**Lecture 7 Outline**

**Hemostatic Disorders of Bleeding**

1. General information:
   1. Disorders can be inherited or acquired.
      1. Small percentages are alright as long as they are working properly (adaptation)
2. Definitions:
   1. Hematoma:
   2. Hemarthroses:
   3. Hemorrhage:
3. Treatment options:
   1. FFP (Fresh Frozen Plasma)
      1. Blood product from a single donor containing all clotting factors, including labile V and VIII
      2. Good for deficiencies other than hemophilia, vWD, and afibrinogenemia
   2. Cryoprecipitate
      1. Concentrated source of VIII, but also contains fibrinogen, XIII, and vWF
      2. Prepared from a single unit of donor blood
   3. Prothrombin complex concentrates
      1. Pooled donor concentrates which contain factors II, VII, IX, X (sometimes one brand may have more VII than others, and sometimes has VIIa)
      2. Names such as:
         1. Konyne (lower level of VII)
         2. ProplexT
         3. FEIBA (=Factor Eight Inhibitor Bypass Activity) (factor VII in this is most VIIa- Hemophilia or VII defieciency
      3. These are recommended for VII deficiency, IX deficiency, and bleeding episodes in patients [hemophiliacs] with inhibitors to factor VIII
4. Hereditary Disorders – see chart A 🡪 I

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Factor | Inheritance | Bleeding | Diagnosed at birth? | Treatment | Notes |
| A | Prekallekrein (Fletcher) |  |  |  |  | 1. Will have extremely long PTT times. 2. Incubate PTT (plasma + activator) for 10 minutes, then add Ca++, PTT will shorten 3. XII🡪XIIa 4. XIIa + HMWK🡪 5. Prekallekrein🡪kallekrein 6. Kallekrein feeds back to further activate XII + XI |
| B | HMWK (Fitzgerald) |  |  |  |  |  |
| C | XII (Hageman factor) |  |  |  |  |  |
| D | XI (PTA-plasma thromboplastin antecedent) |  |  |  |  |  |
| E | X  (Stuart Prower) |  |  |  |  |  |
| F | VII (proconvertin) |  |  |  |  |  |
| G | V (proaccelerin) |  |  |  |  |  |
| H | II (prothrombin) |  |  |  |  |  |
| I | XIII (fibrin stabilizing factor) |  |  |  |  |  |

J. I (Fibrinogen)- Deficiencies

1. 3 types
2. Afibrinogenemia:
3. Hypofibrinogenemia:
4. Dysfibrinogenemia:
5. Afibrinogenemia
6. Hypofibrinogenemia
7. Dysfibrinogenemia
8. Hyperfibrinogenemia

K. VIII (AHF)

1. Called: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
2. Decreased amount of VIII:c (decreased synthesis)
3. Inheritance? \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
4. Diagnosed in levels
   1. <1% 🡪 severe
   2. 1-5% 🡪 moderate
   3. >5% 🡪 mild
5. In factor VII, you can develop an alloantibody or autoantibody. (Considered to be acquired)
   1. In pregnancy, a woman can develop antibodies against her own will
   2. Penicillin can cause development of antibodies
   3. Aging can cause development of antibodies
   4. Mutation of a gene can cause a person to be born with hemophilia A.
6. Treatment
   1. Recombinant VIII is preferred product [pure protein synthesized in the lab instead of being extracted from blood]
   2. Monoclonal VIII is next best
   3. Human VIII is third choice
   4. Porcine VIII available, but not widely used
   5. Recombinant VIIa used for hemophiliacs who have antibodies to VIII or IX (Novoseven)
      1. Under N conditions, about 1% of the VII in the blood circulates in an activated form – VIIa
      2. This small circulating concentration of VIIa by itself does not initiate coagulation until it binds to tissue factor (TF) exposed by vascular injury
      3. The VIIa-TF complex activates more VII🡪VIIa, IX🡪IXa, and X🡪Xa
      4. IXa in conjunction with VIIIa then initiates coagulation
      5. In patients with VIII inhibitor, infusion of Novoseven typically increases concentration of VIIa by 10-100 fold. This high concentration of VIIa bypasses the VIII inhibitor, stimulating hemostasis at vascular wound sites
   6. Proplex (II, VII, IX, X concentrate) also can be used to treat patients with VIII inhibitors. Similar bypass mechanism [FEIBA- Factor Eight Inhibitor Bypassing Activity]
   7. All these products are packaged and given the same way- they come as a lyophilized, frozen material that needs to be solubilized in reagent water that comes with the product. It is all mixed in a syringe that comes with the product. Once mixed, the shelf like is about 3 hours. They are all given to the patient IV push. They can also be given IV drip at some rate to provide continuous infusion. Dosing is based on the desired level of factor.

L. IX (Christmas factor)

1. Called: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
2. Inheritance? \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

M. von Willebrand’s Disease

1. Called: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
2. Inheritance? \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Acute Phase Reactant = when these situations occur in the body, you can have more VIII.

* Levels will fluctuate.
* Platelet function assays will be normal (bleeding time/PFA)
* Most bledding will be under the skin.

1. Acquired Disorders of Bleeding
   1. Trauma
   2. Exposure to drugs
      1. Antibiotics kill bacteria. If drug kills bacteria that make vitamin K, need vitamin K for prothrombin group
   3. Chronic diseases
      1. Liver diseases: maybe VIII:c molecule is not being made or working right, possible decrease in production
      2. Renal disease: abnormal vessel interaction
   4. Development of antibiotics
   5. People on Coumadin
2. Distinguishing Hemophilia A from Classic (Type 1) von Willebrand’s Disease

|  |  |  |
| --- | --- | --- |
| **Test** | **Hemophilia A**  (normal, prolonged, or decreased) | **von Willebrand’s Disease** (normal, prolonged, or decreased) |
| Platelet Count |  |  |
| Bleeding Time or PFA |  |  |
| Platelet retention to glass beads |  |  |
| Platelet aggregation with ristocetin |  |  |
| PT |  |  |
| PTT |  |  |
| Factor VIII assay (VIII:C) |  |  |
| Factor VIII antigen (VIII:vWF) |  |  |
| Ristocetin cofactor assay |  |  |
| vWF multimers |  |  |