory responde during acute injury. However, whether DIC in trauma patients exists is a controversial topic, and some authorities have preferred to differentiate the two entities, preferring the term Trauma Induced Coagulopathy (TIC).

3. Diagnosis of DIC

First, think whether DIC could be a possible complication of the patient's presenting condition. In other words, are there underlying risk factors that are associated with DIC? Check the patient for signs of DIC and possible trombotic or bleeding complications. A single laboratory marker to diagnose DIC is not available. DIC is a clinical-pathological diagnosis, with a specific pattern of laboratory results, but unfortunately these coagulation results can look the same as the coagulation defects associated with advanced liver disease. It should also be taken into consideration that laboratory results may vary over time as DIC is a dynamic condition. However, abnormal coagulation lab results combined with a clinical presentation known to be linked to DIC supports the diagnosis.

Prothrombin time (PT), activated thromboplastin time (aPTT), fibrinogen and platelet count provide useful information concerning the activation of coagulation and consumption of procoagulant factors. Fibrin related markers (D-dimer, fibrin degradation products) indicate the state of fibrinolysis. Typical abnormalities in DIC are prolonged PT, prolonged aPTT, thrombocytopenia, elevated fibrin related markers and reduced fibrinogen levels.

⚠️ **Warning**

Note that these abnormalities resemble that of liver disease.

◎ **Task**

Test your ability to diagnose DIC

A female of 30 yrs of age with a recent history of joint pains (not yet with an established cause) presents to the Emergency Department with fatigue, muscle pain, fever and confusion. She is in haemodynamic shock with low blood pressure and a lactate level of 6 mmol/L. Platelet count is 80×10^9 /L, PT is 14 sec, WBC is 14×10^9 /L, and there are some fragments (schistocytes) in the smear. She is diagnosed with sepsis, resuscitated and intubated. Broad spectrum antibiotics are administered. Renal replacement therapy is started because of anuria. In the following hours, her shock stabilizes. The next morning, lab results are repeated and it appears that platelet count has dropped further to 15×10^9 /L. This worries you and you re-think the cause of thrombocytopenia.

❓ *what is your differential diagnosis of the thrombocytopenia?*

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

A

- DIC, because sepsis is a risk factor and tests can be compatible with consumption coagulopathy
- Sepsis associated thrombocytopenia not meeting DIC criteria (increased consumption and sequestration, decreased production)
- consumption of platelets due to the RRT filter, because these filters can remove platelets from the circulation and PT count can be prolonged with anticoagulation for the RRT
- Hemolytic Uremic Sydrome or Thrombocytopenic Thrombotic Purpura. (Though the vast majority of TTP cases are idiopathic, there is some association with lupus.).
  - Caveat: This degree of thrombocytopenia would be atypical for HUS, and the degree of renal injury would be uncommon in TTP.

? Which test needs to be done without delay?

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

A ADAMTS13. Activity levels of less then 10% indicate TTP, a disease condition characterized by a deficiency of the enzyme ADAMTS13. The purpose of ADAMTS13 is to cleave ultralarge von Willebrand Factor multimers which easily stick to platelets due to a high affinity. If there is not enough ADAMTS13 activity, these ultralarge vWF multimers form micro thrombi, which disturb the microcirculation. Plasma exchange is life-saving in TTP by removing inhibitory antibodies and ULVWF from the circulation, in addition to replenishing ADAMTS13 enzyme activity. Therefore, this treatment should be initiated immediately in case of TTP.

In sepsis, there is excessive endothelial secretion of vWF while ADAMTS13 activity is reduced, resulting in a similar imbalance as seen in TTP. Note also the similarities in coagulation adnormalities between DIC and TTP (Table 2). However, ADAMTS13 levels in sepsis usually remain >

20-30%, which can be used to differentiate DIC from TTP. In this case, TTP is less likely because the degree of renal failure is usually not present and HUS is less likely as this usually does not present with such low platelet counts.

