Pathogenetic Mechanisms And Contemporary Management Of Disseminated Intravascular Coagulation

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ABSTRACT

A defining characteristic of disseminated intravascular coagulation (DIC)—an acquired syndrome arising in the context of severe illness—is the widespread activation of coagulation pathways within the vasculature, culminating in extensive fibrin deposition throughout the circulatory system. This dysregulated hemostatic response not only precipitates microvascular thrombosis and subsequent tissue ischemia but also exhausts platelets and clotting factors, leading to paradoxical bleeding. Moreover, the interplay between procoagulant stimuli and impaired fibrinolysis amplifies organ dysfunction, underscoring the importance of comprehensive laboratory assessment (including D-dimer, fibrinogen levels, and thrombin–antithrombin complexes) and the early institution of targeted therapies—such as anticoagulants, natural anticoagulant supplementation, and supportive transfusions—to restore hemostatic balance and improve clinical outcomes.

Keywords: *disseminated intravascular coagulation, Bleeding, Tissue factor, Multi organ failure, fibrin, scoring system.*

Purpose of the study: The objective of this study is to conduct a comprehensive critical appraisal of the existing literature on disseminated intravascular coagulation (DIC), with a focus on its underlying pathophysiological mechanisms, diagnostic evaluation techniques, and clinical management strategies. In addition, we will assess emerging biomarkers and therapeutic modalities, evaluate the efficacy and safety of current treatments, and identify key gaps to inform future research directions.

Materials and methods: A comprehensive narrative review was conducted by searching PubMed/MEDLINE, Embase, and the Cochrane Library for English-language publications from January 2000 to March 2025 using MeSH terms and keywords such as "disseminated intravascular coagulation," "pathogenesis," "diagnosis," and "management." Titles and abstracts were screened independently by two reviewers, with full-text assessment for studies meeting predefined inclusion criteria (original research, systematic reviews, clinical guidelines, and meta-analyses in human subjects) and exclusion of small case series (<10 patients), non-English articles, abstracts without full text, and animal-only studies. Data on pathogenic mechanisms (e.g., tissue factor activation, anticoagulant depletion), laboratory and point-of-care biomarkers (including D-dimer, soluble fibrin monomers, and thrombin–antithrombin complexes), therapeutic interventions (anticoagulants, transfusions, natural anticoagulant supplementation), and clinical outcomes were extracted, with disagreements resolved by consensus or a third reviewer. Methodological quality was appraised using the Newcastle–Ottawa Scale for clinical studies and

PRISMA/AGREE II checklists for reviews and guidelines. Extracted findings were synthesized narratively across three domains—pathogenetic pathways, diagnostic frameworks, and therapeutic strategies—to identify areas of consensus and remaining gaps in the evidence base.

Introduction. In disseminated intravascular coagulation (DIC), uncontrolled activation of the coagulation cascade within the vasculature leads to extensive formation of fibrin-rich microthrombi, thereby impairing tissue perfusion and provoking bleeding due to consumption of platelets and clotting factors [1]. The syndrome was first characterized by Landois in 1875, when experimental infusion of human blood into canines produced hyaline thrombi in mesenteric vessels [2]. Beyond its dual thrombotic and hemorrhagic presentations, excessive fibrin deposition contributes directly to multiorgan dysfunction, while the cascade's generation of proteolytically active enzymes amplifies systemic inflammatory responses, exacerbating end-organ injury [3]. DIC may be precipitated by a variety of severe insults—sepsis, malignancy, trauma, or obstetric complications—and in early or subclinical phases standard coagulation assays can remain deceptively normal; nonetheless, progressive thrombocytopenia and prolongation of global clotting times eventually emerge as the consumptive process intensifies [4]. Definitive management hinges on prompt treatment of the underlying disorder, but supportive measures—replacement of depleted coagulation components and natural anticoagulants, as well as judicious use of anticoagulant and antifibrinolytic therapies—are critical to restore hemostatic equilibrium [5]. A deeper appreciation of the intricate interplay between coagulation activation and inflammatory modulation not only enhances diagnostic precision but also paves the way for novel targeted interventions, such as recombinant anticoagulants and modulators of fibrinolysis, that may improve clinical outcomes in DIC.

