Aging and Hemophilia: 25 Years of Experience with HIV and HCV

HTRS
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GO RAMS!
Objectives

- Discuss the incidence of cardiovascular, renal and liver disease and its implications in the aging hemophilia population.
- Describe the current research and 25 year experience of the effects of HCV/HIV disease on clinical care for older patients with hemophilia.
- Describe health maintenance strategies to prevent and manage the effects of aging and promote good mental and physical health in this population.

Risk factors for Ischemic Heart Disease in the general aging population

- Cigarette smoking
- Arterial hypertension
- Diabetes
- Obesity
- Hyperlipidemia
Is the risk for heart disease less in patients with hemophilia?

- Ischemic heart Disease may be just as common among persons with hemophilia (PWH) as in the general population, the rate of complications from heart disease might be less.
- CVD events and its risk factors are at least equally prevalent among PWH and might even be higher than US non-Hispanic white males (NHWM).

Is there less risk?

- If there is a protective effect by hypocoagulable state it does not exert a protective effect on thrombus formation;
  - Studies of carotid and femoral artery intimal-medial thickness as a surrogate of atherosclerosis show that hemophilia does not protect from atherosclerosis
    - Sramek, A, Reiber, JHC, Gerrits WBJ, Rosendall, FR. Decreased coagulability has no clinically relevant effect on atherogenesis: observations in individuals with a hereditary bleeding tendency. Circulation. 2001;104 (7): 762-767.
Are risk factors different for People with Hemophilia?

- PWH diagnosed with ischemic heart disease (acute MI, acute/subacute ischemic, angina pectoris, old MI, chronic ischemic heart disease) were more likely to be:
  - Older
  - White
  - Have Hemophilia B
  - Have mild disease
  - Diabetic
  - Have hypertension
  - Have hyperlipidemia
  - Be uninfected with either hepatitis C or HIV

Kulkarni R, Soucie, JM, Evatt, BL and the Hemophilia Surveillance System Project Investigators

- UNCLEAR – small cohort size, few cardiovascular events, and differing age, decade of study, and proportion HIV infected or on antiretroviral therapy

- Ragni, MV, Moore, CG. Atherosclerotic heart disease: prevalence and risk factors in hospitalized men with haemophilia A. Haemophilia (2011), 1-5
What about Factor levels??

**Factor IX**
- High levels of FIX have been shown to be a risk factor for thrombogenesis.
- FIX is activated to FIXa by tissue factor/FVIIa complex. High levels of FIXa, as found in prothrombin complex concentrates, have been associated with arterial and venous thromboses and accounted for the majority of hemophilia B cases with thromboses.
  - Kulkarni et al
- Is this true for purified products??

What about Factor VIII

- A study of hemophilic mice evaluated the role of the intrinsic coagulation cascade in apolipoprotein E and FVIII double-deficient mice (E/-)/(FVIII/-) found:
  - FVIII deficiency delays but does not eliminate the early phase of atherosclerosis through delayed activation of the intrinsic coagulation pathway
  - This protective effect of FVIII deficiency declines with time.
  - Does replacement therapy with clotting factor concentrates, especially use of prophylactic regimens, further diminish a protective effect of FVIII/FIX deficiency on atherosclerogenesis?

What about Factor VIII?

Replacement therapy has been shown to exert a predominant triggering role in the acute vascular event in several reported cases

What about risk factors with aging PWH who also have HIV Disease?

Cardiovascular disease in patients with HIV is increased can be attributed to:
- inflammatory cascade and endothelial activation precipitated by HIV replication
- adverse effects of various antiretroviral agents
- greater rates of infection by hepatitis C virus (HCV)
- increased use of tobacco and recreational drugs.

HIV, aging and CVD

- For each year of exposure to protease inhibitors there is a 15%-16% increase in the adjusted relative rate of myocardial infarction.
- Associated with certain protease inhibitors

Hypertension, HIV and aging

- Hypertension
  - Present in 15%-45% of HIV-infected men \(\geq 50\) years of age versus 3%-5% of HIV-infected men who \(\leq 30\) years of age
  - Associated with lipoatrophy
Diabetes, Metabolic syndrome and lipodystrophy and CVD