⚠ **Warning**

Both HUS and TTP are medical emergencies, and immediate consultation should be sought for the consideration of plasmapheresis if they are suspected.

Table 2: Similarities between TTP and DIC

Parameter	TTP	DIC
Cause	Abs against A13	Cons of A1
ADAMTS13 levels	<10%	20-8(
VWF	High	High
PT	NL	Incre
Fibrinogen	NL	Decr
Platelets	Low ++	Low
D-dimers	Normal/increased	Incre
Fragmentocytes	++	++
Microthrombi	++	++

3. 1. Scoring systems for the diagnosis of DIC

None of the mentioned laboratory values (platelet count, PT, APTT, fibrinogen and fibrinogen degradation products) alone is specific enough to determine whether DIC is present or not. Therefore, scoring systems have been developed to assess the diagnosis. The International Society on Thrombosis and Haemostasis (ISTH) DIC score is widely used to diagnose patients with overt DIC (ISTH score ≥5). The Japanese Association for

Acute Medicine (JAAM) score is specifically designed for the acute onset of "sepsis-induced coagulopathy". This score may be useful to identify non-overt DIC (ISTH score 1-4). This may be relevant, as recent studies suggest that anticoagulant therapy may improve outcomes in septic patients with SIC or DIC, although the evidence is still not robust. Thereby, it was felt important to identify sepsis patients with DIC at an earlier stage in order to include them into trials investigating anticoagulant interventions. In 2017 the SIC score was developed, which resembles the JAAM score but is simplified (see Table 3).

Also, whereas deranged PT and platelet count are associated with mortality in sepsis, fibrinogen and D-dimer levels are not. In the JAAM definition, scoring for fibrinogen is eliminated but scoring for systemic inflammatory response syndrome (SIRS) is added.

For the ISTH DIC score, 4 laboratory values (platelet count, PT, D-dimer or another fibrin degradation marker, and fibrinogen) are required in order to score between 0 and 8 points. An ISTH DIC score ≥5 supports the diagnosis of DIC.
The JAAM DIC score consists of a systemic inflammatory response syndrome criteria score (SIRS criteria) and 3 laboratory values (platelet count, PT and fibrin marker). A JAAM DIC score of ≥ 4 supports the diagnosis of DIC. See Table 3.

Use of the different scoring systems:
Since no gold standard for DIC diagnosis exists, comparison of the scoring systems is challenging.

In September 2019, updated guidelines from the ISTH proposed a 2 step scoring system, with the SIC score to screen for SIC and if present, to further screen for DIC using the ISTH criteria.

🗒 Note
> The SIC criteria have lower diagnostic specificity, and the clinical utlity of the SIC scoring system has not yet been proven.

⚠ Warning
> These scoring systems should only be used IF risk factors for DIC are present!

Table 3: DIC scoring systems		
ISTH DIC score	**JAAM DIC score**	**SIC sco**
	Platelet count	Platelet

Parameter	Points	Parameter	Points	Parameter	
Platelet count • > 100/µL • 50 - 100/µL • < 50/µL	• 0 points • 1 point • 2 points	• ≥120 /µL • 80 -120/µL or > 30% decrease in 24h • < 80/µL or > 50% decrease in 24h	• 0 points • 1 point • 3 points	**count** • > 150/µL • 100-150/µL • < 100/µL	
FDP/Ddimer • No change • Moderate rise • Strong rise	• 0 points • 2 points • 3 points	**Fibrin/FDP (mg/L)** • < 10 • 10 - 25 • ≥25	• 0 points • 1 point • 3 points		
PT prolongation • ≤ 3 sec • 3 - 6 sec • > 6 sec	• 0 points • 1 point • 2 points	**PT (value of patient/normal value)** • < 1.2 • ≥ 1.2	• 0 points • 1 point	**PT-INR** • <1.2 • 1.2-1.4 • >1.4	
Fibrinogen level • > 1g/L • < 1g/L	• 0 points • 1 point	**SIRS criteria** • 0-2 • ≥3	• 0 points • 1 point	**SOFA score** • 0 points • 1 point • ≥2 points	

◎ **Task**

Learn to appreciate the differences between the existing DIC scoring systems

?