Pathogenesis. DIC complicates approximately 1.72 % of hospital admissions, most commonly in patients with fulminant hepatitis, sepsis, or acute promyelocytic leukemia [6]. In fact, hepatocellular carcinoma, non-Hodgkin's lymphoma and systemic infections account for the majority of cases. During the initial "thrombotic" phase, widespread microvascular fibrin deposition—particularly in the renal and pulmonary capillary beds—leads to acute kidney injury and acute respiratory distress syndrome. This is followed by a consumptive phase in which platelets and coagulation factors are rapidly depleted, often accompanied by secondary activation of fibrinolysis to clear microthrombi; clinically, this may present as spontaneous bleeding into soft tissues, the gastrointestinal tract, or the central nervous system and can exacerbate organ dysfunction [6]. Endothelial injury, leukocyte activation and release of pro-inflammatory mediators further amplify both coagulopathy and vascular permeability in DIC [7, 8].

A central driver of this dysregulated hemostasis is tissue factor, the principal initiator of the extrinsic coagulation pathway. In DIC patients, circulating tissue factor activity rises sharply in response to endothelial damage and monocyte stimulation, correlating with disease severity [6]. Elevated expression of tissue factor in leukemic blasts and in malignant solid-tumor cells—such as those from gastric carcinoma—underscores its pivotal role in malignancy-associated DIC [9]. Monitoring tissue factor levels, alongside conventional coagulation assays, may therefore enhance risk stratification and guide the implementation of targeted anticoagulant therapies in diverse clinical settings.

DIC in septic condition.

Septicaemia, in particular, is the most frequent clinical complication linked to drug-induced diarrhea. While almost any microbe has the ability to induce DIC, bacterial infection is typically linked to the onset of the syndrome [1]. Thirty to fifty percent of patients with Gram negative sepsis may experience clinically overt DIC [10–12].

Contrary to popular assumption, patients with Gram positive sepsis appear to have clinically over DIC just as frequently as those with Gram negative sepsis [13]. Different processes underlie the start of DIC linked to sepsis than

those linked to leukemias and solid tumors [6]. Individuals suffering from DIC-related septicemia often exhibit higher lipopolysaccharides [6] levels. Furthermore, inflammatory cytokines [14,15] produced by activated leukocytes are among the stimuli and chemical mediators that activate blood and vascular endothelial cells after burn injury, trauma, and major surgery. Lipopolysaccharides are a consequence of Gram-negative bacterial infection in sepsis. On the other hand, septic infection with Gram-positive bacteria exposes peptidoglycan, which might subsequently activate the receptor that is toll-like [16,17]. The production of several inflammatory cytokines, including tissue factor, is stimulated by the activation of toll-like receptor, which in turn promotes nuclear factor-kappa B [14, 15].

Numerous proinflammatory cytokines mediate DIC [18,19]. Interleukin-6 seems to be the main mediator of coagulation activation. because it is the primary mediator of the fibrinolytic deficiency and the deregulation of the physiological anticoagulation pathways [1]. The aforementioned processes' effects result in microcirculation failure, which culminates in DIC and multiorgan failure [6].

Vascular endothelial cells [6], the fibrinolytic system, and a number of protease inhibitors are the primary defense mechanisms against DIC. The pathogenetic mechanisms of DIC have been elucidated by research conducted on people and animal models. Increased thrombin production, concurrent suppression of physiological anticoagulation mechanisms, and delayed fibrin clearance as a result of compromised fibrinolysis1 all contribute to the systemic development of fibrin.

