HEMOPHILIA 101 FOR NON-CLINICIANS
THE U.S. HEMOPHILIA TREATMENT CENTER NETWORK
AUTHORS/PRESENTERS

Brenda Riske, MS, MBA, MPA
University of Colorado

Regina Butler, RN, MSN
Children’s Hospital of Philadelphia

Jim Munn, RN, MSN
University of Michigan

Special thanks to:
T. Wood-Lively, A. Shapiro, J. Maahs, C. Joiner

Revised from numerous sources including Partners, NHF, CDC, HRSA/MCHB
LEARNING OBJECTIVES
FOR SECTION I

- Identify different parts of the organization of the federally funded U.S. hemophilia treatment center network
- Examine the key components of the hemophilia comprehensive care model
- Evaluate data collection requirements for linking the comprehensive care model to health outcomes
- Identify general scientific precepts of bleeding disorders
- Evaluate how data and clinical care are integrated and pertinent to non-clinical role
ESTABLISHMENT OF COMPREHENSIVE CARE CENTERS IN THE USA

1975: HRSA—HTC funding initiated
1983: HRSA established regions
1995: CDC Surveillance
1998: CDC UDC
FEDERAL FUNDING SOURCES

Centers for Disease Control and Prevention (CDC)
- National Centers on Birth Defects and Developmental Disabilities (NCBDDD)
  - Division of Blood Disorders

Health Resources and Services Administration (HRSA)
- Genetic Services Branch
  - Maternal and Child Health Bureau
MISSION

To facilitate early identification of children with special health care needs and those with genetic conditions and integrate them into systems of service and care that are population- and community-based and family-centered.
HRSA HEMOPHILIA PROGRAM

- Assure access to care
  - Women, non-English speaking, racial/ethnic minorities, rural populations

- Improve health care financing issues

- Encourage consumer participation

- Collaboration with community providers

National annual funding FY2011-- $4.76 million*

VETERAN’S HEALTH CARE ACT
340B

Factor Distribution Programs/Pharmacies

“Discounts” on outpatient drugs to certain federal grantees

Dual purpose

• Lower pricing for patients
• Provide revenue to support HTCs

Patient Choice

Critical source of funding for HTCs

FEDERAL FUNDING SOURCES

Centers for Disease Control and Prevention (CDC)
- National Centers on Birth Defects and Developmental Disabilities (NCBDDDD)
  - Division of Blood Disorders

Health Resources and Services Administration (HRSA)
- Genetic Services Branch
  - Maternal and Child Health Bureau
Priorities
- Public health surveillance
- Prevention of complications of bleeding disorders

Promote and support data collection and research
- Universal Data Collection (UDC) project
- Cooperative agreements structured around data collection and research using UDC data

Blood safety

Annual funding ~$3.7 million per year nationally to HTCs

* CDC/NCBDDD Sept 2011
Standards and Criteria for the Care of Persons with Congenital Bleeding Disorders

Formally developed by NHF Medical and Scientific Advisory Council (MASAC)

Both HRSA and CDC grants require that HTC care be provided in conformity with these guidelines

MASAC recommendation #132. NHF, 2002.  
http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=57&contentid=220.
COLLABORATION WITH CONSUMER ORGANIZATIONS

GOALS:

• Advocacy

• Patient education

• Regulation and product safety
THE COMPREHENSIVE CARE MODEL
HTC SERVICES

- Diagnosis
- Treatment
- Prevention of morbidities
- Education
- Care coordination
- Outreach
- Research
- Pharmacy
COMPONENTS OF COMPREHENSIVE CARE MODEL

- **Multidisciplinary**: MD, RN, SW, PT
- **Comprehensive**: Physical and psychosocial needs of patients are met, either by clinic staff or by referral if services fall outside HTC scope
- **Prevention-focused**: Care delivered to prevent or reduce complications
- **Coordinated** within HTC and with outside providers and service agencies
- **Focused on education** to encourage patient involvement in care, promote independence, and educate larger community about bleeding disorders to improve quality of life and access to appropriate services
Family-Centered Care

- Social Worker
- Hematologist
- Nurse
- Physical Therapist
- Psychologist
- Orthopedist
- Genetic Counselor
- Dental Hygienist
- Infectious Disease Specialist
- Data Manager
HOW DO TEAM MEMBERS PARTICIPATE IN FAMILY-CENTERED CARE?