Think how would these tests yield different estimates of the incidence of DIC in a ICU patient population?

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

A The SIC and the JAAM score will both detect DIC associated with severe infection more easily then the ISTH score because of the use of the SIRS score in the JAAM score and the SOFA score in the SIC score. In line with this, the JAAM score has a high sensitivity, but rather low specificity for DIC. Vice versa, the ISTH DIC score displays a high specificity, but a low sensitivity.

In text References

(Taylor FB et al. 2001; Iba et al. 2017; Gando et al. 2006)

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3. 2. Differential diagnosis of DIC

The differential diagnosis relates to other conditions that can cause thrombocytopenia. In the critically ill, thrombocytopenia most often is due to consumption, which is related to the degree of illness. However, there are some specific conditions causing thrombocytopenia that should not be missed, such as TTP, as already outlined. Consider these conditions in your workup of thrombocytopenia (Table 4).

Table 4: Specific conditions to consider in the Differential Diagnosis of DIC
HITT
Thrombotic thrombocytopenic purpura
Mechanical circulatory support devices
Hemophagocytic lymphohistiosis (HLH)
Hematological malignancies
Drug-induced
Alcohol-induced
Idiopathic thrombocytopenic purpura (ITP)
Post transfusion purpura
Hypersplenism

◎ Task

Test your knowledge of the workup of a patient with suspected DIC

❓

An elderly patient with pneumonia and sepsis is admitted to your ICU. He is on mechanical ventilation, vasopressors and renal replacement therapy, for which he receives continious unfractionated heparin infusion. Complete blood count including platelets have been low since admission. Think of a list of diagnostic tests you consider to order in your workup of the thrombocytopenia.

A

- DIC could be possible. Order lab tests to calculate the DIC score.
- HITT could be possible if platelets drop following heparin or LMWH administration. This seems unclear in this case. An ELISA to detect anti platelelet factor 4 antibodies can be ordered but it often falsely positive in septic patients (and acutely ill patients in general). If this is positive, a functional platelet aggregation test can be done. In functional tests, donor platelets are incubated with patient serum or plasma and heparin. If HIT antibodies are present in the patietns serum, this leads to the formation of a heparin–antibody–PF4 complex that will bind to FcγRIIa receptors on the platelet and induce donor platelets activation. Platelets then release serotonin in the supernatant, which can be detected with the serotonin release assay (SRA).
- HLH is possible though not probable, as a clear risk factor is not present in this case. A complete blood count, liver function tests, levels of triglycerides, ferritin level, fibrinogen level can be ordered. If HLH is suspected based on these test results, NK cell activity and soluble CD25+ levels can be ordered additionally. Phagocytizing cells can be seen in bone marrow aspirate or lymph node.
- Hematologic malignancy is possible though not probable. An aspirate can be considered as well as a leucocyte differentiation and LDH levels.
- For drug-induced thrombocytopenia, no specific lab tests exist.
- ITP is an isolated disorder so not probable in this case. For ITP no specific lab tests exist. A workup of causes of secondary ITP can be considered, these include viral infections and lupus.

In text References

(Zarychanski and Houston 2017)

References

- Zarychanski R, Houston DS, Assessing thrombocytopenia in the intensive care unit: the past, present, and future., 2017, PMID:29222318

4. The coagulation cascade in DIC

4. 1. Normal coagulation cascade

In order to understand the pathological activation of the coagulation cascade which appears in DIC, the physiological coagulation cascade should be understood first. There are three main pillars: the procoagulant system, the anticoagulant system and the fibrinolytic system (Figure 2).