DIC in acute leukemia

Hypercoagulable condition and increased risk of thrombo-hemorrhagic consequences are linked to malignancy [20]. Clinical signs and symptoms may range from life-threatening bleeding due to DIC to localized deep vein thrombosis, which is more common in solid tumors. The thrombotic or bleeding symptoms are really the "tip of the iceberg" of a chronic or subclinical form of DIC that is usually linked to various forms of cancer [20]. In fact, abnormalities in laboratory blood coagulation tests are frequently observed in patients with solid tumors and leukemias, even in the absence of clinical manifestations [20]. These anomalies represent the so-called hypercoagulable state in these individuals and show varying degrees of blood clotting activation [21–23]. In acute leukemias, especially acute myeloblastic leukemia, bleeding symptoms are common and indicative of an early stage of disease [20]. Hypofibrinogenemia, elevated levels of fibrin degradation products, and extended PT and PTT [24] are among the anomalies of the blood clotting system that underlie the clinical features of the coagulopathy well-described in acute promyelocytic leukemia. Severe hemorrhagic problems frequently occur when cytoxic treatment is started because these laboratory parameters tend to become more abnormal. The prothrombin fragment F1 + 2, the thrombin-antithrombin complex, and the fibrinopeptide A are examples of well-known plasma markers of clotting activation that have abnormally elevated levels in this condition, according to the results of new tests to detect enzyme inhibitor complexes and activation peptides [25, 26]. Furthermore, there are plasma indicators that show continuous hyperfibrinolysis, such as low levels of plasminogen and a2-antiplasmin and high amounts of fibrin breakdown products and urokinase plasminogen activator [27–29]. Acute leukemia consistently exhibits thrombin production, as demonstrated by new laboratory techniques for subclinical DIC20.

The main factors that determine the pathogenesis of the coagulopathy associated with acute leukemia are: (1) leukemia cell-associated factors, such as procoagulant, finrinolytic, and proteolytic properties expressed, and the secretion of inflammatory cytokines, i.e., tumor necrosis factor and interleukin-1β; (2) cytoxic therapy; and (3) concurrent infectious complications [20].

DIC in traumatic patients

The ability of trauma patients to manage bleeding and sustain essential organs by averting multiorgan dysfunction syndrome following DIC [30] is critical to their survival. Hemostatic action is essentially limited to the

site of the wound. DIC [30] is occasionally caused by control mechanisms that are unable to confine the hemostatic processes to the site of tissue destruction, allowing them to spread throughout the systemic circulation.

The activation of coagulation in DIC [31] does not seem to be significantly influenced by the intrinsic coagulation pathway. Everyone agrees that the contract system's job is to produce bradykinin, which is a strong inducer of systemic hypotension and local edema [8,31]. The tissue factor-dependent pathway plays a crucial role in the start of thrombin production, according to multiple lines of evidence [30]. After trauma, this idea holds true for DIC patients.

On the day of trauma and the first four days following admission, DIC patients' tissue factor levels were consistently greater than those of non-DIC patients' [30,32]. The findings imply that in post-trauma DIC [30], there is widespread activation of the intrinsic coagulation system. Post-trauma DIC patients were reported to have significant changes in three important physiological anticoagulants: protein C, tissue factor pathway inhibitor, and antithrombin [30] Gando et al. [32] discovered that in post-trauma individuals with DIC, the typical tissue factor pathway inhibitor is insufficient in blocking an activated tissue factor-dependent pathway. Additionally, they demonstrated that protein C activity and antigen levels in trauma patients with complicated DIC were much lower than in patients without DIC [33]. Owings and Gosselin [34] demonstrated that trauma patients also had considerably lower levels of antithrombin.

