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New Anticoagulants In Intensive Care Unit

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List of abbreviations

ACCP: American College of Chest Physicians

ACE: Angiotensin-Converting Enzymes

ACS: Acute Coronary Syndrome

ADP: Adenosine Diphosphate

APC: Activated Protein C

aPTT: Activated Partial Thromboplastin Time

AT: Antithrombin

C_{max}: maximal plasma Concentration

CRRT: Continuous Renal Replacement Therapy

DTIs: Direct Thrombin Inhibitors

DVT: Deep Vein Thrombosis

ECT: Ecarin Clotting Time

FBC: Full Blood Count

FDA: Food and Drug Administration

FFP: Fresh Frozen Plasma

Fp: Fibrinopeptide

gla: Glutamic acid

HIT: Heparin Induced Thrombocytopenia

HITTS: Heparin-Induced Thrombocytopenia Thrombosis Syndrome

ICU: Intensive Care Unit

INR: International Normalized Ratio

LFTs: Liver Function Tests

LMW: Low Molecular Weight

MI: Myocardial Infarction

NSAIDs: Non-Steroidal Anti-Inflammatory Drugs

PCC: Prothrombin Complex Concentrates

PCI: Percutaneous Coronary Intervention

PE: Pulmonary Embolism

PF_4: Platelet Factor 4

PT: Prothrombin Time

PTCA: Percutaneous Transluminal Coronary Angioplasty

SC: Subcutaneously

TAFI: Thrombin Activatable Fibrinolytic Inhibitor

TFPI: Tissue Factor Pathway Inhibitor

tPA: Tissue Plasminogen Activator

TT: Thrombin Time

UFH: Unfractionated Heparin

VTE: Venous Thromboembolism

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Introduction

Anticoagulants are unique compared with most pharmacological agents because even small deviations from therapeutic levels place patients at risk for life-threatening complications. Whereas critically ill patients are particularly susceptible to thrombosis, they also have higher risks of bleeding than the general medical or surgical patients. Although the choices for anticoagulant therapy are expanding with the development of new parenteral and oral agents, rigorous clinical trials of their use in the intensive care unit population are lacking. **(Rajasekhar et al.,2012).**

The anticoagulants heparin and dicumarol were discovered by chance. Both of these anticoagulants have been used effectively to prevent clots since 1940. In the 1970s, three different groups of researchers in Stockholm, London, and Hamilton, Ontario, began work on low-molecular-weight heparin (LMWH). LMWH is produced by chemically splitting heparin into one-third of its original size. It has fewer side effects than heparin and produces a more predictable anticoagulant response **(Hirsh et al., 2008).**

With the biotechnology revolution has come genetically engineered anticoagulant molecules that target specific clotting enzymes. The first successful synthetic anticoagulants were fondaparinux and bivalirudin. Fondaparinux is a synthetic analogue of the antithrombin-binding pentasaccharide sequence found in UFH and LMWH while lepirudin, bivalirudin, and argatroban, are based on antithrombin-independent inhibition of thrombin. **(Nagler et al.,2012).**

Newer designer drugs (as dabigtran,Rivaroxaban and Apixaban) that target single clotting factors and that can be taken by mouth are undergoing clinical testing. If successful, we will have safer and more convenient replacements for warfarin, the only oral anticoagulant available for more than 60 years **(Hirsh , 2008).**

Aim of the work

The aim of the work is to highlight updated anticoagulant drugs in critical care.

Physiology of coagulation system

Hemostasis is the process that maintains the integrity of a closed, high-pressure circulatory system after vascular damage, it is a critical event in the arterial diseases associated with Myocardial Infarction (MI) and stroke, and venous thromboembolic disorders account for considerable morbidity and mortality. A review of recent advances in knowledge about thrombus formation is included, plus new hypotheses and some speculations about thrombus formation and the prevention and treatment of thrombosis **(Bruce and Barbara, 2008)**.

Constituents of the hemostatic system:

With the evolution of vertebrates and their pressurized circulatory system, there had to arise some method to seal the system if injured; hence, the hemostatic system. Interestingly, there is nothing quite comparable to the vertebrate hemostatic system in invertebrate species. In all vertebrates studied, the basic constituents of the hemostatic system appear to be conserved.

Figure 1 illustrates the three major constituents of the hemostatic pathways and how they are interrelated. Each element of the hemostatic system occupies a site at the vertex of an equilateral triangle. This representation implies that each system constituent interacts with and influences all other constituents. In the normal resting state, these interactions conspire to maintain the fluidity of the blood to ensure survival of the organism. Normally, only at the site of an injury will the fluidity of the blood be altered and a blood clot form **(Colman et al., 2006)**.