In response to trauma or inflammation-induced endothelial damage, Tissue Factor (TF) is expressed. TF initiatites coagulation by activating Factor VII then Factor VIIa activates FX. Activated factor X then induces the conversion from prothrombin into thrombin. Thrombin formation is a key step as it initiates a series of reactions which amplifies the procoagulant response including activating platelets, white blood cells and endothelium. Thrombin also acts on fibrinogen to form fibrin, which together with activated platelets form a stable clot.

The anticoagulant system is triggered by activated coagulation factors. The proteins that compose this anticoagulant system primarily act by inactivating coagulation factors ("procoagulants"). The main physiological anticoagulant proteins are protein C, protein S and antithrombin (AT). In addition, tissue factor pathway inhibitor (TFPI) inhibits the early stages of the coagulation cascade by blocking the TF-factor VII complex. Together, these pathways form the anticoagulant system.

The fibrinolytic system is responsible for clot degradation, and results in the formation of fibrin degradation products (FDP). The primary human fibrinolytic enzyme is plasmin, which is formed from when plasminogen is activated by tissue plasminogen activator (TPA). Inhibitors of fibrinolysis are thrombin activatable fibrinolysis inhibitor (TAFI) and plasminogen activator inhibitor (PAI-1).
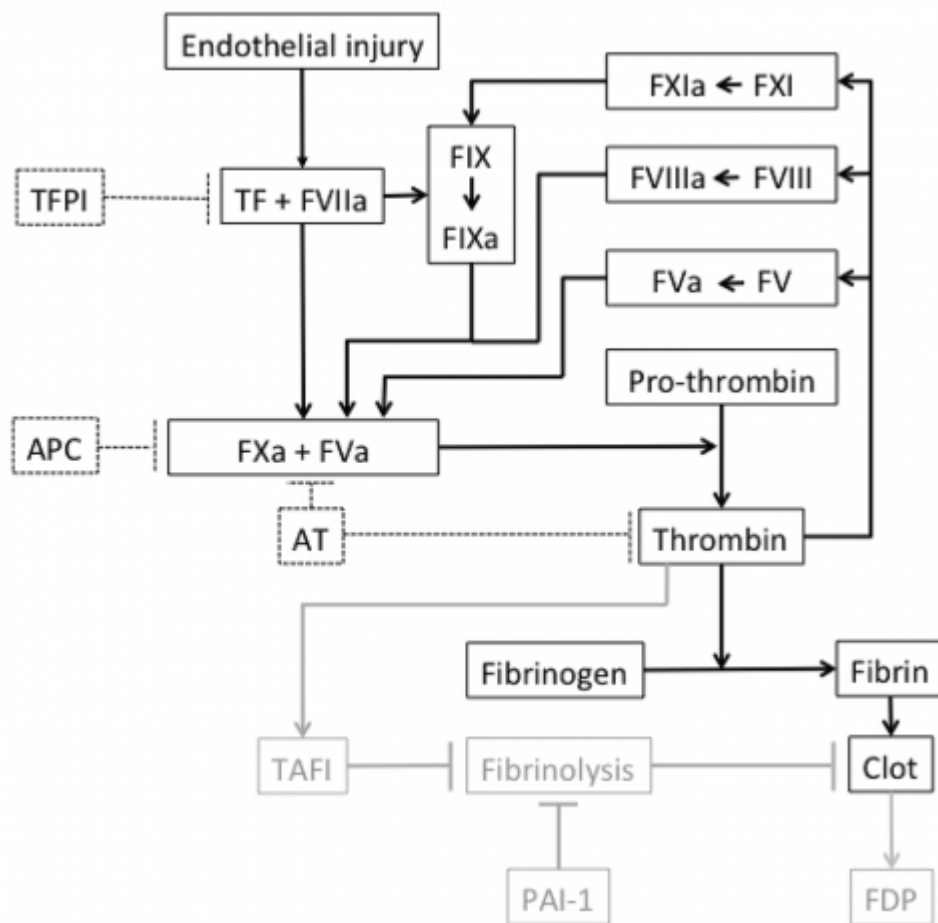
Figure 2:This scheme illustrates the coagulation pathways in black, the anti-coagulant pathways in dashed and the fibrinolytic system in gray.From: Müller, M. C. A. (2014). Coagulopathy and plasma transfusion in critically ill patients.

