

Factor Concentrates.

More is better?

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Scenario -1

- Call from OR !
 - Patients is bleeding out !
 - Don't' ask why, what rate what's been done!
 - We need blood now !
 - What kind of blood would that be ?
 - Just Everything !!!
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Wrong Scenario

- Why in this day and age do medical professionals have such a poor understanding of blood and blood products?
 - Whose job is it to decide what is the most appropriate therapy ?
 - **Answer – he who controls the product. !!!**
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Needed Background Information

- Was the patient normal before surgery.
 - Did he have any underlying coagulopathy ? Liver disease !
 - Did he have any drugs that inhibit platelet function ?
 - Do you have any recent labs !
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Management of Bleeding

- Most bleeding that occurs in hospitalised patients is not anticipated, but is because of what we do to them !
 - Predictable bleeding patients such as hemophilia (factors VIII, IX and XI) & Von Willebrand's disease are very different.
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The Hemophilias

- Factor VIII & XI deficiency is limited to about 30-40,000 male patients in the US, with most about 30K being F VIII.
 - Factor XI deficiency occurs almost exclusively in Ashkenazi Jews & is rare outside Israel.
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Hemophilia Treatment

- ❑ Focused on replacing the missing factor by purified or recombinant specific Factor.
 - ❑ Patients can treat themselves at home for small bleeds.
 - ❑ For surgery, will need hospitalisation and prolonged treatment (usually 10-14days) till wound heals.
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Hemophilia Problems

- About 25 % of them will develop an antibody /inhibitor to the transfused material recognising it as “foreign”
 - They can be very difficult and expensive to treat.
 - Specific strategies have been developed to “bypass” or hyperactivated the clotting system.
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Hemophilia Treatments

- ❑ Human and recombinant F VIII and Factor IX are widely available.
 - ❑ Factor IX concentrate available in Israel.
 - ❑ All work predictably.
 - ❑ Formation of inhibitors is only marginally less with recombinant products.
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The Inhibitor Patient

- ❑ The blood banks worst financial nightmare!
 - ❑ Inhibitor bypassing products include FEIBA and Autoplex.
 - ❑ Exact mechanism of they work is not known, but thought to be focused through factor Xa.
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Ultimate Inhibitor Patient

- ❑ Resistant to FVIII and bypassing products.
 - ❑ Now use NovoSeven (rec. F VIIa)
 - ❑ Doses of 90 -300 μ g/kg are required every 2 hours.
 - ❑ This can cost up to \$30,000 per dose in a 100kg male.
 - ❑ This represents >\$250, 000/day !!
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Rarer Concentrates

- ❑ C1-esterase inhibitor concentrate for patients with hereditary angioedema.
 - ❑ Not FDA approved in US but is allowed in through Argentina for “off label use” through Angioedema Foundation.
 - ❑ Used mainly for patients in high risk situations i.e pregnancy delivery
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More Rarer Concentrates

- ❑ Protein C concentrate available for compassionate use in US for babies with homozygous Protein C deficiency.
 - ❑ Can get life threatening thrombosis at birth if not treated.
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Unique Concentrates

- ❑ Rec. Activated Protein C (Xigris)
 - ❑ Specifically designed to prevent micro thrombi in the septic patient by inhibiting thrombin generation.
 - ❑ Clinical trials highly successful, but poor utilisation in US, probably due to poor validation of bacterial sepsis & fear of “bleeding” from anticoagulant.
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Different Concentrates

- ❑ Three plasma derived factor IX concentrates (Bebulin, Alphanine & ?) are in reality "PCCs"
 - ❑ They contain not only FIX, but high doses of F II & F X and low doses of F VII.
 - ❑ Bebulin also contains Proteins C & S, making it very useful for acute reversal of Coumadin Overdose.
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Oldies but Goodies

- ❑ Antithrombin concentrates have been available for 15 years as a plasma derived product, in this past year as transgenic material from goats milk.
 - ❑ Developed specifically for the congenital AT deficient patient but useful also in acquired deficiency such as DIC and Liver Transplantation.
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More Oldies but Goodies

- ❑ Fibrinogen Concentrates were approved recently in the US.
 - ❑ They were available many years ago but were withdrawn because of their high viral disease transmission.
 - ❑ New products are safe even though still plasma derived.
 - ❑ Should prove very useful.
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All Hail the New King !

- ❑ The mantra for most surgeons in a bleeding patient is it's not their fault.
 - ❑ If they are losing blood then give blood back !
 - ❑ Problem is we don't have blood any more, we have bits of blood.
 - ❑ Surgeons and anesthesiologists don't really know how to dose bits of blood
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All Hail the New King !

- How much of a “bit to give” depends on who is shouting the most.
 - The famous “just keep me 5 units ahead”
 - Ahead of what !!
 - Trauma protocols have developed good strategies that provide products in a balanced manner
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All Hail the New King !

- ❑ Most blood product ordering is done without any real thought.
 - ❑ The 2,2 and 1 (FFP, Cryo & platelets) is “routine” but not logical.
 - ❑ If that does not work, give twice as much !!
 - ❑ If it’s going to hell in a hand basket, order the **“King of Clots” !!**
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The King is NovoSeven !!

- ❑ Recombinant FVIIa is the most potent hemostatic agent we have.
 - ❑ It is not used at physiological dose but at pharmaceutical doses (20 x higher)
 - ❑ It was not developed to plug holes in patients put there by surgeons.
 - ❑ It is however effective used correctly.
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More King

- It use needs to be controlled by transfusion medicine physicians who understand its benefits & limitations.
 - It can and does cause thrombosis in off label use (new FDA Black Box Warning last week)
 - Most of it's use in US is "off label"
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Even More King

- It is very effective in long surgeries with a lot of tissue damage and exposure.
 - Good examples are Aortic Aneurysms and Cardiac bypass.
 - We allow 3 small 2mg doses to be given by defined Cardiac Anesthesia MD in a 24 hour period.
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The King Again !

- ❑ It is not a panacea for all bleeding that is uncontrollable.
 - ❑ More surgery is usually needed also.
 - ❑ It needs to be give with an adequate level of Fibrinogen ($> 100\text{mg/dL}$).
 - ❑ It can and does activate platelets.
 - ❑ It can be truly life saving !
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The Future

- ❑ More is not better .
 - ❑ Use of the correct product will work better than loads of everything.
 - ❑ Stuff rarely work .
 - ❑ Some concentrates will recycle as anti-inflammatories with anticoagulant overtones (AT rec & rAPC).
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More Future

- ❑ New unique concentrates will continue to be developed.
 - ❑ Active site blocked r FVIIa.
 - ❑ Genetically matched recombinant /human FVIII to prevent inhibitor.
 - ❑ Plasmin as an antifibrinolytic (drug)
 - ❑ Things you can't imagine.
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