Natural Anticoagulant as Modulators of the Inflammatory Response

Natural anticoagulants have the ability to lessen the coagulant reaction, lessen DIC clinical symptoms, and, in certain situations, increase sepsis survival [35]. According to experimental data, decreased inflammatory responses could be the reason for the mortality decrease rather than the inhibition of coagulation per se [35]. Studies have demonstrated that various activated coagulation factors, including thrombin, factor VI-Ia, and factor Xa, can trigger cells to produce cytokines, which may be the direct cause of the reduced inflammatory response [63]. Nevertheless, even while tissue factor pathway inhibitors, protein C, and antithrombin [64–66] prevented DIC and death, In lethal primate models of sepsis, native anticoagulant therapies with heparin [67] and active site-inhibited factor Xa [68] likewise effectively blocked the activation of coagulation, but they had no effect on lethality. Therefore, it seems that the natural coagulation inhibitors' control of the inflammatory response is related to their other, non-coagulant functions [35]. Antithrombin possesses direct anti-inflammatory properties, independent of coagulation factors through an unclear mechanism. Moreover, research indicates that the tissue factor pathway inhibitor suppresses factor VI-Ia, which can cause proinflammatory alterations in mononuclear cells.

Fibrinolysis and Fibrin Degradation Products

Many studies show that at the moment of greatest activation of coagulation in DIC [1], the fibrinolytic system is mainly repressed. This reluctance is brought on by a persistent rise in the plasma concentration of plasminogen activator inhibitor 1, the primary fibrinolytic system inhibitor [70,71]. Clinical investigations have established that plasminogen activator inhibitor type 1 is the mediator of the suppression of fibrinolysis. They have also demonstrated that, despite the presence of fibrinolytic activity in response to fibrin formation, this activity is not high enough to offset systemic deposition [1,12,72, 73].

Research using experimental models of sepsis, which is the most prevalent cause of deep vein thrombosis (DIC), has proposed the idea of a procoagulant condition, which is defined by thrombin production that is higher than plasmin [74]. Numerous investigations have demonstrated that sepsis patients have activated the fibrinolytic system, as indicated by elevated plasmin-a2-and plasmin complex levels [75,76]. Comparable elevations of similar complexes have been noted in DIC [77,78] that are unrelated to Sep-Si. However, due to a more noticeable general rise in thrombin-antithrombin complexes, the majority of these patients are in a procoagulant state.

Furthermore, most patients have low levels of plasminogen and a2-antitplasmin, which somewhat correlate with result [35]. But it's still unclear if this is merely a result of decreased synthesis or consumption due to a negative phase behavior. These levels have been repeatedly shown to be correlated with outcome in patients with DIC who have causes other than sepsis [80, 81]. It's interesting to note that some research has indicated that administering tissue-type plasminogen activator to animals suffering from inflammatory conditions can improve certain signs of organ failure and reduce inflammation. This suggests that increasing fibrinolysis may help treat multiple organ failure [74]. Fibrinogen is broken down by thrombin into fibrin monomer, which quickly polymerizes to form a clot [83]. Tiny quantities can circulate in plasma as soluble fibrin, which can comprise fibrinogen and varying degrees of cross-linking [83]. Its composition can be complicated.

A heterogeneous collection of degradation products reactive in D-dimer assays is formed by plasmic breakdown of cross-linked fibrin, and their levels indicate the extent of fibrin formation and lysis [83]. In experimental animal models of DIC, significant increases of the products of fibrinogen breakdown are consistently observed. D-dimer is raised early and stays high in human models of DIC brought on by endotoxin injection, indicating the lysis of microvascular disseminated intravascular coagulation fibrin deposits [83]. For the diagnosis of DIC, elevated levels of D-dimer and soluble fibrin are highly sensitive, and a normal level has a high negative correlation is the predicted value. Additionally, D-dimer tests or serial monitoring of soluble fibrin may be useful in assessing the therapeutic response [83]. Their sensitivities range from roughly 90 to 100% [84-88], depending on the assay and the level selected to distinguish between normal and abnormal.

As a result, an increased amount of soluble fibrin or fibrin breakdown product should be present in all or almost all DIC patients. Because mechanisms other than DIC may generate increases, fibrinogen degradation products, D-dimer, and soluble fibrin tests have higher sensitivity than specificity [83]. For example, hepatic illness and renal insufficiency can both result in increased fibrinogen breakdown. For example, elevated levels of D-dimer and fibrinogen degradation product can result from both renal insufficiency and liver disease [89,80]. Because of this, it is always best to utilize these assays in conjunction with other markers [83] rather than using them alone.