- 4.6-fold higher prevalence of diabetes among HIV-infected men on cART than among HIV negative
- Metabolic syndrome
  - Dyslipidaemia, abdominal adiposity, elevated blood pressure and insulin resistance, occurs in 17%–24% of HIV-infected patients.
  - Associated with increased age and the use of stavudine, didanosine and protease inhibitors (particularly lopinavir/ritonavir)
  - Central obesity
  - BP > 130/85
  - Triglycerides > 150
  - HDL < 50
  - Fasting blood glucose > 100

Management of Cardiovascular Disease in the Aging PWH

Lack of evidence-based guidelines or safety recommendations for the acute treatment and secondary prophylaxis of cardiovascular disease in PWH

- Bleeding risk excludes from participation in trials
- Need for prospective clinical trials

Mannucci, PM, Schutgens, EG, Santagostino, Mauser-Bunschoten. How I treat age-related morbidities in elderly persons with hemophilia, Blood 114: (26), 2009 5256-5263
Coppola, A, Tagliaferri A, Franchis, M The management of cardiovascular diseases in patients with hemophilia. Seminars in Thrombosis and Hemostasis. 31 (1) 91-102
General principles

- Indications for treatment of PWHs should be similar to their age-group peers without hemophilia, provided replacement therapy is adapted to the baseline plasma factor deficiency
- Consider the risk of bleeding carried by therapeutic procedures and antithrombotic drugs
- Consider other concomitant coagulation defects
  - Thrombocytopenia
  - Vit K Deficiency (not uncommon with HCV)
  - Other clotting factor deficiencies

- Consider types of Factor concentrates
  - Inhibitor treatment; aPCCs
- Consider other risks for clotting
  - HIV disease
- Consider continuous infusion vs. bolus for prolonged therapy
- Consider higher peaks during highest bleeding risk
- Modify procedures to minimize risk
The perfect anticoagulant...

- Shorter half-life
- Reversible
- Does not interfere with routine factor monitoring
- Fewer major bleeding events (esp. ICH)
- Oral

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**Table III: Properties of Major Anticoagulant Drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Most Important Applications</th>
<th>Route of Administration</th>
<th>Laboratory Monitoring</th>
<th>Adverse Effects and Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coumadin (Warfarin)</td>
<td>Thrombosis prophylaxis in outpatients</td>
<td>Oral</td>
<td>Prothrombin time, INR</td>
<td>Bleeding with overdose, skin necrosis and gangrene</td>
</tr>
<tr>
<td>Unfractionated heparin</td>
<td>Thrombosis prophylaxis in hospitalized patients</td>
<td>Intravenous</td>
<td>aPTT, anti-factor Xa assay</td>
<td>Bleeding, thrombocytopenia, acute systemic reaction, skin necrosis and gangrene; bleeding during long-term use</td>
</tr>
<tr>
<td>Low Molecular Weight Heparin</td>
<td>Total knee replacement, high-risk abdominal surgery, liver or hip replacement, abdominal surgery, DVT treatment, unstable angina, Non-C wave MI</td>
<td>Subcutaneous Subcutaneous Subcutaneous</td>
<td>aPTT, ACT, Anti-factor Xa assay</td>
<td>Bleeding, thrombocytopenia, osteoporosis (long-term use)</td>
</tr>
<tr>
<td>Tricaban</td>
<td>Treatment of HIT, Treatment of MI</td>
<td>Subcutaneous</td>
<td>aPTT, ACT, Anti-factor Xa assay</td>
<td>Contraindicated in renal disease, Contraindicated in hepatic disease, Contraindicated in renal disease</td>
</tr>
<tr>
<td>Direct thrombin inhibitors</td>
<td>Lepidran, Argatroban, Bivalirudin</td>
<td>Subcutaneous</td>
<td>aPTT, ACT, Anti-factor Xa assay</td>
<td>Contraindicated in renal disease, Contraindicated in hepatic disease, Contraindicated in renal disease</td>
</tr>
<tr>
<td>Antiplatelet agents</td>
<td>Aspirin, Clopidogrel, Ticlopidine, GP IIb/IIIa blockers, Dipyridamole</td>
<td>Oral</td>
<td>PLT function status if needed</td>
<td>Bleeding, GI hemorrhage, Not in pregnancy or hepatic disease, neutropenia (folic acid only)</td>
</tr>
<tr>
<td>Factor Xa inhibitors</td>
<td>Fondaparinux, Thrombosis prophylaxis in hip fracture, hip replacement</td>
<td>Subcutaneous</td>
<td>Usually not required, PLT function status if needed</td>
<td>Bleeding, GI hemorrhage, Not in pregnancy or hepatic disease, neutropenia (folic acid only)</td>
</tr>
</tbody>
</table>