Figure 2: This scheme illustrates the coagulation pathways in black, the anti-coagulant pathways in dashed and the fibrinolytic system in gray. Coagulation is initiated through endothelial injury which leads to the formation of a tissue factor and factor VIIa complex. Subsequently factor Xa and factor Va form a complex which leads to the transition of pro-thrombin into thrombin. Thrombin plays a keyrole in an amplification loop and furthermore initiates the formation of fibrin eventually leading to stable clot formation.

The anti-coagulant pathways consist of tissue factor pathway inhibitor (TFPI), activated protein C (APC) and anti-thrombin (AT).

The fibrinolytic system is inhibited by thrombin activated fibrinolysis inhibitor (TAFI) and plasminogen activator inhibitor 1 (PAI-1), both leading to inhibition of fibrinolysis.

4. 1. 1. Pathophysiological changes in coagulation during DIC

In DIC, all 3 pillars of the coagulation system are affected.

Microorganisms and their components (such as lipopolysaccharides, described as pathogen-associated molecular patterns or PAMPs), induce the expression of tissue factor on monocytes and macrophages by binding to pattern-recognizing receptors. Tissue factor, a major initiator of coagulation, and the tissue factor-initiated pathway induce both prothrombotic and proinflammatory responses in part via protease-activated receptors (PARs). Phosphatidylserine on cellular membranes can also active PARs. Tissue factor and phosphatidylserine in extracellular vesicles also contribute to the activation of coagulation. In sepsis induced coagulopathy (SIC or DIC, which are a continuum), plasminogen activator inhibitor-1 (PAI-1) release in turn suppresses the release of the key fibrinolytic enzyme tissue-plasminogen activator (t-PA). As a result, the fibrinolytic system is suppressed by PAI-1, producing microcirculatory thrombosis, which is the hallmark of SIC.

Additionally, in sepsis induced DIC substances that are released from damaged cells, such as free-DNA, histones and high-mobility group box 1 protein (collectively termed damage-associated molecular patterns, DAMPs) will contribute to thrombus formation. Neutrophil extracellular traps (NETs) are mesh-like DNA fibers comprised of histones that can prevent bacterial dissemination, but also damage the endothelium.

In non-sepsis induced DIC, fibrinolysis is more prominent. In hematologic disease related DIC, TF initiates systemic coagulation that is insufficiently contained by the physiological anticoagulant pathways and is amplified by impaired endogenous fibrinolysis. Hematologic tumor cells and their derived vesicles can increase plasminogen activation. Plasmin degrades fibrin and thereby increases the risk of bleeding.

◎ [Task]

Test your knowledge of the coagulation abnormalities in DIC.

This is a schematic representation of a blood vessel (Figure 3). Which enhanced or inhibited processes in the 3 pillars (procoagulant, anticogulant and fibrinolytic) lead to the disturbed coagulation assays that underlie a diagnosis of DIC. Indicate in the figure whether a process is enhanced or diminished in DIC by placing arrows up or arrows down.
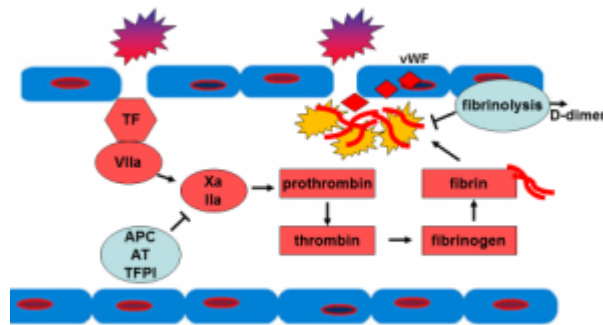

Figure 3:Blood vessel in which coagulation and anticoagulant processes are depicted. ESICM Academy 2020.

