

Everything You Always Wanted To Know About Prophylaxis, PORTs & Immune Tolerance

But

Were Afraid To Ask

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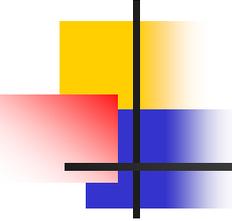
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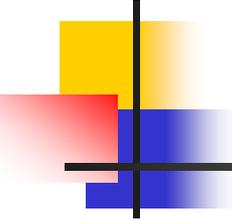
MSU Center for Bleeding &
Clotting Disorders

National Hemophilia Foundation Meeting 2003



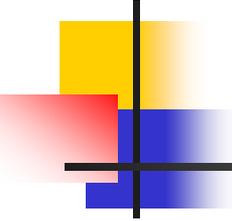
Prophylaxis

- What is prophylaxis?
 - Prophylaxis is the regular infusion of clotting factor administered to prevent or suppress bleeding episodes
 - Prophylactic infusions are given when a patient is not bleeding
 - Prophylaxis may be given before surgery, exercise, to suppress bleeding in a problem joint, or as part of a program to prevent joint disease



Prophylaxis

- Is prophylaxis for all patients regardless of severity?
 - Not indicated for mild deficiency
 - May be indicated in some forms of moderate deficiency if frequent bleeding occurs especially in joints
 - Some severe deficient patients don't bleed into joints enough to warrant prophylaxis



Prophylaxis

- Are there different kinds of prophylaxis?

Model

Revised Definition

Primary prophylaxis determined by age

Long-term continuous* treatment started before 2 years of age and prior to clinically evident joint bleeding

Primary prophylaxis determined by first bleed

Long-term continuous* treatment started prior to the onset of joint damage,[†] irrespective of age

Secondary prophylaxis

Long-term continuous* treatment not fulfilling the criteria for primary prophylaxis

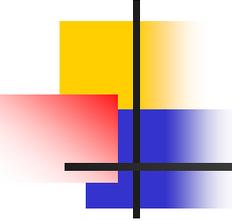
Short-term prophylaxis

Short-term treatment to prevent bleeding

*With intent of treating 52 weeks/yr up to adulthood, minimum treatment of 46 weeks/yr.

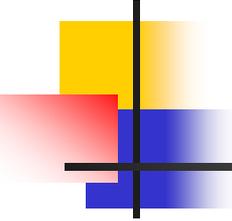
[†]Presumptively defined as having had no more than one joint bleed.

Berntorp et al. *Haemophilia*. 2003;9 (suppl 1):1-4.



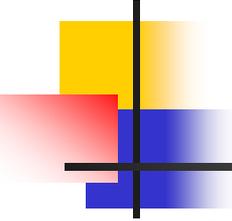
Prophylaxis

- Does it matter how often I am infused when on prophylaxis?
 - Yes!
 - Breakthrough bleeding
 - Amount of concentrate used
 - No?
 - If started at a very young age and frequency increased as tolerated and joint bleeding suppressed



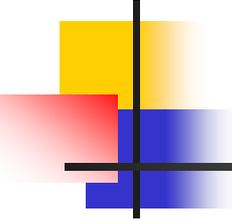
Prophylaxis

- Are there ways to decrease the amount of factor I use on prophylaxis?
 - The shorter the infusion interval the less factor used
 - Twice a week uses more than 3 times a week uses more than every other day uses more than daily
 - If a target joint has developed it will take more factor concentrate meaning a higher level to suppress bleeding episodes
 - Healthy joints use less factor to suppress bleeding



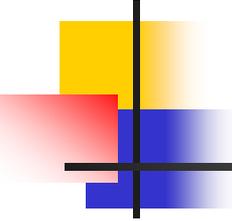
Prophylaxis

- What benefits has prophylaxis been shown to provide?
 - Only method to date **proven** to prevent musculoskeletal disease
 - If prophylaxis successful in suppressing bleeding episodes to less than 12 a year, academic achievement is improved
 - Increased freedom and more normal psychosocial functioning for the child and family
 - Unproven benefits
 - Decreased inhibitors



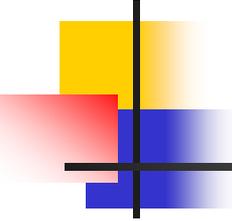
Prophylaxis

- Do I have to have a central venous access device to do prophylaxis?
 - No
 - But it may not be easy
 - It takes dedication and patience
 - Not all children are good candidates
 - Not every family is successful up front with peripheral venipuncture even with great effort



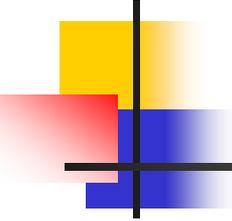
Prophylaxis

- When should my child start primary prophylaxis?
 - What is your child's bleeding pattern?
 - Do you have a family history by which the risk of musculoskeletal complications can be judged?
 - When did or will the first joint bleed occur?



