The Bleeding Bunch: Hemophilia

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Assignment: Presentation
SBS11QHG2
Period 6

Headings till the very end

Physiology

Figure 1

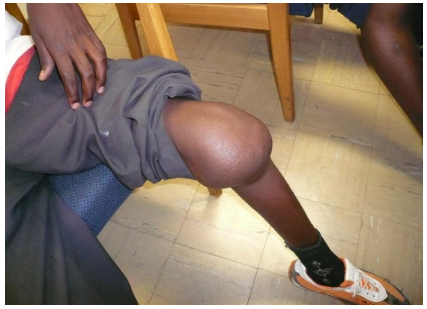


Figure 2

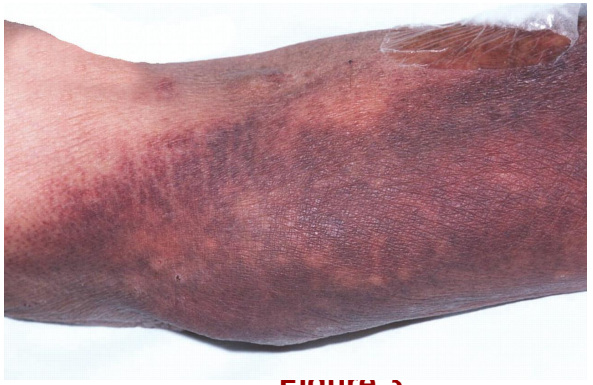


Figure 3

- 3 Types: A, which affects 1 in 5,000 males/ B, which affects 1 in 20,000 males/ and C, which affects 1 in 100,000 individuals. (Focusing on A for most of this presentation)
- Hemophilia B is also called the Christmas disease because it was named after Stephen Christmas, the very first patient that was diagnosed with this disease
- Hemophilia A is the second most common bleeding disorder next to von Willebrand disease
- Symptoms include mad bleeding everywhere and can't stop (F1), hematomas (F2), contusion (F3), swelling, joint pain, sudden nosebleeds, and blood in urine/stool
- Early onset but symptoms don't form until after infancy, when the child's motor skill begin to develop
- All these symptoms are caused by a deficiency in clotting factors 8 or 9, depending on which type of hemophilia one has
- Clotting factors aid in coagulation, the process of blood clotting