Clinical Picture

Individuals with deep vein thrombosis (DIC) may have clinically less obvious microvascular thrombosis or develop thromboembolic illness mostly manifests as a dysfunction of various organs [8,91]. This means that DIC should be considered one of the causes of organ failure, although other theories contend that DIC is only a symptom of organ failure (failure of the microvasculature, which includes dysfunctional endothelial cells). Stimulated blood cells, and thus an active coagulation system) [94]. In actuality, it's possible that both mechanisms are involved. On the other hand, significant bleeding could be the primary symptom. Patients with DIC may experience simultaneous thrombosis and hemorrhage, which does not assist a clinician in selecting the most appropriate course of treatment [92]. In actuality, bleeding and thrombosis can happen in different places and to differing degrees. The thrombotic spectrum includes large intravascular deposition of fibrin that can impair circulation to laboratory evidence of hypercoagulability without significance [92]. In a similar vein, bleeding can range in severity from minimal blood loss that occurs only after an injury to enormous, spontaneous, and potentially fatal bleeding [92]. Infection [92] is the most common underlying cause of DIC in most cases. Thirty to fifty percent of patients with gram-negative sepsis may experience clinically overt DIC [10–12]. Contrary to popular assumption, patients with gram-positive sepsis appear to have clinically overt DIC just as frequently as those with gram-negative sepsis [13].

A number of processes, such as physical force, burns, or heat stroke, can generate polytrauma, which can lead to DIC. Hemolysis, phospholipid release, endothelial activation, and acidosis due to hypoperfusion [92] are the consequences of

hemolysis. Although almost all patients with advanced malignant illness have enough evidence for a procoagulant condition, the frequency of overt DIC appears to be substantially lower [93]. The literature does not provide a precise incidence of DIC in patients with solid tumors, but it can be identified in 15–20% of patients presenting with leukemia [92,94].

Local stimulation of coagulation may be caused by vascular illnesses such as big hemangiomas (Kasabach-Merritt syndrome) or huge aortic aneurysms [14,15,95]. Additionally, hemangiomas of the liver and spleen, hemangioendotheliosarcoma, Osler's disease, and Klippel-Trenaunay syndrome have all been linked to signs of DIC [96–100]. A tiny percentage of patients with aneurysms in major vessels, such the aorta, may also develop DIC. A 25% incidence of clinically significant DIC has been observed in patients with massive hemangiomas [92]; however, a recent analysis of individuals with more frequent aortic aneurysms demonstrated an incidence of systemic activation of coagulation in just 1% of cases [15].

The most prevalent obstetric disorder is pre-eclampsia, which is linked to blood coagulation activation and, in severe situations, macroscopic fibrin deposits in multiple organs [101–102]. Placental abruption and amniotic fluid emboli [103] may result in acute DIC. Within four hours of the insult, women who survive severe amniotic fluid emboli are at a 50% or higher chance of developing diabetic ketoacidosis (DIC) [104].

Diagnosis

The International Society of Thrombosis and Hemostasis' Scientific Standardization Committee proposed that DIC be defined as an acquired syndrome that is characterized by intravascular activation of coagulation and loss of localization resulting from various causes. The harm it causes can start with the microvasculature and lead to organ dysfunction if it is bad enough [105].

As of right now, there isn't a single laboratory test or set of assays that is sensitive and specific enough to provide a conclusive diagnosis of DIC. Nonetheless, the majority of the time, a combination of laboratory and underlying illness results can be used to make an accurate diagnosis [106]. Numerous assays have been developed to detect the generation of thrombin (e.g., prothrombin fragment 1 + 2, thrombin-antithrombin complexes), its activation of the protein C and fibrinolytic pathways (e.g., activated protein C and inhibitor and plas-min-antiplasmin complexes), and the resulting end products of its activity (e.g., fibrinopeptide A, soluble fibrin) [107] as a result of the recognition of the pivotal role played by thrombin in the pathophysiological process of DIC. Thrombin-antithrombin complex, F1 + 2, D-dimer, soluble fibrin, and activated protein C protein C inhibitor complex [108] are examples of sensitive indicators.