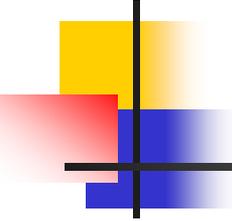
Prophylaxis

- When can I stop prophylaxis?
 - Do you have musculoskeletal problems?
 - Is insurance an issue?
 - How active are you?
 - How often do you bleed off prophylaxis and can you readily infuse if bleeding occurs?
 - Have you finished growing?



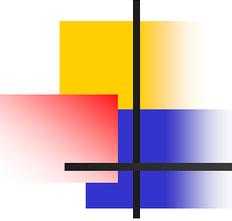
Prophylaxis

- What do I do when my child has a bleed?
 - Treat
 - Quickly and adequately
 - Discuss how to return to your regular schedule with your health care provider
 - Report breakthrough bleeds
 - Was it spontaneous or associated with injury?
 - What day of the week did the bleed occur?
 - How many breakthrough bleeds have been experienced on the current regimen?
 - Does the regimen need to be altered?
 - Dose
 - Frequency



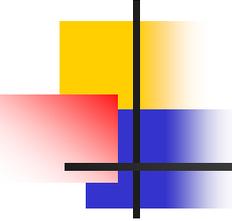
Prophylaxis

- What is hard about prophylaxis?
 - Administration of factor
 - PORTs require attention to good care
 - Peripheral venipuncture requires being comfortable, confident
 - In some the transition may take months, be patient
 - Factor should optimally be given in the morning
 - Compliance with any long term regimen of care requires work and knowledge of goals
 - Very young children
 - Adolescence
 - Insurance costs



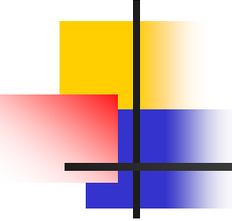
Prophylaxis

- Does prophylaxis cost more?
 - Yes
 - Putting money up front for disorder rather than paying for treatment of consequences
 - What is the cost to society of a person who does not function optimally?
 - Physical perspective
 - Achievement perspective?



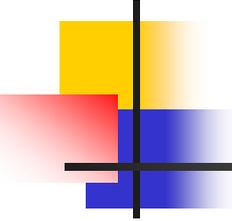
PORTs

- What is a PORT?
 - Implantable venous access device
 - Several types available
 - Port-a-cath: completely under the skin
 - Broviac™, Hickman™ : catheter extends out through the skin
 - Peripheral intravenous access devices: P.A.S. ports™, SlimPorts™
- Arterio-venous fistula?



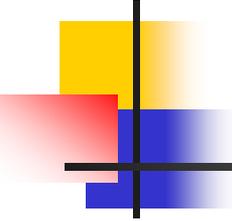
PORTs

- When is a PORT used?
 - Poor venous access
 - Usually in the very young
 - If daily or frequent treatment is necessary



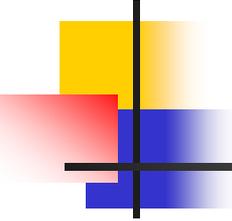
PORTS

- What things should I consider before my child gets a PORT?
 - The medical goal
 - My child's bleeding tendency
 - My social situation
 - The expected risk of complications



PORTs

- What information do I need to know about my PORT?
 - Proper technique of accessing port
 - Proper care of the port
 - Recognizing the early signs of complications
 - Know that PORTs are temporary solutions
 - Prepare your child by always saying that the PORT will eventually be removed, it cannot stay in forever



PORTs

- What are problems associated with PORTs?

Principal

Early

Late

Infection

Hemothorax

Thrombosis

Thrombosis

Pneumothorax

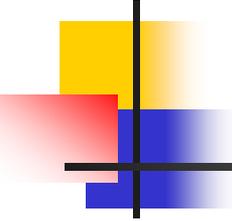
Infection

Hematoma

Mechanical problems

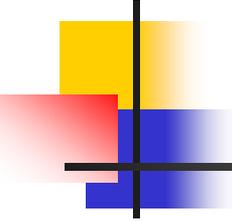
Infection

- Fracture with/without embolization
 - Line migration
 - Separation of catheter from reservoir
 - Erosion of skin over port
-



