



Disorders of Coagulation and Flow

Week 4– Disorders of Coagulation and Flow

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Intended Learning Outcomes

At the end of this lecture you should be able to:

- Describe the process of haemostasis and in particular the role of platelet activation and coagulation in achieving effective haemostasis
- Explain how a thrombus is dissolved in biological settings
- Describe the mechanism of action of classes of drugs used to reduce risk of thrombosis
- Describe the mechanism of action of anticoagulant drugs and their application in veterinary settings
- Describe the mechanism of action of fibrinolytic drugs and their application in veterinary settings

Keywords

Anti-coagulant, aspirin, coagulation, clot, factor Xa inhibitors, fibrin, fibrinolytic, heparin, plasmin, plasminogen, platelet, thrombin, thrombolytic agents, vitamin K, warfarin

Lecture 19 – Anticoagulants: prescriptions and poisons

As was discussed in lecture 15, there are three components to the process of haemostasis, namely vasoconstriction, platelet activation and coagulation (fibrin formation). Understanding how drugs work to increase or reduce coagulation, or to modify platelet activation, requires a sound understanding of these processes.

Drugs can be used to improve coagulation (in the case of some bleeding disorders), or to reduce coagulation, either in vitro, where an unclotted blood sample is required for examination of cell types or for plasma analysis, or in vivo where an increased risk of thrombosis is identified. Drugs can also be used clinically to help dissolve a thrombus.

Drugs that affect coagulation

In veterinary medicine the drugs of most importance are those that affect coagulation. Their application is not so much in the clinical context of reducing risk of coagulation (hence increasing clotting time), as in preservation of collected blood samples for examination (heparin) and as toxic agents (warfarin and other coumarin derivatives) that are used as rodenticides.

- **Injectable anticoagulants (heparin):** in human medicine, heparin is used acutely to reduce the risk of thrombosis post surgery and following implantation of thrombogenic prostheses such as metallic heart valves. Heparin is a large molecular weight glycosaminoglycan. As a consequence, when it is used therapeutically it must be administered by injection.
- **Oral anticoagulants (warfarin):** warfarin impairs the clotting cascade because it competes with vitamin K and inhibits gamma carboxylation glutamate- an essential step in formation of clotting factors II, VII IX and X. Although

commonly used in human medicine, warfarin is not used therapeutically in animals. However understanding of its mechanism of action is important in managing rodenticide poisoning in dogs and cats- a common toxicological presentation.

Antiplatelet drugs

Coagulation can also be manipulated using drugs that affect platelet activation. The most commonly used of drugs in this category is the nonsteroidal anti inflammatory drug (NSAID) aspirin. Aspirin is a cyclooxygenase (COX) inhibitor, that binds irreversibly to COX and prevents formation of thromboxane, through the arachidonic acid cascade. Thromboxane is a potent activator of platelets, promoting their endothelial adhesion and the formation of a platelet plug.

Fibrinolytic drugs

In some situations, (for example thrombosis of the iliac arteries in cats), it may be necessary to dissolve a thrombus that has formed. Drugs that achieve this do so by activating the normal biological pathways responsible for lysis of the fibrin clot by promoting the activation plasminogen to plasmin, that is fibrinolytic. Streptokinase and alteplase are examples of fibrinolytic agents.

Further Reading

Rang and Dale's Pharmacology. Elsevier (2020) Ch 25 **Available as e-book from Unimelb library**

Katzung BG and Trevor's Pharmacology. (2019) (12th ed). Appleton Lange. Chapters 34. **Available as e-book from Unimelb library**

Riviere JE and Papich MG (2008). *Veterinary Pharmacology and Therapeutics*. 9th edition. Wiley-Blackwell. Chapters 16-18.