- Develop plan with patient and family
- Provide education
- Detect potential complications of bleeding or treatment
- Assist with home treatment goals
- Remain available for triage and assessment 24 hours per day for social issues and anticipatory guidance
- Manage data to ultimately improve health related outcomes
EXTENDED MULTIDISCIPLINARY TEAM

- Dental professionals
- Genetic counselors
- Infectious disease specialists
- Research coordinators
- Liver specialists
- Nutritionists
- Data managers
COMPREHENSIVE CLINIC

- Multidisciplinary evaluation
  - Minimally occurs yearly for severe patients
    - May be less often for mild patients
  - Opportunity to identify emerging or existing problems

- Includes written comprehensive clinic report
  - Should include clinical assessment and changes from prior visits
  - May be provided to the patient and other medical providers, depending on HTC practices and permissions granted by the patient

- Other Data (labs, radiology, demographics)
DATA COLLECTION AND RESEARCH
Quality of Care
- Expand our knowledge of best treatments, practices
- Assess/monitor risk factors for complications

Advocacy
- Preserve choice and access to therapies
- Defend against cost-driven care decisions being made by insurers and state payers
- Retain current levels of federal funding
DATA COLLECTION AND RESEARCH

- Hemophilia surveillance datasets
  - Hemophilia Data Set (HDS)
  - Universal Data Collection (UDC) Project
- Hemophilia surveillance outcomes
- Information infrastructure for data collection and management
CDC 6 STATE SURVEILLANCE STUDY

- 1995 – 1997 data collection
- 6 states – CO, GA, LA, MA, NY, OK
- Statute – hemophilia was reportable condition
- Collected HTC and non-HTC patient data (~20% US population)

Soucie, JM et al. Blood 2000, 96,2, 437-442
SURVEILLANCE STUDY RESULTS

- 67% received HTC care
- 8% patients died during study period
- HIV/AIDS was immediate cause of death for 52.5% of persons and 12% underlying cause
- HTCs served larger % of persons with severe disease and with those with inhibitors and/or HIV and liver disease
- Persons receiving care at an HTC were 30% less likely to die than those receiving care outside HTCs
Established in early 1980’s to track numbers of patients seen in HTCs

Annual submission voluntarily submitted by all HTCs in network

Aggregate, de-identified descriptive patient data

Requires routine use and incorporation of data collection and entry as part of clinic operations

Revisions 2011
## 2011 HDS
### PATIENT PROFILE (ALL PATIENTS)

<table>
<thead>
<tr>
<th>General Demographics: Active patients by age, gender, and race</th>
<th>0-2 yrs</th>
<th>3-12</th>
<th>13-17</th>
<th>18-21</th>
<th>22-24</th>
<th>25+</th>
<th>Total by gender</th>
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## 2011 HDS HEMOPHILIA A & B TABLE

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<tr>
<th>Active patients by age, gender, and bleeding disorder diagnosis</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Total Hemophilia A</th>
<th>Total symptomatic acquired FVIII inhibitors</th>
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## OTHER FACTOR DEFICIENCIES

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<th>Active patients by age, gender, and bleeding disorder diagnosis</th>
<th>Factor I</th>
<th>Factor II</th>
<th>Factor V</th>
<th>Factor VII</th>
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## ACTIVE AND INACTIVE PATIENTS

### ACTIVE MULTI-YEAR PATIENTS

<table>
<thead>
<tr>
<th>Number of active patients that are seen on a multi-year schedule (maximum of 3 years)</th>
<th>Total</th>
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### INACTIVE PATIENTS

