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PATHCHAT

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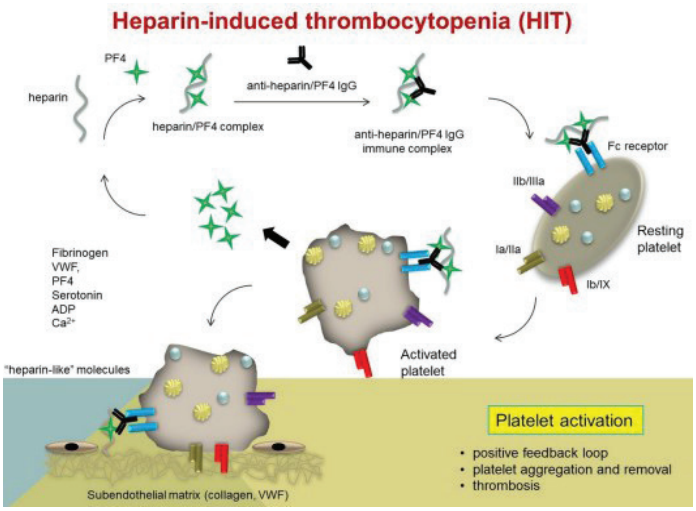
Heparin-induced thrombocytopaenia – HIT happens!

Most patients who receive unfractionated heparin experience a small, quick drop in their platelet count. This is called Type 1 HIT and is clinically insignificant. Heparin is widely used in clinical practice and particularly in patients with cardiovascular disorders. A more serious form of thrombocytopaenia – known as **Type II HIT** – is seen in 0.3 to 3% of patients. This disorder can cause catastrophic arterial and venous thrombosis with a mortality rate as high as 20%.



Unfractionated heparin has a higher risk (1 to 5%) than low molecular weight heparin (0.1 to 1%).

Diagnosis

The diagnosis of HIT is primarily a clinical one. The diagnosis and management of the patient should be the following: Probability scoring with the 4Ts as described below. If positive, then withdraw warfarin and all forms of heparin. Confirm that a laboratory test is available from the pathology laboratory. There is no single laboratory test that can be performed with sufficient speed, sensitivity and specificity to positively guide the primary decision to stop heparin. The decision to perform laboratory tests and the interpretation of the results should always be performed after the clinical scoring system of the 4 Ts system, which has been devised and tested for this purpose. Please note: It is important to note a 50% or more drop in platelet count, but mostly not severe initially, for example, 350, dropped to 150 x 10^9/l.

SCORE	2	1	0
Thrombocytopaenia	>50% platelet count drop to nadir >20 x 10^9/l	30 to 50% platelet count drop or nadir 10-19 x 10^9/l	<30% platelet count drop or nadir <10 x 10^9/l
Time of platelet drop	Day 5 to 10 or Day 1 with recent prior heparin (previous 30 days)	Day 10 or later timing unclear, or Day 1 with less recent heparin (previous 31 to 100 days)	Day 4 or earlier (but no recent prior heparin)
Thrombosis	Proven new thrombosis, skin necrosis or acute systemic reaction after intravenous UFH bolus	Progressive or recurrent thrombosis, erythematous skin lesions, suspected thrombosis (not proven)	None
O**T**her causes of thrombocytopaenia	None evident	Possible	Definite

UHF – unfractionated heparin **pre-test probability score: 6-8 indicated high, 4-5 intermediate and 0-3 low.**

Laboratory diagnosis

The antibody and ELISA tests available have sufficient sensitivity to reliably exclude the diagnosis, while they lack the specificity to positively identify HIT. The serotonin release assay is the gold standard, but is cumbersome and inconvenient for routine use. The simplest method for routine use is a modified platelet aggregation method. Reported studies using this test indicate that it has a high specificity at >90%. However, the sensitivity of the test is more variable, and although >80% most of the time, is frequently nearer to 50 to 60% and therefore cannot reliably exclude HIT.

Specimen requirement

1x citrated blood. It is preferable to use an exact sample of the heparin infused into the patient as an agonist in the test system. Enhanced aggregation (>20%) of normal platelets in the presence of heparin and the patient plasma indicates a positive result.