A platelet count, measurements of global clotting times (pro-thrombin time [PT] and activated partial thromboplastin time (aPTT), measurements of antithrombin III and/or 1 or 2 clotting factors, and a test for fibrin degradation products can all be used to diagnose DIC in a routine setting1. In clinical practice, the disorder can be diagnosed based on the following findings: low levels of coagulation inhibitors like antithrombin III [1], prolongation of clotting times like the PT and aPTT, elevated INR, presence of fibrin-degradation products in plasma, an underlying disease known to be associated with DIC, an initial platelet count of less than 100,000 per cubic milliliter or a rapid decline in platelet count. It should be noted that in most cases, multiple coagulation tests are more beneficial in diagnosing DIC [106] than are single laboratory results. An unusual clotting profile has recently been reported, as determined by variations in light transmittance on the aPTT or PT [109,110]. With a sensitivity and specificity of more than 90%, this unusual waveform has been demonstrated in prospective trials to be a reliable, quick, and easy way to identify DIC. It also happens independently of clotting time prolongation [107,111]. Additionally, it has been described as a pre-DIC, or early predictor of imminent DIC, with implications for monitoring and prognosis in the critical care situation.

For the purpose of diagnosing DIC [112], the Japanese Ministry of Health and Welfare has

created a scoring system that includes laboratory testing. An accumulation of

A score of seven or higher indicates DIC. A score of five or more is consistent with DIC, while a value of less than five may be suggestive of non-overt DIC [106], albeit it is not conclusive.

Plasma and Platelets

The risk of bleeding increases in patients with DIC who consume coagulation factors and platelets. The clinical state of the patient directs plasma or platelet concentrate treatment, which shouldn't be started based only on test results [5]. It has been demonstrated that patients requiring an invasive surgery but with poor laboratory values can benefit from therapy with plasma and platelets [93,113]. Patients who are not bleeding and who are not at high risk of bleeding should not receive platelets or plasma as a preventative measure, according to the available data1.

Risk assessment: Does the patient have a underlying disorder known to be associated with overt DIC? If yes: proceed; if no: do not use this algorithm Order global coagulation tests (platelets count, PT, fibrinogen, soluble fibrin monomers or fibrin degradation products)

Score global coagulation test results Platelet count (> 100 = 0; < 100 = 1; < 50 = 2)

• Elevated fibrin-related marker (e.g. soluble fibrin monomers/fibrin degradation products) (no increase= 0; moderate increase = 2; strong increase = 3)

• Prolonged PT (< 3 sec = 0; > 3 sec but < 6 sec = 1; > 6 sec = 2)

• Fibrinogen level (> 1 g/L = 0; < 1 g/L = 1) Calculate score

If ≥ 5: compatible with overt DIC; repeat scoring daily.

If < 5 suggestive (not affirmative) for non-overt DIC; repeat next 1-2 days

It could be necessary to use significant amounts of plasma—up to six units per 24 hours—to adequately cure the coagulation defect1. This requirement may be met by using coagulation factors concentrates, although individuals with DIC5 may be especially vulnerable to their potentially hazardous residues of activated coagulation factors. Cryoprecipitate is also used as replacement therapy; it contains fibrinogen in addition to factor VIII, von Willebrand factor, factor XIII, and fibronectin. However, controlled trials have not supported its use [5].

Anticoagulants

In patients with DIC, thrombolysis should theoretically be beneficial. In fact, Heparin can partially limit the activation of coagulation in situations related to sepsis or other reasons, according to experimental studies [1]. To completely eliminate the risk of venous thromboembolism, adequate prophylaxis is also required1. Since 1959 [114], heparin has been used to treat diabetic ulcer disease. According to research on animals, this medication can prevent experimental septicemia by blocking the coagulation process, but it has no effect on mortality [115,116]. Heparin has not been found to be helpful in controlled clinical trials, but it has been in small, uncontrolled investigations including patients with DIC [117,118].