<table>
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<tr>
<th>Number of inactive patients</th>
<th>Total</th>
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<tr>
<td>Active patients by age, gender, and bleeding disorder diagnosis</td>
<td>HIV Negative</td>
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<tr>
<td>Hemophilia A</td>
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<td>Hemophilia B</td>
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<tr>
<td>VWD</td>
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<td>Other factor deficiency</td>
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<td>Total</td>
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<th>Primary cause of death</th>
<th>Hemophilia</th>
<th>VWD</th>
<th>Other factor deficiencies</th>
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<td>HIV related</td>
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<tr>
<td>Liver disease related</td>
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<tr>
<td>Bleeding related</td>
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<td>HTC SERVICES</td>
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<table>
<thead>
<tr>
<th>Number</th>
<th>Other</th>
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<tbody>
<tr>
<td><strong>Number of unduplicated patients that received an annual comprehensive evaluation</strong>*</td>
<td></td>
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<tr>
<td><strong>Number of comprehensive evaluations conducted</strong>*</td>
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<tr>
<td><strong>Diagnostic evaluations (unduplicated patients)</strong></td>
<td></td>
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<tr>
<td><strong>Number receiving consultations only (unduplicated patients)</strong></td>
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</table>

*Please refer to the HDS Glossary for the definition of this data element

<table>
<thead>
<tr>
<th>Number</th>
<th>Other</th>
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</thead>
<tbody>
<tr>
<td><strong>Number of patients with an unidentified primary care physician outside of the HTC</strong></td>
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<tr>
<td><strong>Number of patients whose primary care physician was sent a written summary from the HTC</strong></td>
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<tr>
<td><strong>Number of group educational sessions or support groups sessions provided by the HTC</strong></td>
<td></td>
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### HTC SERVICES

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>Does your HTC/institution offer interpretative services?</td>
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<tr>
<td>Do patients participate in development of their own care plan?</td>
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<tr>
<td>For those HTCs providing services to pediatrics, what is the average age at which pediatric patients begin to participate in their own care?</td>
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<tr>
<td>Does your HTC offer weekend, evening, or alternative clinics?</td>
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<tr>
<td>Does your HTC provide transportation assistance to patients?</td>
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<tr>
<td>Does your HTC have an advisory board? (See glossary for definition of an advisory board.)</td>
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<tr>
<td>Does your HTC review a patient choice policy with patients/families?</td>
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<tr>
<td>Does your HTC participate in collaborative activities with your local chapter/consumer group(s)?</td>
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<tr>
<td>Does your HTC receive financial support from the state Title V program?</td>
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## OTHER BLEEDING DISORDERS

<table>
<thead>
<tr>
<th>Other bleeding disorder patients by age and gender</th>
<th>Osler Weber Syndrome</th>
<th>Alpha 2 Antiplasmin</th>
<th>Storage Pool Disease</th>
<th>Glanzmann Thrombasthenia</th>
<th>Bernard Soulier</th>
<th>Other Inherited Platelet Disorders</th>
<th>Acquired Functional Platelet Disorders</th>
<th>Total by Gender</th>
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<tbody>
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<td>Clotting disorders patients by age and gender</td>
<td>Thrombophilia</td>
<td>Other clotting disorders</td>
<td>Total by Gender</td>
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# Clotting Disorders

## Patients by Age and Gender

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<th>P20210</th>
<th>Prot C Def</th>
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<th>LA / ACA</th>
<th>Homocyst</th>
<th>Factor XII</th>
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<td>Age 18 – 21</td>
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<td>Age 22 – 24</td>
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<td>Age 25+</td>
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<td><strong>Total</strong></td>
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<td></td>
<td>37</td>
</tr>
</tbody>
</table>
US HTC PATIENT POPULATION BY DIAGNOSIS

2011 Compiled by Shearer, Riske U of CO
US HTC HEMOPHILIA & VWD POPULATION BY GENDER

Hemophilia A/B

Von Willebrand Disease

Female
Male

2011 Compiled by Shearer, Riske U of CO
HDS: VALUABLE TOOL WITH LIMITATIONS

👍 Valuable in tracking regional and national trends
  • Population served
  • Need
  • Impact of initiatives: women with bleeding disorders
  • Trends over time

