3.1.5

Acquired (Secondary) Disorders NOT Directly Involving Platelets

Liver Disease

Because clotting factors are synthesized in the liver, liver disease and decreased function leads to a clotting factor shortage. A shortage of clotting factors makes it more difficult for blood to clot. However, sometimes a surprising issue of excessive clotting can also arise with liver disease. We call this DIC, which will be explained shortly in this chapter. DIC with liver failure likely occurs because even though the liver is no longer making clotting factors, it is also no longer producing anticoagulant proteins.

Vitamin K Deficiency

Vitamin K deficiency is another acquired coagulation disorder. As you have previously read, many clotting factors are dependent on vitamin K, so a deficiency in vitamin K leads to a reduced production of clotting factors. Symptoms of this deficiency include bruising, petechiae, and oozing of blood at surgical sites. Because as much as 50% of our vitamin K is made in the gut by bacteria, vitamin K deficiency is more common in infants because they don't have fully established gut flora. As a result, infants often get a vitamin K injection when they are born to facilitate a healthy clotting system. A good source for Vitamin K is found in leafy green vegetables.

Vascular Disorders Relating to Collagen

One acquired vascular disorder that can lead to bleeding is scurvy. **Scurvy** is a relatively rare condition caused by a severe lack of vitamin C in the diet. Without vitamin C, the body cannot make collagen. A diminished production of collagen leads to possible hemorrhage as blood vessels are weakened.

Cushing disease that causes hypercortisolism can be responsible for bleeding because under the influence of high levels of cortisol, the body breaks down more protein including collagen.

Sentinel purpura is another cause for bleeding and happens because as we get older, our collagen gets weaker. This includes the collagen in our vessel walls. This weakening can lead to bleeding and easy bruising.

Disseminated Intravascular Coagulation (DIC)

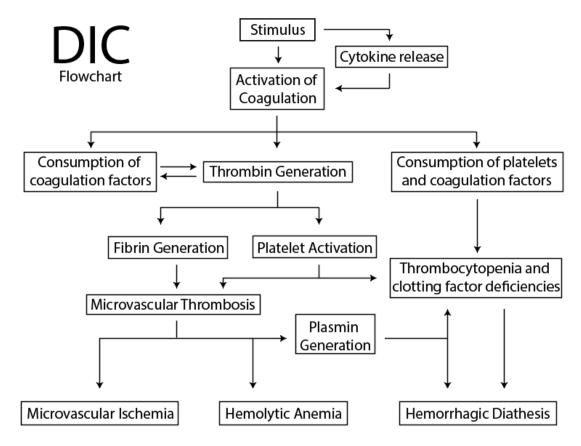


Image by Becky T F19

Disseminated intravascular coagulation (DIC) is characterized by abnormal activation of clotting factors throughout the body rather than in just one localized area surrounding a lesion. The underlying cause of DIC is usually due to large amounts of inflammation, infection, or cancer. Anything that creates an environment where large areas of the body can participate in activating the clotting cascade creates a high risk for DIC. Examples of some things that can do this include necrotic or dying body tissues, tumors that expose collagen and tissue factor to circulating blood, and large burns. As multiple fibrin clots form in the blood, red blood cell fragments called schistocytes may be observed as the cells are sliced when they travel through the clots.

There are two effective treatments for DIC. The first is a transfusion of fresh frozen plasma (FFP) to replace the clotting factors that have been used up in the excessive clotting. The other treatment is use of heparin to try and prevent clots, but if too much heparin is given, excessive bleeding can occur. To decide which treatment approach to take, it is important to figure out where the patient is in the disease process. If excessive clotting has taken place and the clotting factors are depleted, then there is a concern of hemorrhage so plasma would be given to replace clotting factors. However, if clotting factors are still relatively available and there is a concern of clot formation and ischemia development, then heparin could help prevent further excessive clotting.

A patient may arrive with petechiae and purpura and appear to have symptoms of excessive bleeding. How do you know if it is DIC or some other bleeding disorder? A blood test that reveals the concentrations of platelets and clotting factors can help determine the etiology of the condition. TTP and HUS, discussed below, would reveal rapidly depleting platelets but clotting factors remaining more stable. DIC would reveal rapidly depleting clotting factors and increased D dimers (the name for broken down products of clotting factors) because the clot dissolving elements of the blood would also be working overtime trying to take care of the sudden increase in clots. Platelets would be a bit more stable with DIC, although they can also diminish with time as the fibrin clots trap and activate them (via thrombin binding).



Petechiae and Purpura: Tiny (1-3 mm) red dots called **petechiae** can form in pinpoint patterns due to bursting of small capillaries. Blood can also collect under tissue due to vessel breakage within the skin in larger and typically raised purple spots called **purpura**, which involve inflammation of the blood vessels or vasculitis. Blood can also pool in very large bruised areas called **ecchymosis** (not pictured). *https://commons.wikimedia.org/wiki/File:Purpura.jpg; Hektor; GNU Free Documentation License, Version 1.2 or any later version published by the Free Software Foundation* Antiphospholipid Syndrome

Antiphospholipid syndrome is an autoimmune disease in which the body produces autoantibodies directed against several species of negatively charged phospholipids. Ultimately, this leads to tissue damage, inflammation, and even direct activation of platelets. Common manifestations of antiphospholipid syndrome are recurrent thrombosis (venous and arterial), repeated fetal loss, and thrombocytopenia.

Exogenous Estrogen and Pregnancy

During pregnancy and while using exogenous estrogen as a contraceptive or medication for various conditions, estrogen levels are high. Estrogen is a potent stimulator of the liver and increases the number of blood proteins that the liver makes. Since many of the clotting proteins are made in the liver, a relatively hypercoagulable state develops in the circulatory system of individuals experiencing high levels of estrogen.

Stasis of Blood

Stasis of blood may occur in patients who are experiencing prolonged bed rest or immobility. The decreased circulation causes an excessive number of platelets and clotting factors to accumulate near each other and spontaneous clots may arise.

Cancer

Neoplasms and malignant cancer cells can recruit large numbers of new blood vessels that may be fragile and more likely to break. Healthy tissue is also compromised by cancer tissue such that tissue factor may be produced

excessively and exposed to the blood. Connective tissue like collagen may also be exposed to the blood more readily in tumors.

Lifestyle

Smoking, obesity, and insulin resistance all promote endothelial cell injury which increases the risk for triggering a clotting process.



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