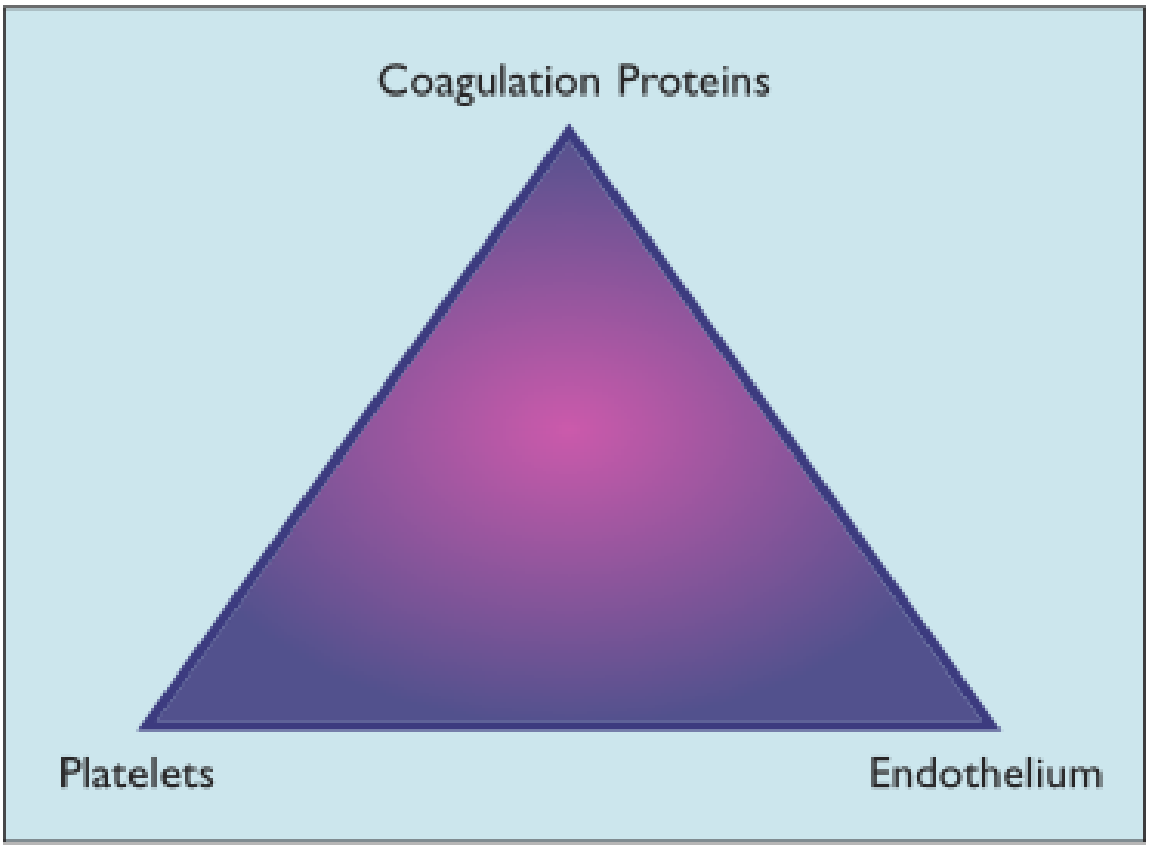

Figure (1): Basic representation of the elements of hemostasis

1- Endothelium:

Figure 2 shows some of the basic properties of the endothelium. The endothelium normally promotes blood fluidity, unless there is an injury. With damage, the normal response is to promote coagulation at the wound site while containing the coagulation response and not allowing it to propagate beyond this site **(Aird, 2005)**.

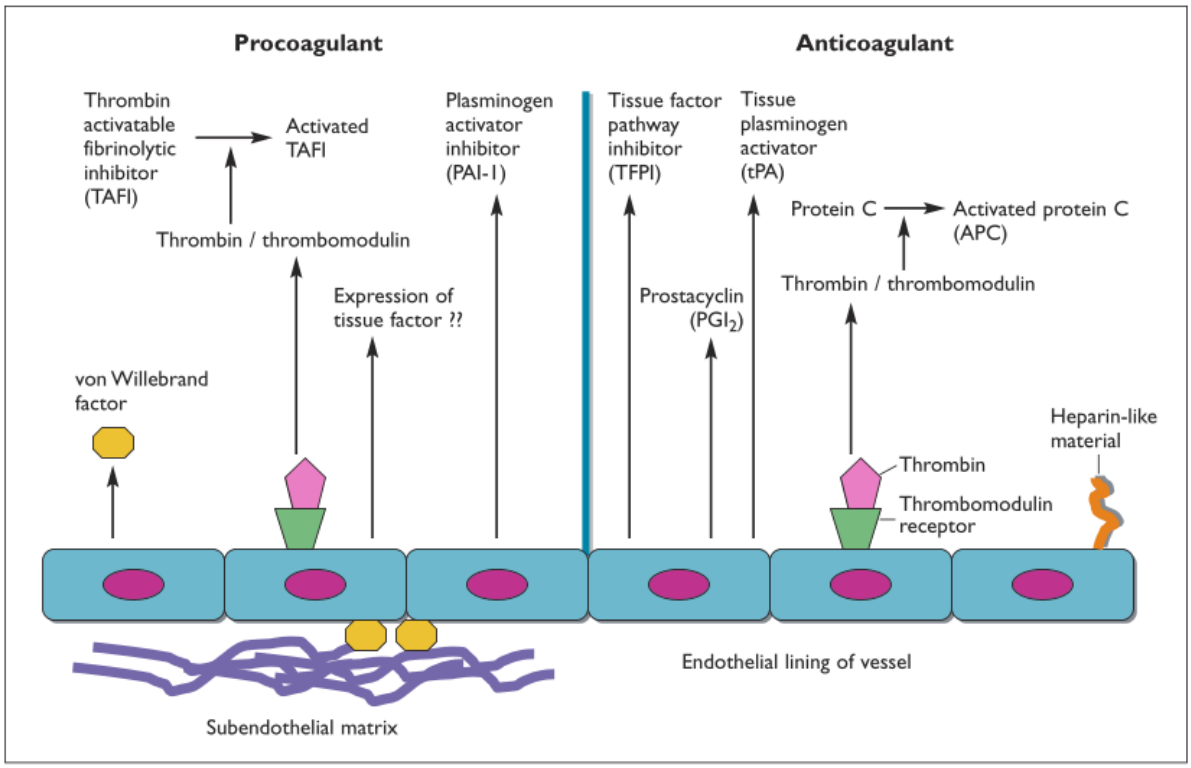

Figure (2): A stylized view of endothelial functions related to procoagulation and anticoagulation. The subendothelial matrix, represented by the purple interlocking lines, is a complex of many materials.The most important constituents of the subendothelial matrix related to coagulation function are collagen and vonWillebrand factor.