👍 National statistics used to continued allocation of federal funding

👎 Does not provide information about effectiveness of treatment or patient outcomes
Acknowledgements

- HTC staffs from 1990 – present
- HTC Regional Coordinators
- CDC staff
- HRSA
5 year randomized clinical trial of 65 children with severe hemophilia A

Comparison of prophylaxis vs. on-demand, enhanced

Baseline, end of study MRI, x-rays, physical evaluation

Funded by CDC, Bayer

Manco-Johnson, et al. NEJM 2007 357;6, 535-544
Using MRI, relative risk for joint damage in enhanced episodic is 6.29 (CI 1.6-26.6) using MRI

Proportion of children with normal bone and cartilage by MRI in all six index joints at study exit

Episodic – 58%
Prophylaxis – 93%

p < 0.01
UNIVERSAL DATA COLLECTION PROJECT (UDC)

- **Purpose**
  - Monitor blood safety among recipients of blood products
  - Monitor extent and progression of joint disease
  - Identify issues for further study

- **Collect**
  - Routine clinical data on an annual basis
  - Blood sample for HIV, hepatitis A, B & C testing and serial sample storage
    - Test results of patients re-enrolled are monitored by CDC to detect new infections
    - All seroconversions are investigated to determine if the infection was due to transmission through blood products

September, 2011 update

- New UDC will be developed based on discussion between HTC staff and CDC

- Once identified, data elements will be part of two systems
  - CDC/UDC online data collection
  - WebTracker for electronic submission to CDC

- Keep track of updates, via ATHN or Regional Coordinators
UDC ENROLLMENT

Since May 1998 – Aug 2011
- > 27,054 persons with bleeding disorders enrolled
- 92078 UDC visits

More than 70% of all patients with hemophilia are enrolled

Most annual UDC visit data submitted electronically

UDC RESEARCH PRIORITIES

1. Joint outcomes
2. Women with bleeding disorders
3. Socioeconomic factors impacting outcomes
4. Rare bleeding disorders
5. Inhibitors
6. Healthy weight
7. Baby studies
OTHER UDC SPECIAL DATA COLLECTION

- Baby Form
- Mortality Form
- Quality of Life
- Inhibitor Project

Clinical outcomes data and research
Data to support evidence-based clinical standards
Consolidation/conservation of efforts and resources
Collaboration to form one national clinical database


2000-2004: Development and rollout of Lab Tracker to HTCs

2003: UDC forms incorporated into Lab Tracker

2005: Regions adopt Lab Tracker as national information platform
2006: ATHN established to support data collection infrastructure
2008: ATHN funding for HTC data coordinators initiated
2009: Beta testing of WebTracker, initial data migration
2010: National Rollout of WebTracker
2011: >85 sites using WebTracker

CDC developed online data entry system
Review of Objectives

- Identify different parts of the organization of the federally funded U.S. hemophilia treatment center network
- Examine the key components of the hemophilia comprehensive care model
- Evaluate data collection requirements for linking the comprehensive care model to health outcomes
- Identify general scientific precepts of bleeding disorders
- Evaluate how data and clinical care are integrated and pertinent to non-clinical role
ACKNOWLEDGMENTS

- CDC Division of Blood Disorders
- HRSA Maternal and Child Health Bureau Genetics Services Branch
- U.S. Hemophilia Treatment Center Network Regional Coordinators and Directors
- Judith Baker
- The Indiana Hemophilia & Thrombosis Center
- National Hemophilia Foundation
- Tami Wood-Lively, Colleen Joiner, Chris Roberson
THANK YOU, TAMI, FOR YOUR YEARS OF SERVICE, DEDICATION, AND FRIENDSHIP TO ALL IN THE HEMOPHILIA COMMUNITY.

WE WILL MISS YOU!