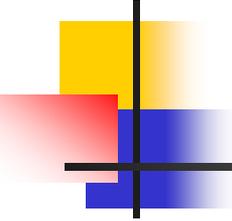
PORTs

- Who is at risk for these complications with PORTs?
 - Everyone with a port
 - Especially patients with an inhibitor
 - Maybe those who use EMLA cream
 - Patients with other coagulation disorders
 - Virally infected patients



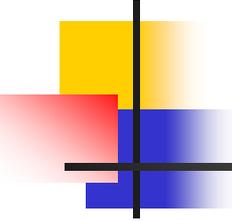
PORTs

- When should a PORT be removed?
 - As soon as feasible
 - When there is infection that can not be cleared
 - When the catheter is occluded
 - When a thrombosis in the vessel has occurred



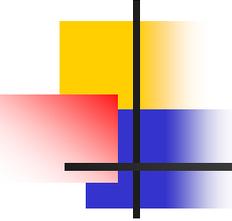
PORTs

- When should peripheral venipuncture be considered?
 - As soon as possible
 - When the child has adequate peripheral veins
 - When the child is cooperative
 - Have a positive attitude about learning peripheral access
 - Better attitude increases chance of success
 - Children know when you are anxious and they become anxious as well



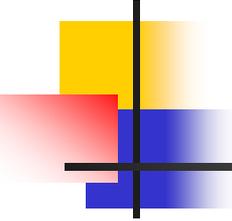
PORTs

- Can my child swim with a PORT?
 - Yes: if it is not accessed
 - No: If the PORT is accessed
 - If the catheter extends through the skin
 - Broviac™, Hickman™, PICC



PORTs

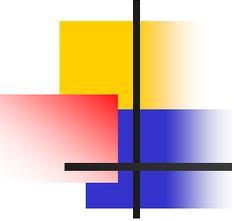
- Does a child have to go to surgery to get a PORT?
 - Usually yes
 - Unless a peripheral access device is placed which is used for a shorter period of time



PORTs

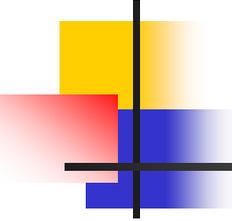
- What if something hits the PORT?
 - Ouch!
 - A hematoma may develop
 - Do not access PORT when hematoma present as blood is a good culture medium for bacteria
 - Uncommon to have mechanical problems due to direct injury but possible
 - If no blood return when accessed after injury, stop and call your healthcare provider





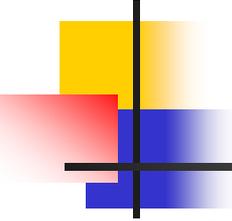
PORTs

- Who will teach me how to access my child's PORT as I live so far from the HTC?
 - Knowledgeable medical staff most often nurses teach these skills
 - Personnel may come from your hemophilia center, but may be hospital staff as well
 - If homecare nursing staff assist with this process, the teaching should be consistent and coordinated



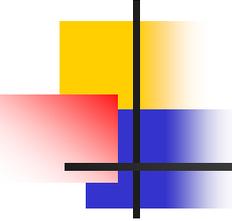
PORTs

- Can I train multiple people in my family to use the PORT?
 - Yes: *But* the more people who access the PORT the higher the risk of complications



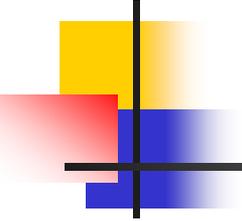
PORTs

- What do I tell my child's school or daycare?
 - Your child has a PORT
 - If an injury occurs call immediately
 - If a fever develops call immediately



Immune Tolerance

- What is an inhibitor?
 - An inhibitor is an antibody that develops against the factor that is deficient