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VCU Virginia Commonwealth University
Newer agents: Dabigatran

- Randomized Evaluation of Long-Term Anticoagulation trial (RE-LY)
  - Large international study
  - Non-valvular atrial fibrillation and at least one additional risk factor for stroke
  - 150mg dose Dabigatran twice daily vs. warfarin

Dabigatran vs. Warfarin

- Given at a dose of 110 mg was associated with rates of stroke and systemic embolism that were similar to those associated with warfarin, as well as lower rates of major hemorrhage.
- Dabigatran administered at a dose of 150 mg, as compared with warfarin, was associated with lower rates of stroke and systemic embolism but similar rates of major hemorrhage.
Dabigatran: Problems for PWH

- No antidote
- Prolongs aPTT, ECT, and TT
- Renal metabolism
- GI bleeding higher than warfarin
Changing the procedure

- Choice of arterial access site: femoral vs. radial for percutaneous coronary intervention (PCI)
  - Up to 70% of all bleeding episodes in the general population are related to access site hematomas and retroperitoneal hemorrhage.
  - Most retroperitoneal hemorrhage is diagnosed before discharge; VAS are not!
    - 172 pts: At the time of telephone follow up bruising was reported in 68.6% of all patients (n=118) with 47% of those reporting bruises greater than 7.5 cm. 73% with femoral; 60% with radial at 5-7 days post discharge.
  - Cosman, T, McArthur H. Prevalence of bruising at the vascular access site one week after elective cardiac catheterisation or percutaneous coronary intervention. Journal of Clinical Nursing March 2011

Changing the procedure

- Choice of stent
  - While drug-eluting stents have a lower two year repeat revascularization procedures than bare-metal stents, they require longer antiplatelet therapy.
    - Usually treat one month with ASA and P2Y12 inhibitor (clopidogrel or prasugrel.)
**Guidelines: PCI**

- **PCI with metal stents** (Mannucci)
  - Peak factor at 80%
  - If dual antiplatelet, treat for trough above 30%
  - If single antiplatelet, treat for trough above 5%

**Guidelines: Cardioversion**

Cardioversion (Mannucci)

- If >48 hours from onset,
  - Exclude thrombus
  - Factor levels to 80% during heparin treatment during cardioversion and 5 days post, followed by vit K antagonists for 4 weeks with target of 2.5 INR

**Case study:**
- 67 year old white male with very mild FIX Deficiency who was seen by cardiology incidentally for afibrillation
- Negative HCV; HIV; CHAD score 1; failed multag
- Treated with coumadin 4 weeks before and two weeks post; changed to 81 mg ASA daily
- Treated with recombinant FIX to 100% correction; daily 30 units/kg for four days.
**Guidelines: Cardiac surgery**

- Small case reports (CABG, valve, ASD closure)—Mannucci
- Treatment for 7-14 days; target 100% operatively
- Warfarin target at 2.0-2.5
- Consider Continuous Infusion
- Cautions with DDAVP (increase HR, DBP, antidiuretic effect and risk of arterial thrombus—Schutgens)

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**Case Study**

38 year old male with mild FVIII Deficiency; chronic HCV (failed), HIV Disease (on HAART)
- Had chest pain, failed stress test
- Had cardiac cath (femoral stick; with factor coverage to peak of 80-100% and trough at 50%; no bleeding noted
- Did not need stent; but plan was to also monitor TEG testing and cover with factor while on anticoagulants
Case Study continued

- Triple bypass surgery two days later
- Factor coverage with troughs above 50 for one week; daily treatment at 35 units/kg for one week and then every other day treatment at 25 units/kg
- No bleeding or clotting complications

Guidelines: Valve prosthesis:

Consider valve prosthesis that do not require anticoagulation (Dolan)
Implications for health care maintenance

- Monitoring cholesterol levels
  - Many patients perceive staff at an HTC as their PCP, but HTCs may not perceive this as their role (~70% at subspecialists; 15% never received cholesterol testing)