1967 - 2011
BLOOD CLOTTING BASICS
LEARNING OBJECTIVES
FOR SECTION II

- Identify basic components necessary for blood to clot
- Examine the key components considered in treatment of hemophilia
- Identify general scientific precepts of bleeding disorders
- Evaluate how data and clinical care are integrated and pertinent to non-clinical role
HEMOSTASIS AND COAGULATION

A complex series of reactions that leads to the control of bleeding at the site of injury
HEMOSTATIC SYSTEM COMPONENTS

- Blood vessels
- Platelets

- Plasma coagulation system
  - Factors (II, V, VII, VIII, IX, XI, XIII)

- Proteolytic or Fibrinolytic system
  - Form mature clot and begin to breakdown
HOW BLEEDING STOPS

- Vessel wall damage
- Vasoconstriction
- Platelet plug formation
- Clotting cascade activated to form fibrin clot
Laboratory evaluation of pathways

- Extrinsic pathway: Prothrombin time – PT
- Intrinsic pathway: Activated partial thromboplastin time – aPTT

PT and aPTT

- Measured in seconds
- Normal ranges are individual laboratory and reagent dependent
- Prolongation suggests factor deficiency or inhibitor of coagulation
Late Joint Bleeding in Hemophilia: Knee

- Increased pain
- Increased swelling
- Decreased range of motion
- Therapy initiated at this time results in prolonged treatment and greater risk for sequelae

Osteoarthritis

Healthy knee joint

Hypertrophy and spurring of bone and erosion of cartilage
HEMOPHILIA

- Factor VIII deficiency: Hemophilia A
- Factor IX deficiency: Hemophilia B or Christmas disease
- Factor XI deficiency: Hemophilia C or Rosenthal’s disease

<table>
<thead>
<tr>
<th>Factor VIII</th>
<th>&gt;</th>
<th>Factor IX</th>
<th>&gt;</th>
<th>Factor XI</th>
<th>&gt;</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>→</td>
<td>1</td>
<td>→</td>
<td>?</td>
<td>→</td>
<td>?</td>
</tr>
</tbody>
</table>

**Affected males**
- All daughters are carriers
- No sons are affected

**Female carrier**
- 50% risk for carrier daughter
- 50% risk for affected son
DETECTION OF HEMOPHILIA

- Family history
- Symptoms
  - Bruising
  - Bleeding with circumcision
  - Muscle, joint, or soft tissue bleeding
- Hemostatic challenges
  - Surgery
  - Dental work
  - Trauma, accidents
- Laboratory testing
### RANGE OF FACTOR VIII OR IX ACTIVITY

<table>
<thead>
<tr>
<th>Activity Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over 200%</td>
<td>High levels found in pregnancy</td>
</tr>
<tr>
<td>50% - 200%</td>
<td>Normal range of FVIII &amp; IX</td>
</tr>
<tr>
<td>25% - 49%</td>
<td>~1/3 of carriers have levels in low or below normal range</td>
</tr>
<tr>
<td>6% - 24%</td>
<td>Mild hemophilia</td>
</tr>
<tr>
<td>1% - 5%</td>
<td>Moderate hemophilia</td>
</tr>
<tr>
<td>&lt;1%</td>
<td>Severe hemophilia</td>
</tr>
</tbody>
</table>

Level above which bleeding after injury is unlikely

---

Hemophilia A: 20.6 per 100,000 males
- Severe: 50-60%

Hemophilia B: 5.3 per 100,000 males
- Severe: 44%
Physical consequences

- Musculoskeletal issue
- Functional disability
- Consequences related to treatment
  - Disease transmission
  - Inhibitor development
    - Treatment and other factors
CONSEQUENCES OF HEMOPHILIA

- Psychosocial
  - Effects on the family
  - Effects on the individual

- Societal systems
  - Effects on the healthcare system
  - Effects on educational systems
TYPES OF BLEEDS

- Joint bleeding - hemarthrosis
- Muscle hemorrhage
- Soft tissue
- Life threatening-bleeding
PRINCIPAL SITES OF BLEEDING