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

The procoagulant pathways are excessively enhanced. TF expression and vWF expression are increased, due to activation by tumor cells, vascular endothelial cells and activated monocytes. TF activates coagulation factors which are then consumed resulting in low coagulation factor levels. vWF binds to platelets, also resulting in low platelet counts in the circulation.

The anti-coagulant pathways do not function properly as the protein C-based system is impaired due to low concentrations of protein C. Protein S, which is essential for the formation of activated protein C, is decreased as well. Additionally, cytokines lead to a downregulation of expression of thrombomodulin, an important "brake" on thrombus formation. Thereby, essential components in the formation of activated protein C are compromised. Finally, antithrombin levels are reduced.

The fibrinolytic process which breaks down clots is impaired. In particular, in sepsis-induced DIC, there is an increase in PAI-1, resulting in the inhibition of tPA that in turn leads to inhibited fibrinolysis. In malignancy-associated DIC, suppression of fibrinolysis is less prominent.

The presence of DIC is probably not an "on or off" phenomenon but a continuum, ranging from mild thrombocytopenia to overt DIC. Due to the pathophysiologic processes in the 3 pillars as described above resulting in the consumption of procoagulant proteins, anticoagulant proteins and platelets in the formation of (micro)thrombi, the net decrement in coagulant proteins means the individual with DIC is more prone to bleeding events. However, it should be noted that both, thrombo-embolic events as well as hemorrhage can occur, and can occur simultaneously. Typically, organ dysfunction often develops in sepsis-associated DIC due to reduced tissue perfusion due to the predominance of microthrombus formation, while in (non-septic) DIC with more prominent fibrinolysis, systemic bleeding is a more common feature.

> **Note**
>
> there are of course, exceptions to this rule, as there are pathogens that are known to accelerate fibrinolysis, and many cases of non-sepsis DIC where thrombosis predominates. There is no stereotypical presentation of DIC, whatever the root causes may be.

5. Management of DIC

Hallmark of treatment is management of the underlying disorder that is triggering DIC. If that disorder is eliminated, DIC will resolve.

5. 1. Prophylactic Anticoagulation

In the non-hemorrhaging patient with DIC, the initiation of prophylactic anticoagulation with low doses of unfractionated heparin (UFH) or low molecular weight heparins (LMWH) should be strongly considered, and if prophylactic anticoagulation is already being administered should not be stopped. This recommendation holds even if the patient is already thrombocytopenic (though a "cut-off" platelet count is controversial). Anticoagulation therapy is important because patients with DIC are fundamentally in a procoagulant state and thus at risk for micro- and macro-thrombosis. In addition, in a large retrospective study thromboprophylaxis reduced the development of thrombocytopenia in DIC, presumably because it diminishes consumption of platelets by slowing thrombus formation (Williamson et al, 2013). Besides pharmacological thromboprophylaxis, mechanical thromboprophylaxis with pneumatic compression devices can be considered.

It is also recommended to administer stress ulcer prophylaxis in DIC patients to reduce bleeding (Williamson et al. 2013).

📰 **References**

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5. 2. Platelet Transfusion

In the ICU, platelet transfusions are given prophylactically to correct a low platelet count in the setting of a pending hemostatic challenge or to prevent "spontaneous" haemorrhage – most current guidelines recommend <10 x 10^9 /L for the former though the evidence for these thresholds are limited. In non-bleeding patients, DIC is **NOT** a reason to transfuse platelets at a higher threshold than in patients without DIC. Also, the presence of DIC alone is not a reason to transfuse platelets prior to an invasive procedure. While these patients are at an overall higher risk of bleeding, it is unclear whether prophylactic platelet transfusions reduce this risk.

In patients with DIC who are on anticoagulant medication, it is general practice to maintain a somewhat higher trigger for prophylactic platelet transfusion than in non-anticoagulated patients, although evidence to support this practice is absent.