Implications for health care maintenance at HTC

- Healthy Weight Management
  - Obesity and PWH...besides heart disease
    - Type 2 Diabetes
    - Asthma
    - Sleep Apnea
    - Depression
    - Fatty liver disease
    - Joint disease
    - Cost of treatment
Distribution of BMI in VA Adults with Hemophilia

BMI by severity in Adults

<table>
<thead>
<tr>
<th></th>
<th>Severe</th>
<th>Moderate</th>
<th>Mild</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>48 (27)</td>
<td>9 (23)</td>
<td>10 (32)</td>
<td>29 (27)</td>
</tr>
<tr>
<td>Overweight</td>
<td>62 (35)</td>
<td>17 (44)</td>
<td>10 (32)</td>
<td>35 (34)</td>
</tr>
<tr>
<td>Normal weight</td>
<td>65 (37)</td>
<td>13 (33)</td>
<td>11 (36)</td>
<td>41 (38)</td>
</tr>
<tr>
<td>Underweight</td>
<td>1 (1)</td>
<td>--</td>
<td>--</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>
What can HTCs do about healthy weight management

- Virginia Hemophilia Advisory Board Subcommittee
  - Tracking BMI and assessing activity
  - Providing resources for patients and referral sources for HTC staff
  - Partnering with chapters for targeted programming
  - Reconsidering clinic lunches and clinic environment to support healthy weight education
  - Reconsidering messages about sports
  - Consider ideal weight dosing
  - Nutritionists in clinic

Implications for health care maintenance at HTC

- Glucose monitoring and management
- Blood pressure management
  - Accurate measurement and reporting
- Smoking avoidance
- Other meds: fish oil
  - The high amounts of omega-3s that are present in fish oil can increase the risk of bleeding or affect the time it takes blood to clot. Fish oil supplements interact with medicines for high blood pressure, so taking them together might lower a person's blood pressure too much.
  - People who decide to use fish oil should look for products made from fish with lower mercury levels.
Changes in our practice: Bleeds vs. Clots

“When in doubt, treat”

...is it always true?

Bleed vs. Clot

Clots:
- About half of people with DVT have no symptoms at all.
  - Swelling
  - Pain
  - Tenderness
  - Redness of the skin

Joint or muscle bleeds:
- Warmth
- Pain
- Swelling
- Decreased ROM
- Redness
Liver Disease and Aging population with Hemophilia

- Between 85% and 93% of all US males with hemophilia born before 1975 have been found to be positive for HCV infection
  - Phillip, C. The aging patient with hemophilia: complications, comorbidities and management issues, Hematology 2010
- Most acquired their HCV in the first year of life with their first infusion.
- Hemophilic men who develop ESLD now account for 10% of all liver transplants performed in HIV/HCV co-infected individuals in the U.S.
Liver Disease and Aging population with Hemophilia

- Survival among co-infected hemophiliac transplant candidates awaiting transplantation is significantly shorter than that in those without hemophilia
- Among older patients with hemophilia and chronic HCV infection, the prevalence of cirrhosis increases to as high as 60%
- Liver-related diseases are the most common non-AIDS-related cause of death among persons with HIV infection (Zhoo)

Liver Disease and Aging population with Hemophilia

- Independent predictors of liver-related death in patients with HIV include:
  - Older age, IVDU, HCV and HBV infection, decreased CD4 and increased viral loads
- Hepatocellular carcinoma has become an increasingly important cause of death in patients with hemophilia as life expectancy has increased.

Liver Disease and Aging population with Hemophilia

- HAART contributes to liver injury by
  - Mitochondrial toxicity (NNTIs such as zalcitabine, didanosine and stavudine)
  - Complications of the immune reconstitution inflammatory syndrome and hypersensitivity reactions.

Liver Disease and Aging population with Hemophilia

- HAART treatment negates the effect of HIV on coinfected patients.

- HAART does decrease the progression of HCV-related fibrosis, cirrhosis-related complications including cancer
Liver Disease and Aging population with Hemophilia

- More than 1 million patients nationwide could develop HCV-related cirrhosis, hepatic decompensation, or HCC by 2020 increasing the demand for liver transplant

Current treatment for HCV

Pegylated interferon alfa and nucleoside analogue ribavirin

- Rapid viral response (RVR) at 4 weeks suggests strong chance for viral cure at 48 weeks.
- If do not achieve 2 log drop in viral load by week 12 (early viral response or EVR), generally considered treatment failure.
- If negative VR at week 48, considered End Treatment Response. Discontinue treatment and monitor for 24 weeks.
Current treatment for HCV

- If no viral load at 24 weeks, considered sustained viral response (SVR)
- Many permutations to protocols to maintain platelet and RBC counts (side effects of med)
- Rates vary with genotype: 1: 45%; 2/3: 75%.