70-80% of bleeding episodes are into joints

Acute
• Pain, swelling, interference with normal activities

Chronic
• Synovial hypertrophy and synovitis leading to hemophilic arthropathy, disability

<table>
<thead>
<tr>
<th>Common bleeding sites:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knees</td>
</tr>
<tr>
<td>Elbow</td>
</tr>
<tr>
<td>Ankle</td>
</tr>
<tr>
<td>Shoulder</td>
</tr>
<tr>
<td>Wrist</td>
</tr>
<tr>
<td>Hip</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>


## COMMON SITES OF BLEEDING IN HEMOPHILIA: FVIII REPLACEMENT GUIDELINES

<table>
<thead>
<tr>
<th>Site of Bleeding</th>
<th>Typical Target FVIII Range %</th>
<th>Typical Duration of Replacement Therapy, days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint (70-80% of bleeding episodes)</td>
<td>40-60</td>
<td>1–2</td>
</tr>
<tr>
<td>Muscle* (10-20% of bleeding episodes)</td>
<td>40-60</td>
<td>2–3</td>
</tr>
<tr>
<td>*except for iliopsoas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral mucosa</td>
<td>30–50</td>
<td>Until bleed cessation</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>30–50</td>
<td>Until bleed cessation</td>
</tr>
<tr>
<td>Renal/Hematuria</td>
<td>50</td>
<td>3–5</td>
</tr>
<tr>
<td>Deep laceration</td>
<td>50</td>
<td>5–7</td>
</tr>
<tr>
<td>Retroperitoneal</td>
<td>50–100</td>
<td>7–10</td>
</tr>
</tbody>
</table>

### COMMON SITES OF BLEEDING IN HEMOPHILIA: FVIII REPLACEMENT GUIDELINES

<table>
<thead>
<tr>
<th>Site of Bleeding</th>
<th>Typical Target FVIII Range %</th>
<th>Typical Duration of Replacement Therapy, days</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS* (&lt;5% of bleeding episodes)</td>
<td>60–100</td>
<td>7–10</td>
</tr>
<tr>
<td>• initial</td>
<td>80–100</td>
<td>1–7</td>
</tr>
<tr>
<td>• maintenance</td>
<td>50</td>
<td>8–21</td>
</tr>
<tr>
<td>Throat and neck</td>
<td>80–100</td>
<td>1–7</td>
</tr>
<tr>
<td>• initial</td>
<td>50</td>
<td>8–14</td>
</tr>
<tr>
<td>• maintenance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal tract</td>
<td>80–100</td>
<td>1–6</td>
</tr>
<tr>
<td>• initial</td>
<td>50</td>
<td>7–14</td>
</tr>
<tr>
<td>• maintenance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery (major)</td>
<td>80–100</td>
<td>1–3</td>
</tr>
<tr>
<td>• Pre-op</td>
<td>60–80</td>
<td></td>
</tr>
<tr>
<td>• Post-op</td>
<td>40–60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30–50</td>
<td></td>
</tr>
</tbody>
</table>

* CNS = Central nervous system

World Health Organization (WHO). *Delivery of Treatment for Hemophilia 2002.*
The knee is a common target joint in hemophilia.
EARLY JOINT BLEEDING IN HEMOPHILIA: KNEE

- Warmth, tingling
- Optimal time to initiate treatment
LATE JOINT BLEEDING IN HEMOPHILIA: KNEE

- Increased pain
- Increased swelling
- Decreased range of motion
- Therapy initiated at this time results in prolonged treatment and greater risk for sequelae
LIFE-THREATENING BLEEDING

- **Head / Intracranial**
  - Nausea, vomiting, headache, drowsiness, confusion, visual changes, loss of consciousness

- **Neck and Throat**
  - Pain, swelling, difficulty breathing/swallowing

- **Abdominal / GI**
  - Pain, tenderness, swelling, blood in the stools

- **Iliopsoas Muscle**
  - Back pain, abdominal pain, thigh tingling/numbness, decreased hip range of motion
OTHER BLEEDING EPISODES