Molecular Cause

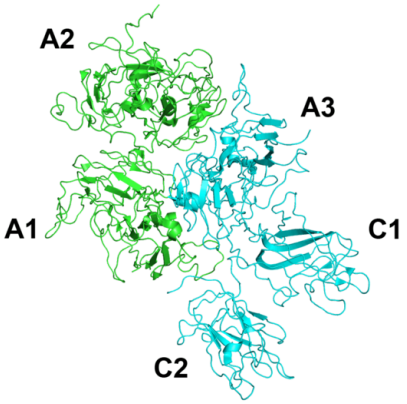


Figure 4

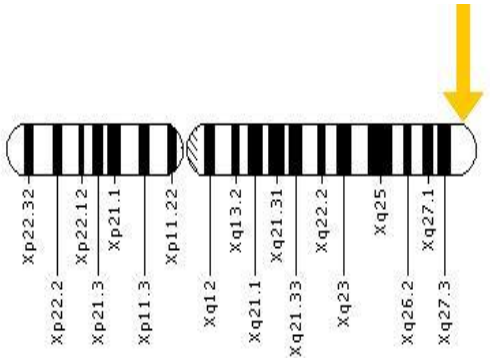


Figure 5

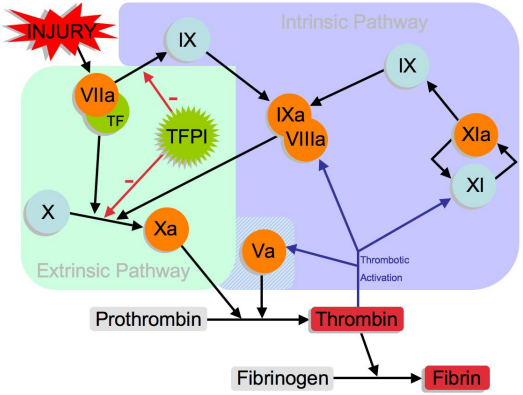


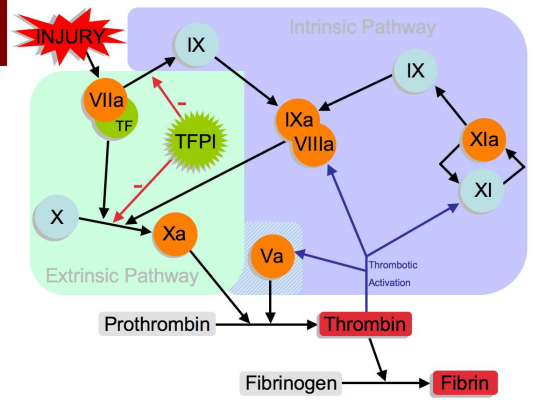
Figure 6

- Hemophilia Is a sex-linked recessive disorder. More males than females
- In hemophilia A, huge inversion on exons 1 - 22 and 23 - 26, which accounts for 50% of mutation. Another 30% are non-familial plus spontaneous and the others are usually point mutations but not always
- Mutation occurs at the location Xq28 on the F8 gene on the X chromosome
- 10% of defects are unusable clotting factors while the other 90% make insufficient amount of them
- The role of the clotting factors in the coagulation cascade is to react with aggregated platelets to amplify production of thrombin
- Thrombin cleaves fibrinogen into fibrin, the material that does most of the clotting

Treatments/Risk/Limits

- Standard of cure: replacement therapy: shooting up missing recombinant/plasma-derived clotting factors up a vein
- Some risks are that immune system might start attacking these factors and that the plasma-derived clotting factors might contain pathogens such as HIV
- A limitation of this treatment is that the clotting factors will eventually break down, depending on the person, usually in a month and must be readministered. If not, the patient might have another episode of bleeds
- Medications that supplement this treatment include desmopressin, a synthetic hormone that stimulates the production of clotting factors 8 and von Willebrand factors (factors that bind to clotting factors 8 to slow down clotting factors' 8 degradation), and antifibrinolytic medicine, pills that neutralizes chemicals that break down clots.
- Hormones are potent and affect a lot of other cells. This is why desmopressin include a lot of the usual side effects such as headaches, nausea, and seizures
- Another known treatment is to receive a liver transplant because that is where the clotting factors are made. One would be using another's DNA to produce the clotting factors for them
- Many, many risks and limits arise from the transplant
- The immune system might reject the liver, attacking it. If so, the immune system must be suppressed by drugs which the patient will constantly have to take time to time, degrading the quality of life. Also, the a person has to die because the liver is a vital organ
- There are known cases definitely in mice where a liver transplant worked where the scientists were able to implant endothelial cells of a healthy mouse onto the liver of a hemophiliac one. The mice was able to produce clotting factors that it was missing prior to the surgery

Proposal Cure/Limits



- Thrombin is the key source to clotting blood
- Let's save as much thrombin as we can! (without killing the patient. If thrombin is introduced before the patient needs it, a clot will form and possibly obstruct the arteries)
- Thrombin is practically used at all stages of the coagulation cascade such as activated factor 5 to 5a, 7 to 7a, 8 to 8a, aggregating platelets, and fibrinogen to fibrin.
- Another way to activate factor 5 to 5a and factor 7 to 7a without "wasting" thrombin is to activate it using factor 10a. Factor 10a is able to cleave both factor 5 and 7 at specific areas which allows them to be in their activated form.
- I propose to use a porous chamber that contains stationary, beaded form of factor 10a which will allow smaller proteins such as factors 5, 5a, and 7, 7a to filter pass it while preventing the factors 10a from leaving it. That way when the clotting factors filter through this chamber, they would activate by the factors 10a so they would not need to be activated by thrombin later on. This method relies on the thrombin produced by the reaction between factor 10a and factor 5a
- This apparatus would be located near the liver because not only this is the location that the factors are produced, eventually all blood will be filtered at this point
- Reasons why this will not kill the patient: I will point through the coagulation cascade but general idea is that the activated clotting factors need a tissue factor to start the cascade which is not available until the subendothelial tissue is exposed, basically, if one gets wounded
- Limitations of this cure may include the fact that the patient will have to go through surgery, and for a hemophilia, this could mean certain death if procedures are not followed. Another limitation would be that the amount of thrombin saved will never compare to the thrombin explosion generated by the factor 8 and 9 reacting with aggregated platelets.

References

Slide 1:

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Figure 1 http://diseasespictures.com/hemophilia/

Figure 2 http://drugline.org/medic/term/hemophilia/

Figure 3 http://biol1020-2.blogspot.com/haemophilia-b.html

Slide 2:

Kliegman, Robert (2011). *Nelson textbook of pediatrics.* (19th ed. ed.). Philadelphia: Saunders. ISBN 978-1-4377-0755-7.

Figure 4 http://www.personal.psu.edu/jzs5510/table.html

Figure 5 http://ghr.nlm.nih.gov/gene/F8

Figure 6 http://matthewheron.wordpress.com/2012/01/26/

Slide 3:

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"Result Filters." *National Center for Biotechnology Information*. U.S. National Library of Medicine, n.d. Web. 22 May 2013. http://www.ncbi.nlm.nih.gov/pubmed/9249003

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