New treatments

- Entry inhibitors
- Protease and polymerase inhibitors
- Cyclophilin inhibitors
- NS5a inhibitors
- Interferon enhancers
- Immunomodulators
Protease Inhibitors

- Two agents have entered Phase III trials: telaprevir and bocepravir.
  - Excellent efficacy against HCV
  - Highly susceptible to mutant drug resistant virus emergence, and viral breakthrough has been observed in <1 week when these drugs are used as single-agent therapies [27].
  - Combined with pegylated interferon and ribavirin, and SVR rates of 65-75% have been observed. Shorter duration of therapy may be possible for some patient/agent combinations

Other treatments

- Polymerase inhibitors
  - Somewhat lower efficacy than protease inhibitors
  - May have higher intrinsic barrier to emergence of drug resistance

- Cyclophilin inhibitors
  - Target host proteins that the virus utilizes
  - Potent; good resistance profile
  - Side effects still need more characterization
Management of the aging PWH and HCV: waiting . . . .

- Monitoring the disease progression
  - Liver biopsy: gold standard
    - Percutaneous vs. transjugular
  - MELD (Model for End Stage Liver Disease)
    - Bilirubin, INR, creatinine
    - AFP
    - Abdominal ultrasounds

Table 4. Univariate (crude OR) and multivariate analysis (adjusted OR) of the features associated with the risk of developing hepatocellular carcinoma

<table>
<thead>
<tr>
<th>Variables</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, older than 62 y</td>
<td>7.3 (1.4-38.2)</td>
<td>1.8 (0.1-36.9)</td>
</tr>
<tr>
<td>Age at HCV infection, older than 40 y</td>
<td>6.9 (1.3-35.9)</td>
<td>3.4 (0.2-69.9)</td>
</tr>
<tr>
<td>AFP level at entry, higher than 11 ng/mL</td>
<td>11.6 (2.6-51.5)</td>
<td>15.2 (2.7-65.7)</td>
</tr>
<tr>
<td>ALT level at entry, higher than 175 IU/L</td>
<td>1.3 (0.1-10.7)</td>
<td>1.2 (0.1-11.8)</td>
</tr>
<tr>
<td>Alcohol intake, more than 80 g/d</td>
<td>8.8 (2.0-38.5)</td>
<td>12.9 (2.4-68.7)</td>
</tr>
</tbody>
</table>

*For each variable, ORs are adjusted for the remaining 4 variables considered.
Risk factors for HCC in patients with HCV-related cirrhosis nPWH

- >50 years or those infected when aged > 50 years
- Longer duration of infection
- Men
- Overweight
- Diabetic patients
- Advanced cirrhosis
- Elevated alpha-fetoprotein.
- Other possible risk factors include
  - Steatosis
  - HCV genotype 1b
  - Asian/African American
  - occult HBV infection.
- Possible association with cigarette smoking and HCV-related HCC

Risk factors for fibrosis (Ragni)

- AFP
- Previous treatment
- age
Implications for HTC care

- Close monitoring, even if no treatment options are currently available
- Avoidance of liver toxic meds; monitor HIV closely; avoid Tylenol and alcohol
- Weight management
- Consider mental and psychological health issues
  - Cognitive functioning
  - Decision making

HAV/HBV vaccination

Diagnostic testing
- Endoscopy for varices (combine with colonoscopy if appropriate)
- Glucose testing

Preparation for liver transplant

Supportive care
Renal Disease in the Aging Hemophilia Population

- Hemophilia-related risk factors for renal disease
  - Renal bleeding
  - Acute renal obstruction (antifibrinolytics)
  - HIV related renal diseases: glomerulonephritis,

- Acute renal failure, interstitial nephritis, specific renal lesion termed HIV-associated nephropathy, nephrotoxicity related to antiretrovirals, antifungals and antibiotic treatment