As a general rule, platelet transfusions in DIC should be guided by the recommendations applicable to all critically ill patients. Please refer to ICU transfusion guidelines (Vlaar et al. 2020) for further details. Overall, a restrictive (conservative) threshold is recommended. There is at least a theoretical concern for the acceleration of thrombus formation with the transfusion of platelets or other procoagulant proteins (i.e.: in plasma or cryoprecipitate).

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5. 3. Plasma/Cryoprecipitate/Fibrinogen Concentrate Transfusion

There is no indication for *prophylactic* plasma transfusion in DIC based elevated PT/PTT levels alone, nor for prophylactic cryoprecipitate or fibrinogen concentrates for low fibrinogen levels alone.

Transfusion support with plasma, cryoprecipitate or fibrinogen should only be reserved for the haemorrhaging DIC patient, and should follow the current guidelines for the management of the bleeding critically ill patient. (Of note, evidence that transfused plasma reliably corrects any coagulation disorder is presently absent.)

The use of prothrombin complex concentrates (PCCs) have not been adequately assessed in DIC, and as such, should only be used in DIC after very careful consideration. As common consequence of PCC use is venous thrombosis, the risks posed in DIC by their use may well outweigh potential benefits.

5. 3. 1. Therapeutic Anticoagulation Strategies

Patients with DIC and thromboembolism should be anticoagulated in the absence of hemorrhage. Current guidelines suggest the use of unfractionated heparin (UFH). If there is a strong contra-indication due to active bleeding, a caval vein filter should be placed in case of thrombi in the lower extremities(Konstantinides et al. 2019).

In DIC patients without thromboembolic events, worldwide differences in the use of anticoagulation medication exist, and the availability of these medications is very limited.

- **Antihrombin:** There is a deficit in anticoagulant proteins in DIC, including a deficit of antithrombin (AT). A large RCT on the efficacy of replenishing AT using high dose AT in sepsis (Kienast et al. 2006) was negative overall, but did suggest a survival benefit in the sub-group of patients with DIC. Current sepsis guidelines still recommend against its use in septic patients, however.
- **Activated Protein C:** Trials on the treatment of sepsis with human recombinant activated Protein C (aPC) showed conflicting results on mortality and this drug was taken off the market, though there have been subsequent post hoc analyses that suggested benefits for patients with sepsis and DIC.
- **Thrombomodulin:** Another option that was recently trialled is administration of soluble thrombomodulin (sTM). sTM binds thrombin which serves to augment the conversion of protein C to activated protein C. In addition, sTM inhibits inflammation and organ injury caused by damage-associated molecular patterns. However, despite initially promising study data from Japan, in a multinational RCT in sepsis-induced coagulopathy the use of sTM did not reduce mortality (Vincent et al. 2019).

It merits noting that while European and North American guidelines recommend against anthrombin and aPC use in sepsis and presently make no mention of sTM, the Japanese guidelines differ, and in fact, recommend for the use of AT or sTM for the treatment of sepsis-induced DIC.

❓

If anticoagulant treatment is started in a DIC patient with a deep vein thrombosis, would this affect the platelet threshold at which you transfuse platelets prophylactically in this patient?

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

Ⓐ The risk of bleeding in this patient is increased due to the consumptive coagulopathy and low platelet count due to DIC together with the anticoagulant therapy. There are no data underlying a specific platelet trigger in these patients. It may be prudent to adhere to a higher platelet count as a trigger for platelet transfusion, such as 30-50 x 10^9 /L, though there is little agreement even among experts on this point.

❓

What are the risks and benefits of a platelet transfusion in a non-bleeding DIC patient?

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

Ⓐ The benefit of platelet transfusion is that the risk of bleeding may diminish. The risk of platelet transfusion is thought to be 'fuelling the fire', meaning that platelet transfusions may contribute to ongoing consumption of platelets with formation of microthrombi. The magnitude of these effects are, however, unknown. Additionally, transfusion reactions of varying type and severity are not uncommon with platelet transfusions.

In text References

(Dellinger 2006)

📖 References

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