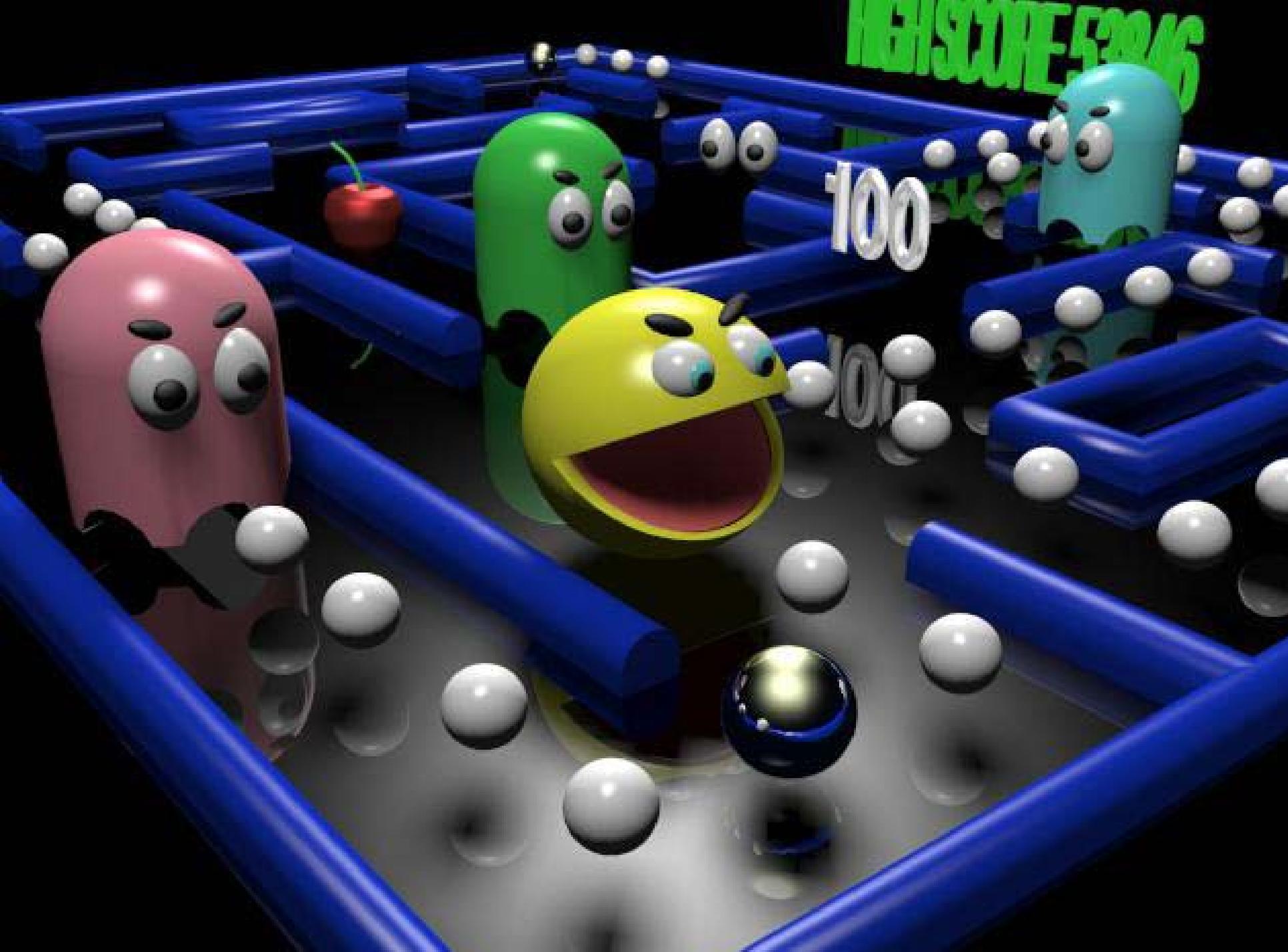


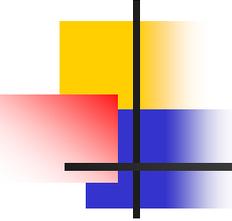
Does the inhibitor impact care?

Yes



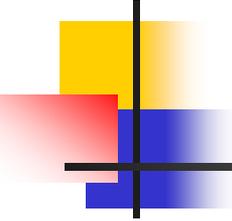
Each BU of inhibitor
consumes a 50% level





The Immune System

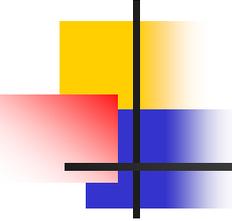
- Function of the immune system
 - Self versus non-self
 - Immune response to foreign substances
 - non-self



Measuring an Inhibitor

- How are inhibitors measured?
 - Measured in Bethesda Unit: BU
 - One Bethesda unit is the amount of inhibitor that will neutralize 50% of factor activity when 1 ml of plasma incubated for two hours at 37° C

Each BU of inhibitor
consumes a 50% level



Immune Tolerance

- Who is at risk of developing an inhibitor?
 - Usually young patients with less than 50 exposure days
 - Usually young
 - Genetic predisposition?
 - Family history
 - Racial differences
 - Patients undergoing intensive treatment especially if “inflammatory condition” present

