

# **Updates in Diagnosis and Management of Disseminated Intravascular Coagulopathy in Septic Patients**

Essay

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

"قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا  
عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ"

صدق الله العظيم

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## *List of Abbreviations*

aPTT	activated partial thromboplastin time
ARDS	Acute Respiratory Distress Syndrome
AT	antithrombin
DIC	disseminated intravascular coagulation
ECCO2R	extracorporeal CO2 removal
ECMO	extracorporeal membrane oxygenation
EGDT	early goal-directed therapy
EHF	Ebola haemorrhagic fever
FDPs	fibrin (-ogen) degradation products
FFP	fresh frozen plasma
HUS	Hemolytic Uremic syndrome
IL	Interleukin
ISTH	the International Society on Thrombosis and Haemostasis
ITP	idiopathic thrombocytopenic purpura
JAAM	the Japanese Association for Acute Medicine
JMHW	the Japanese Ministry of Health and Welfare
LODS	logistic organ dysfunction score
MAHA	microangiopathic hemolytic anemia
MAP	mean arterial pressure
MODS	multiple organ dysfunction syndrome
MOF	The Denver Multiple Organ Failure score
NAPs	nematode anticoagulant proteins
PAR	the pressure adjusted heart rate
PBW	predicted body weight

PC	protein C
PEEP	positive end-expiratory pressure
POC	point of care tests
PT	prothrombin time
rFVIIa	recombinant activated factor VII
rhAPC	recombinant human activated protein C
rNAPc2	recombinant nematode anticoagulant protein c2
rTFPI	Recombinant tissue factor pathway inhibitor
rTM	recombinant thrombomodulin
SCC	the Surviving Sepsis Campaign
ScvO <sub>2</sub>	central venous oxygen saturation
SF	soluble fibrin monomer
SIRS	Systemic inflammatory response syndrome
SOFA	sequential organ failure assessment
TEG	thromboelastography
TF	tissue factor
TFPI	tissue factor pathway inhibitor
TM	thrombomodulin
TNF	tumour necrosis factor
TT	thrombin time
TTP	thrombotic thrombocytopenic purpura
UFH	unfractionated heparin
VAP	ventilator-associated pneumonia

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# Introduction

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## Introduction

Sepsis has been around since the dawn of time, having been described for more than 2000 years. The incidence of sepsis, severe sepsis and septic shock continues to increase. We have made progress over the past half-century in identifying and treating patients with sepsis. However, owing to the increasing incidence of sepsis, the number of people who die each year continues to increase. The mortality with sepsis, particularly related to treating organ dysfunction, remains a priority to clinicians worldwide. (*Greg, 2012*)

Sepsis is the most common cause of death in hospitalized patients and affects >18 million people worldwide; its incidence is expected to increase by 1% annually. (*Ishikura et al, 2014*)

Sepsis is almost associated with haemostatic abnormalities ranging from subclinical activation of blood coagulation (hypercoagulability) to acute disseminated intravascular coagulation (DIC) characterized by massive thrombin formation and widespread microvascular thrombosis, partly responsible of the multiple organ dysfunction syndrome (MODS) and subsequent consumption of platelets and coagulation proteins causing, in most severe cases, bleeding manifestations. (*Semeraro et al, 2010*)

The expression "death is coming" was used to reflect the severity of DIC as a disease with a poor prognosis. The diagnosis and treatment of DIC are therefore important and an early diagnosis of DIC as pre-DIC may help to improve the patient survival. (*Kaneko and Wada, 2011*)

The pathogenetic mechanisms of DIC and MODS may have important implications for the development of new therapeutic agents that could be potentially useful particularly for the management of severe sepsis. The pathophysiology of sepsis-associated DIC is extremely complex and still represents a matter of extensive investigation. The key event is the systemic inflammatory response to the infectious agent. (*Semeraro et al, 2010*)

Early diagnosis and early treatment for DIC are important, and the use of haemostatic molecular markers is necessary to successfully make an early rapid diagnosis. The current widely used diagnostic criteria for DIC are not actually diagnostic criteria, but rather criteria for starting DIC treatment. (*Kaneko and Wada, 2011*)

Although the effectiveness of anticoagulant therapy in septic patients remains controversial, some studies suggest that

rapid diagnosis and early treatment of DIC improve outcomes for these patients. (*Ishikura et al, 2014*)

The goals of pharmacotherapy in cases of DIC are to reduce morbidity and to prevent complications. (*Levi and Besa, 2012*)



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# Aim of Work

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## Aim of work

- ▶ The aim of this essay is to review pathophysiology, diagnosis of septic induced disseminated intravascular coagulopathy and updates in its management.



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# Chapter (1)

Pathophysiology of septic  
induced coagulopathy

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