- Mouth bleeding
- Nose bleeding
- Scrapes and/or minor cuts
- Menorrhagia
COMPLICATIONS OF BLEEDING

- Flexion contractures
COMPLICATIONS OF BLEEDING

- Joint arthritis / arthropathy
COMPPLICATIONS OF BLEEDING

- Compartment syndrome/neurologic impairment
TREATMENT OF HEMOPHILIA

- Replacement of missing clotting protein
  - Factor I, VIII, IX, VII, XIII concentrates

- Other treatments
  - Mild or moderate disease and VWD

- Oral agents
  - Amicar® (Epsilon Amino Caproic Acid)
  - Lysteda ®/Cyclokapron® (Tanexamic acid)

- Supportive measures
  - Icing
  - Immobilization
  - Rest
TREATMENT METHODS

On-demand

• A treatment method which provides replacement therapy for bleeding episodes once they have occurred

Prophylaxis

• Treatment methods that provide replacement therapy in the absence of bleeding of episodes

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1930-50</td>
<td>Whole blood</td>
</tr>
<tr>
<td>1952</td>
<td>Hemophilia A and B differentiated</td>
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<tr>
<td>1950-60</td>
<td>FFP</td>
</tr>
<tr>
<td></td>
<td>Cryoprecipitate</td>
</tr>
<tr>
<td>1970s</td>
<td>Commercial Plasma-derived factor developed</td>
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<tr>
<td>1985</td>
<td>Heat-treatment of all factor products sold in US</td>
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### PRODUCT CLASSES

<table>
<thead>
<tr>
<th>Source</th>
<th>Purity</th>
<th>Comments/Generation</th>
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</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>Intermediate*</td>
<td>Blood donors versus plasma pheresis</td>
</tr>
<tr>
<td></td>
<td>High+</td>
<td></td>
</tr>
<tr>
<td>Recombinant</td>
<td>High+</td>
<td>1\textsuperscript{st} : Albumin added as stabilizer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2\textsuperscript{nd} : Albumin removed as stabilizer, human/animal protein exposure during production</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3\textsuperscript{rd} : No added human or animal protein during Production</td>
</tr>
</tbody>
</table>

*Intermediate: More than just clotting factor in the vial
  - Activity/protein ratio mid range

+High Purity: Just clotting factor in the vial exclusive of added stabilizers
  - Activity/protein ratio is very high
FACTOR REPLACEMENT PRODUCTS

**FVIII Products**
- Xyntha® [r-3rd gen]
- Advate® [r-3rd gen]
- Refacto® [r-2nd gen]
- Kogenate FS® [r-2nd gen]
  - Helixate FS® [r-2nd gen]
- Recombinate® [r-1st gen]
- Hemophil-M® [pd]
- Monoclate-P® [pd]

**FIX Products**
- BeneFIX® [r-3rd gen]
- Bebulin VH® [pd]
- Mononine® [pd]
- Profilnine® [pd]

**VWF Products**
- Stimate® [drug]
- Humate-P® [pd]
- Alphanate® [pd]
- Wilate® [pd]

**Bypassing agents**
- Novo Seven® [r]
- FEIBA® [pd]

MASAC Recommendations #151, 169, and 195:
http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=157&contentid=347
TREATMENT METHODS

On-demand
• A treatment method which provides replacement therapy for bleeding episodes once they have occurred

Prophylaxis
• Treatment methods that provide replacement therapy in the absence of bleeding episodes

FACTOR VIII CONCENTRATE

- Intravenous infusion
  - IV push
  - Continuous infusion

- Dose varies depending on type of bleeding
  - Ranges from 20-50+ units/kg

- Half-life  8-12 hours

- Each unit infused raises serum factor VIII level by 2 %
FACTOR IX CONCENTRATE

- Intravenous infusion
  - IV push
  - Continuous infusion

- Dose varies depending on type of bleeding
  - Ranges from 20-100+ units/kg

- Half-life 12-24 hours

- Each unit infused raises serum factor IX level by 1%
INFUSIONS OF FACTOR CONCENTRATES