Clinical investigations have not demonstrated that therapy with heparin significantly increased the risk of bleeding, despite disagreements regarding the safety of heparin in patients with DIC who are prone to bleeding1. All things considered, there is no evidence to support the routine use of heparin as therapy in patients with DIC [5], but it is likely helpful in individuals who have severe fibrin deposition, such as in cases of acral ischemia or purpura fulminans, or clinically obvious thromboembolism [1].

Heparin with Low Molecular Weight

Heparin with a low molecular weight has the same antithrombotic capability as unfractioned heparin, but at a lower risk of bleeding.Rabbits have been shown to respond well to treatment for DIC [119]. Two small, uncontrolled human investigations that claimed successful outcomes also included [120,121]. Furthermore, a multicenter, double-blind, randomized trial [122] examined the efficacy of dalteparine sodium in the treatment of DIC. In this trial, dalteparin sodium outperformed unfractionated heparin in terms of reducing bleeding symptoms and raising the subjective score for organic symptoms. Therefore, based on this study, it may be hypothesized that while treating DIC [5], low molecular weight heparin

has less bleeding problems than unfractioned heparin.

Hirudins

In animal experiments, recombinant hirudin showed promise in the treatment of diabetic foot ulcers (DIC) [123–125]. Nevertheless, there isn't a single randomized controlled study on hirudin use in DIC patients. Its usage in patients with DIC [5] may be restricted due to the elevated risk of bleeding.

Coagulation Inhibitors

Low plasma levels of antithrombin III, a significant coagulation inhibitor, are linked to a higher death rate [40]. When this inhibitor was given to animals at supraphysiologic dosages, sepsis-related mortality was decreased [126]. DIC and occasionally organ function have improved in a number of controlled trials, the majority of which involved sepsis patients [43–45]. The trials' meta-analyses revealed a drop in mortality from 56% to 44% [1].

The investigations conclude that antithrombin III can help DIC, while it is less clear if this will have a positive effect on clinical outcomes [5]. The pathogenesis of diabetic eye disease (DIC) may be considerably influenced by the depression of the protein C system. Consequently, supplementing with activated protein C may be advantageous4. Activated protein C has been demonstrated to be useful in lowering mortality and organ failure in experimental sepsis studies [66]. A large-scale randomized controlled trial shown to be clinically effective in treating severe sepsis [55]. Activated protein C group mortality was 24.7%, while placebo group mortality was 30.8%. Subsequent research verified that activated protein C can restore normal coagulation activity in cases of severe sepsis [127]. A prospective trial involving septic patients with relatively moderate illness severity did not demonstrate any advantage of activated protein C [128]; however, activated protein C appears to be more effective in greater disease severity groups [4]. Inhibiting tissue factor's activity may be useful in the treatment of DIC [5] because it is essential to the start of coagulation during DIC.

Recombinant tissue factor pathway inhibitor was infused immediately after endotoxin injection in an animal study [129], and this greatly reduced the consumption of platelets and coagulation factors. Promising outcomes were observed in phase II clinical trials with recombinant tissue factor pathway inhibitor in sepsis patients; however, a phase III trial failed to demonstrate an overall survival improvement in patients treated with tissue factor pathway inhibitor [130–131].

Conclusion. The pathogenesis of Disseminated Intravascular Coagulation (DIC) is a complex interplay of systemic activation of coagulation pathways, widespread formation of microthrombi, consumption of clotting factors and platelets, and concurrent activation of fibrinolysis. Various underlying conditions, such as sepsis, trauma, or obstetric complications, can trigger this dysregulated response, leading to a cascade of events that disrupt the delicate balance between coagulation and fibrinolysis. The resulting clinical manifestations underscore the critical importance of timely recognition and management to mitigate the potentially life-threatening consequences of DIC.

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