Pathogenesis

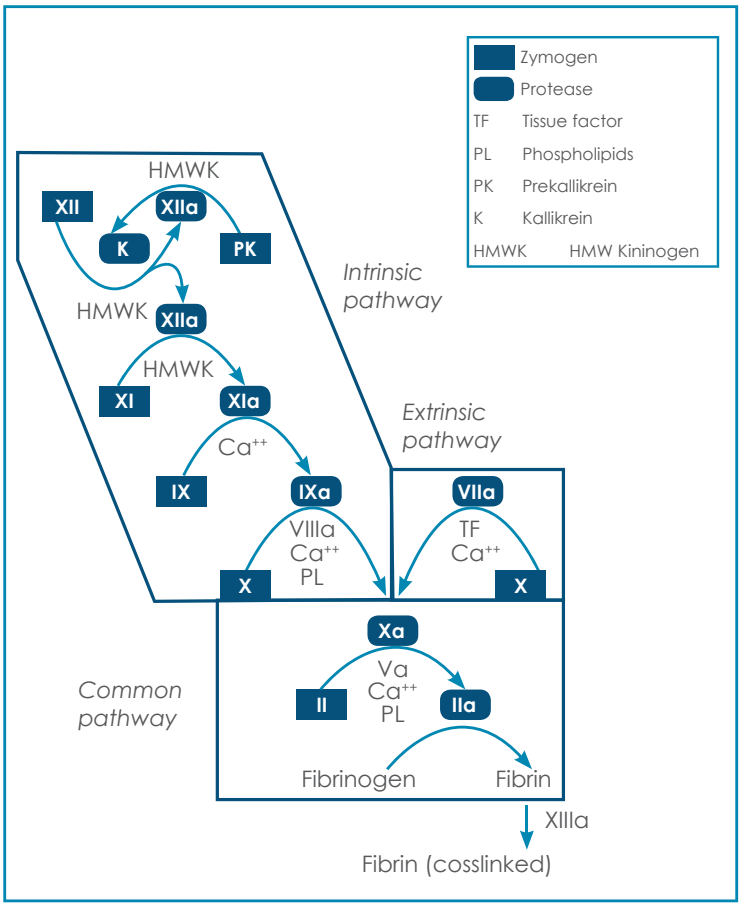
HIT is the result of the development of antibodies against heparin-platelet factor 4 complexes. The antigen-antibody complexes bind to and activate platelets via the FCRγII, resulting in intense platelet activation and the release of procoagulant-rich microparticles. These platelet and monocyte microparticles activate the coagulation cascade by releasing tissue factor, which binds to FVIIa, leading to the activation of factors IX and X. The microparticles also facilitate coagulation by providing an anionic phospholipid membrane surface.

Treatment

Type II HIT develops 5 to 12 days after starting heparin therapy and causes a profound decrease in the platelet count to usually <50 x 10^9/l. This activation results in arterial and venous thrombosis particularly in patients who are ill. This syndrome has a high mortality rate.

Treatment for HIT requires both immediate discontinuation of all heparins and warfarin with the administration of a non-cross-reactive anticoagulant that is capable of interrupting the activated coagulation cascade at the level of thrombin or FX.

The most appropriate anticoagulant for use remains uncertain. It must be immediate acting, associated with a low risk of bleeding, should not require monitoring and – perhaps most important – the physician should be familiar with its use.



Some suggestions

The British Committee for Standards in Haematology (BCSH) recommends the use of fondaparinux. The dosage of Arixtra depends on the initial reason for heparin therapy, renal function and the weight of the patient. The platelet count should be monitored closely and a vitamin K antagonist should be started when the platelet count has recovered to at least 150 x 10^9/l. The administration of fondaparinux and the vitamin K antagonist should overlap for at least five days or until the INR is within the therapeutic range for two consecutive days.

The patient should be advised to avoid heparin, especially in the following three to four months after the diagnosis of HIT and to consult with a specialist if heparin is needed in the future.

The American College of Chest Physicians also recommend lepirudin, argatroban and danaparoid. These drugs are, however, not available in South Africa.

References

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