Heme Testing Aid/APLS

Some PGY-1

Weird But HY Coagulation Pathway Assays

-An Activated Protein C Resistance Assay is an experimental approach that involves the addition of Activated Protein C to a patient's plasma and detecting how long it takes a clot to form. We know that Protein C inhibits Factor 5 (and 8). In the absence of Protein C, a clot forms quickly. The addition of Protein C should inhibit Factor 5 and hence increase the amount of time needed to form a clot. A slight (or no change) in the clotting time after the addition of Activated Protein C is diagnostic of factor V Leiden.

-Mixing studies are essentially studies that involve 2 phases. In Phase 1, an increased PT or PTT is noted. In the 2nd phase, the addition of normal plasma that selectively contains coagulation factors of interest fixes the problem and decreases the PT and PTT back to a normal range.

Antiphospholipid Syndrome 1

-Antiphospholipid syndrome (APLS) is a bizarre autoimmune disease with a poorly understood pathophysiology. What follows is my approach to rationalize the mechanism in my head. This is not necessarily the underlying pathophysiology but it should make do for the USMLEs.

-In the body, APLS autoantibodies bind to and initiate the destruction of “phospholipid binders”. The removal of these “phospholipid binders” from circulation leads to a physiologic excess of phospholipids which leads to an increased activation of the coagulation cascade and thrombosis. In addition, autoantibodies are typically made against Protein C and other anti clotting proteins (pro-thrombotic).

-In test tubes, APLS autoantibodies do not bind “phospholipid binders” but instead bind “actual phospholipids”. The removal of “actual phospholipids” from circulation leads to a decreased activation of the coagulation cascade and hence an increased PT/PTT since it takes longer for a clot to form.

Antiphospholipid Syndrome 2

The **Dilute Russell Viper Venom Time** (DRVVT) is a test often used to assess **APLS**.

Step 1-Add Viper Venom to a sample of the patient's serum. Viper Venom activates Factor 10 and leads to the formation of a clot via the final common pathway. This is a "test tube" test so an individual with APLS autoantibodies would have a low level of phospholipids and hence an increased PT/PTT (clot forming time). Unfortunately, the increased PT/PTT could also arise from a deficiency of any member of the final common pathway of the coagulation cascade (factors 1, 2, and 5).

Step 2-Normal plasma (which contains adequate amounts of clotting factors) is added to the mix from Step 1. An individual that has APLS autoantibodies will not have a decrease in the PT/PTT since these autoantibodies are still present and there's no phospholipid to "fix" the phospholipid deficiency problem. On the flip side, if the increased PT/PTT stems from a final common pathway coagulation factor deficiency, the PT/PTT will be decreased (make sure you understand this).

Step 3-A large amount of phospholipid is added. This addition overwhelms and cancels out the effect of APLS autoantibodies present in the plasma. In this case, the PT/PTT should decrease to a normal range since the underlying problem has been corrected (again, make sure you understand this).