Disseminated Intravascular Dissemination (DIC)

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At the IDG Meeting, I gave a rather long explanation of DIC, on the bequest of Nancy. I wish to give a summary of that talk, to make following these attachments much easier.

01CoagulationPathway.jpg

This slide is the prototypical slide used to instruct students on the coagulation pathway. The best way to approach this slide is to understand that the clotting factors were named in the order in which they were discovered—they are not named in logical sequence. If you start with the Extrinsic pathway, it makes understanding this slide that much easier.

Think of think of this sequence: 7 – (skip 8) – 9 – 10 – (T in ten and T in two) – 2 – 1 – Clot. That is count up from 7 to 10 then down 2 to 1. Remember this sequence, and it makes the rest easier to remember.

Extrinsic pathway: think "E" as external to the body, and this will help you remember that infections and trauma are the major events "external" to the body that initiates the process of DIC. Take infection: E coli, Staph aureus, or any other bacterium that secretes an endotoxin that damages tissue. This creates Tissue Factor (TF) that induces the activation of factor VII to VIIa. This starts the coagulation pathway (the above sequence) that leads to clot formation.

02TNF-Pathway1.png

This slide depicts what happens during an infection. The body produces T lymphocytes (CD14) and macrophages (MD2) to fight the infection, here labeled as "Myeloid cells." The macrophage releases interleukin-6 (IL-6), which is a major mediator of inflammation, and Tumor Necrosis Factor (TNF). IL-6 leads to the expression of Tissue Factor (TF)—remember the discussion from above?—that leads to the clotting sequence—which you have memorized by now: 7 – (skip 8) – 9 – 10 – 2 – 1 – Clot.

TNF leads to the production of tissue Plasminogen Activator (t-PA) which leads to Plasminogen, which leads to Plasmin, which is used to lyse (break up) fibrin, which breaks down clot formation. This can be measures as the release of plasmin degradation products.

Now, you have a model for DIC. It is a race between two systems: the clotting pathway and the lysis of fibrin, or the bleeding pathway. In DIC, usually clotting wins out—hence, the name DIC. However, there are times in which bleeding wins out. Sometimes, clotting proceeds first followed by bleeding. DIC is a terrible disease, it is hard to manage, and mortality in the ICU is as high as 50%.

03TNF-Pathway2.jpg

This is a busy slide. I include it here to show you that there are many other proteins involved. This is a complex process. The bottom line is that you can see the endothelial lining is a busy place with many proteins that are inter related. You can see that TNF leads to many things: expression of proteins leading to clotting: "Procoagulant effects" and promoting bleeding: "Fibrinolysis effects."

04PlasminPathway.png

This slide shows the formation of Plasmin. If you have a clot, you have to break up the clot. Here you can see that tPA, which wee discussed already, leads to Plasminogen converting to Plasmin, which then breaks up Fibrin, releasing fibrin degradation products (again, all discussed above). You should be familiar with tPA and Urokinase used in medicine to reverse clotting, say in patients with acute coronary syndrome, or a patient having a stroke, or to open clogged CVP catheters, as three common examples.

05DIC-Pathogenesis_Levi.pdf

This is an article that was written in 1993, and is fairly easy to read. In Fig 2 it shows the coagulation pathway, which is the first slide that was looked at. In Fig 3 it introduces the concept of Protein C interaction. There is a separate pathway that leads to clotting amplification (and makes DIC that much worse). Thrombin combines to Thrombomodulin to form a complex, which causes Protein C to become activated. This then combines with Protein S to inhibit Factors V and VIII (it shuts down the intrinsic pathway), and leads to more bleeding—not cool! If

you remember, clinically there are people with protein C deficiencies that tend to get DVTs, so activating this system causes bleeding.

The final thing shown in this article is that volunteers who are infused either endotoxin or TNF will first have elevation in plasminogen, leading to bleeding, and later elevation in Plasminogen Activator Inhibitor (PAI-1), leading to clotting.

06DIC-Pathogenesis_Logan.pdf

This is a peer-review article that comments on Levi's article.

07DIC-Cerebral_Neligan.pdf

This is an article showing a case of DIC that resulted in multiple micro-hemorrhages in the brain leading to near death, and permanent brain injury. Given the diffuse nature of the cerebral bleeding, this patient had a long recovery and acted like a post traumatic head injury patient.

08DIC-Gangrene_Davis.pdf

This article features a case of DIC that resulted in gangrene and loss of all four limbs. This is a nightmare scenario.

09DIC-Advances_Madoiwa.pdf

This is an article written in 2015 which is a very difficult read. It shows you how much more information is now known about DIC since the first article written by Levi in 1993. I find Hematology to be one of the most challenging fields, and very difficult to keep current, given the ever-evolving knowledge base. This is why there are specialists in this field. I am a generalist. My knowledge base is only slightly ahead of yours!

I hope this summary helps!!!

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