- HCV associated nephropathy (appears immune complex mediated)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute renal disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV infection</td>
<td>9.1 (3.7-22.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5.2 (1.8-15.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>Inhibitor (vs. none)</td>
<td>3.0 (1.1-8.5)</td>
<td>0.04</td>
</tr>
<tr>
<td>Race (Black/other vs. White)</td>
<td>1.7 (0.7-3.8)</td>
<td>0.2</td>
</tr>
<tr>
<td>Age (per 10-year increase)</td>
<td>0.9 (0.7-1.1)</td>
<td>0.4</td>
</tr>
<tr>
<td>Severity (severe vs. mild/moderate)</td>
<td>0.8 (0.4-1.4)</td>
<td>0.6</td>
</tr>
<tr>
<td>Hepatitis C infection</td>
<td>1.1 (0.6-2.0)</td>
<td>0.7</td>
</tr>
<tr>
<td>Chronic renal disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>15.0 (6.4-34.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HIV infection</td>
<td>5.2 (2.2-12.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (per 10-year increase)</td>
<td>0.8 (0.6-1.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Kidney bleed (vs. none)</td>
<td>3.2 (1.0-10.1)</td>
<td>0.032</td>
</tr>
<tr>
<td>Race (Black/other vs. White)</td>
<td>2.2 (1.0-5.1)</td>
<td>0.036</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.7 (0.9-8.2)</td>
<td>0.08</td>
</tr>
<tr>
<td>Severity (severe vs. mild/moderate)</td>
<td>0.7 (0.3-1.7)</td>
<td>0.4</td>
</tr>
<tr>
<td>Hepatitis C infection</td>
<td>1.1 (0.3-2.5)</td>
<td>0.8</td>
</tr>
<tr>
<td>Inhibitor (vs. none)</td>
<td>1.0 (0.2-4.4)</td>
<td>0.9</td>
</tr>
</tbody>
</table>

*All factors listed were included in a logistic regression model.
Role of hypertension and kidney disease

- Second most common cause of renal disease in elderly patients
- The prevalence of hypertension in PWH admitted for kidney bleeds was 10.1% vs. 4.5% among those admitted for other reasons ($P \leq 0.004$).

Case Study #1

- 32 year old AA male with severe FVIII Deficiency; chronic HCV, HIV Disease (on HAART); PFA normal
  - History of ANCA and needs biopsy to look for vasculitis
  - Treated with Factor VIII to 100% correction to maintain trough above 50% for five days.
Clinical implications

- Early recognition and treatment of hypertension
- Management of renal biopsy
- Management of hemodialysis and bleeding complications
  - Peritoneal vs. hemo
  - Access device if hemo
    - Managing bleeding
  - Timing of infusions
  - Platelet function and DDAVP
    Haemophilia (2009), 15, 33-42

Case Study #2

44 year old white male with severe Factor VIII Deficiency, HIV Disease (on HAART but not always well controlled), chronic HCV and ESRD; lives with brother
- Needs dialysis; failed peritoneal dialysis
- Needs Tenckhoff catheter
  - Covered with factor but had recurrent oozing from site
  - Tried DDAVP without resolution
Case Study #2

- Wound management to the rescue....
  - Gelfoam
  - Pressure dressing
  - Factor VIII replacement

HTC implications

- Reconsider approach to hematuria
- Encourage routinely drinking plenty of fluids
- Consider drug interactions and utilize pharmacist teams in management
- Consider OTCs
Conclusions: What We Know

- Life expectancy for PWH is nearing that of the general population
- PWH are at risk for many of the same aging conditions as Persons without Hemophilia
- HIV, HCV makes treatment challenging for PWH
- Hypocoagulable state complicates treatment
- Reconsider what are “hemophilia norms”

Conclusions: What We Don’t Know

- Lack of evidence-based guidelines cardiovascular disease in PWH
- Lack of long-term data management of HIV or HCV disease
- Need for prospective studies on the treatment of effects of aging
- Need for research on prevention strategies in this population to reduce the risk of cardiovascular, liver, renal other diseases
Conclusions: What Seems Reasonable

- Treat with factor to allow patients the benefits of treating their comorbidities and effects of aging
- Modify procedures/treatment to the extent it is feasible to minimize risk

Conclusions: What Seems Reasonable

- Closely monitor---collaboration with specialty services and PCP
  - Hypertension
  - Obesity
  - Progression of CVD, liver and renal disease
- Enlist guidance from non-traditional services for hemophilia
  - Pharmacy
  - Wound management
  - Nutrition