- Dose may be +/- 10% ordered

- Factor is not wasted even if the dose is not exactly what is ordered

- Document lot number, expiration date, time of infusion, and exact dose given in units
PROPHYLAXIS

- Scheduled infusions of factor concentrates to prevent most bleeding
- Frequency: 2 to 3 times weekly to keep trough factor VIII or IX levels at 2-3%
- Types
  - primary prophylaxis
  - secondary prophylaxis
- Use of access device necessary in some patients
DDAVP (DESMOPRESSIN ACETATE)

- **Synthetic vasopressin**

- **Administration -**
  - Intravenous
  - Subcutaneously
  - Nasally (Stimate)

- **Side effects**
  - Water toxicity
AMICAR
(EPSILON AMINO CAPROIC ACID)

- **Antifibrinolytic**
- **Uses**
  - Mucocutaneous bleeding
- **Dosing:** 50 - 100 mg./kg. q. 6 hours
- **Side effects**
- **Contraindications**
  - Hematuria
LYSTEDA
(TRAXEMAMIC ACID)

- Oral or IV (Cyclokapron) formulation
- Uses
  - Mucocutaneous bleeding (dental, uterine)
- Dosing:
  - 1300 mg three times/day (oral) x 5 days
  - 10 mg/kg 3 – 4 times/day (IV) x 2 – 8 days
- Side effects
  - Renal and retinal impairment
- Contraindications
  - Hematuria
  - Concurrent use of factor replacement products
COMPLICATIONS OF TREATMENT

- Inhibitors/Antibody development
- Hepatitis A
- Hepatitis B
- Hepatitis C
- HIV
INHIBITORS

Definition
- antibody to infused “foreign” factor concentrates

Prevalence
- 20-30% of patients with severe hemophilia A
- 1-4% of patients with severe hemophilia B
HEPATITIS

- **Hepatitis A** - small risk of transmission
  - Vaccination recommended

- **Hepatitis B** - no transmissions since 1985
  - Vaccination recommended

- **Hepatitis C** - no transmissions since 1990
  - ~90% of patients receiving factor concentrates prior to 1985 are HCV antibody positive
No transmissions via factor concentrates since 1985
- viral inactivation procedures

Seropositive rate in concentrate prior to 1985
- 69.6% persons with severe hemophilia A
- 48.6% of persons with severe hemophilia B
WHY IS SOCIAL WORK PART OF TEAM?

- Guilt
- Challenge of hospitalizations
- Control issues
- Financial / insurance challenges
- Feeling different / unable to do certain activities
- Counseling needs
CONSEQUENCES OF HEMOPHILIA

Psychosocial
• Effects on the family
• Effects on the individual

Societal systems
• Effects on the healthcare system
• Effects on educational systems
HEMOPHILIA: THINGS TO REMEMBER

- ~ 50% of patients with severe hemophilia bleed with circumcision
- ~ 30% of cases of severe hemophilia result from spontaneous mutations → negative family history
- When a new patient is diagnosed with mild/moderate disease, other at-risk family members may be tested regardless of prior history

http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=180&contentid=45&rptname=bleeding..
Carriers of hemophilia are at-risk of bleeding

Baseline factor level on carriers are done to determine risk and need for intervention

Genetic testing best for determination of carrier status but reserved until patient is able to decide for themselves

Factor activity level inaccurate for carrier detection unless positive
Physical consequences

• Musculoskeletal issue
• Functional disability
• Consequences related to treatment
  − Disease transmission
  − Inhibitor development
    • Treatment and other factors
LEARNING OBJECTIVES
FOR SECTION II

- Identify basic components necessary for blood to clot
- Examine the key components considered in treatment of hemophilia
- Identify general scientific precepts of bleeding disorders
- Evaluate how data and clinical care are integrated and pertinent to non-clinical role