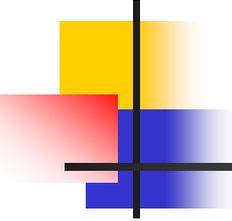
Factor VIII

Severe: ~ 30%

Moderate & mild: 3-13%

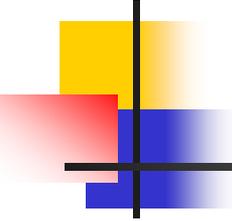
Factor IX

Severe: < 5%



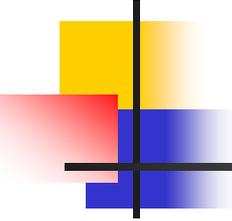
Immune Tolerance

- What kinds of inhibitors are there?
 - Low responders
 - Titer consistently < 5 BU
 - 60% of patients with inhibitors
 - FVIII for replacement therapy may cause little or no increase in titer
 - High Responders
 - Titer **ever** ≥ 5 BU
 - 40% of patients with inhibitors
 - Factor VIII or IX treatment may further stimulate inhibitor



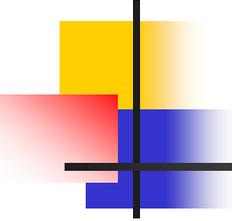
Immune Tolerance

- What treatments are available if I have an inhibitor?
 - Treatment of acute bleeds
 - Define kind of bleeding episode
 - Usual versus life or limb threatening
 - Low responding: Higher doses of factor
 - High responding:
 - APCCs: FEIBA, Autoplex *or* PCCs
 - Recombinant FVIIa
 - High factor doses until inhibitor increases *or* Porcine FVIII
 - Long terms treatments to eradicate inhibitor
 - Immune tolerance



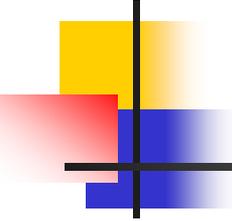
Immune Tolerance

- Are treatments different for inhibitors with factor VIII versus factor IX deficiency?
 - Yes if you have factor IX deficiency and reactions to PCCs and APCCs then rFVIIa is used and the others are not options
 - Response to immune tolerance in factor IX with inhibitors not as good as factor VIII



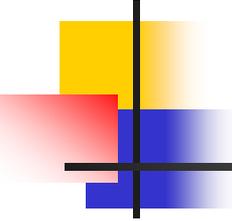
Immune Tolerance

- What is it?
 - Giving repeated doses of factor over a period of time
 - Daily
 - Twice daily
 - Three times a week
 - The idea is to reset the immune system so it stops producing the antibody that is inhibiting the deficient factor
 - Several methods are used
 - Just factor
 - Use of immune suppressive therapy



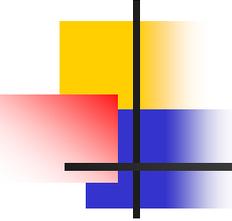
Immune Tolerance

- How often are these treatments successful?
 - Somewhere between 60-80% overall
 - The success rates of all the protocols are a matter of ongoing study and debate
 - Success may be higher if inhibitor treated when it first develops



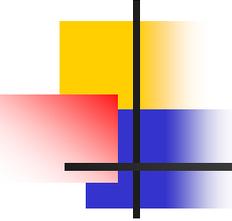
Immune Tolerance

- Is it worth going through these treatments to get rid of an inhibitor?
 - Treatment and outcome is better if you do not have an inhibitor
 - Each person has to make an individual decision weighing their circumstances



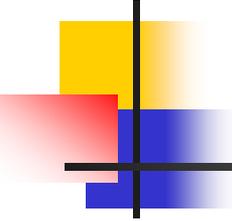
Immune Tolerance

- When is it best to treat an inhibitor?
 - As soon as it develops
 - Titer less than 10 BU
 - If the inhibitor is > 10 BU
 - If inhibitor has just emerged some recommend treatment
 - If inhibitor is long-standing probably best to wait until < 10 BU
 - Once started, do not interrupt therapy!



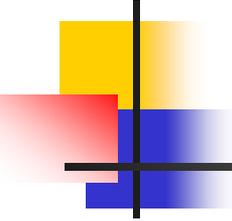
Immune Tolerance

- What should I consider before my child starts Immune Tolerance?
 - Child & family readiness
 - Venous access & central line placement
 - Cost versus potential benefit
 - Potential predictors of success



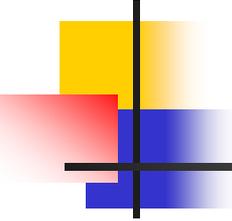
Immune Tolerance

- How will I know if my son has an inhibitor?
 - Routine visits and comprehensive clinic
 - Poor response to usual treatment with factor concentrate



Immune Tolerance

- Can he have surgery if he has an inhibitor?
 - Yes, but
 - The risks are higher
 - A well thought out plan should be developed
 - Know titer before do surgery
 - Discuss treatment options including rescue therapy available for surgery based upon titer
 - Perform surgery for medically important issues



Summary

