Do I really need that test ???

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University of Toronto
St Michael’s Hospital

No relevant conflicts of interest
HEMOSTASIS IS LIKE LOVE

Everybody talks about it, nobody understands it.

JH Levy 2000
SIMPLIFIED CLINICIAN’S VIEW OF HEMOSTASIS

Platelet/coagulation factor activation

Lots of exciting biochemistry

CLOT
- Pre-op identification of individuals at high risk of bleeding is important.
- Extensive hemostatic screening is expensive and inappropriate in low risk groups.
- Multiple retrospective studies indicate that there is no value in routine preoperative coagulation testing.

- There are multiple national and discipline-specific guidelines that also advise against preoperative testing [some guidelines make exceptions for ophthalmic and brain surgery].

- If testing is done to prevent litigation, it may indeed be harmful.
  - Can lead to unnecessary consultation and delay surgery.
Patients taken from National Surgery Quality Improvement Program

46,977 patients studied; 54% had at least one preoperative test with no clear indication for testing

15.3% tested on the day of operation of these, 61.6% had surgery despite an abnormal result

Of all patients tested 0.3% had adverse event

After adjusting for patient profile & procedure characteristics, neither testing nor abnormal results were associated with perioperative complications
British Committee of Standards in Haematology Guidelines

- 3 prospective studies: 12,000 patients
- Abnormal tests had poor positive Predictive Value and low Likelihood Ratio for bleeding
- Perioperative bleeding rates the same in patients with or without an abnormal coagulation test
- The guidelines do not recommend preoperative coagulation testing as a routine
Best practice

- take a good bleeding history
- 25% of the normal population will give a history of abnormal bleeding unless specifically questioned
- Several bleeding score documents are available for use – many are for pediatrics e.g. AHCDC Score Card

Can J Anaesth 2011, 58:74-107
When to suspect a bleeding disorder

- Bleeding which
  - is unprovoked
  - is of unexpected volume
  - is from unexpected, unusual, or multiple sites
  - is delayed after initial hemostasis
  - occurs despite adequate treatment of a known bleeding disorder
Key points on clinical history

- Is there a systemic hemostatic defect?
  - is the patient known to be a clinical “bleeder”?
  - has a bleeding disorder been diagnosed?
  - surgical history, including dental
  - previous treatment for bleeding (include transfusion history)
  - menstrual history
  - medications
  - family history of a bleeding disorder
  - concurrent disease, especially hepatic, renal, or hematological
## Bleeding Assessment Tool

<table>
<thead>
<tr>
<th>Epistaxis</th>
<th>Oral cavity</th>
<th>Surgery</th>
<th>Muscle hematoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>0  No or trivial (less than 5)</td>
<td>0  No</td>
<td>1  No bleeding in at least 2 surgeries</td>
<td>0  Never</td>
</tr>
<tr>
<td>1  &gt; 5 or more than 10’</td>
<td>1  Reported at least one</td>
<td>0  Not done or no bleeding in 1 surgery</td>
<td>1  Post-trauma no therapy</td>
</tr>
<tr>
<td>2  CONSULTATION ONLY</td>
<td>2  CONSULTATION ONLY</td>
<td>1  Reported in &lt;25% of all surgeries</td>
<td>2  Spontaneous no therapy</td>
</tr>
<tr>
<td>3  Packing or Cauterization or Antifibrinolytics</td>
<td>3  Surgical hemostasis or Antifibrinolytics</td>
<td>2  Reported in &gt;25% of all surgeries, no intervention</td>
<td>3  Spontaneous or traumatic requiring Desmopressin or Replacement therapy</td>
</tr>
<tr>
<td>4  Blood transfusion or Replacement therapy or Desmopressin</td>
<td>4  Blood transfusion or Replacement therapy or Desmopressin</td>
<td>3  Surgical hemostasis or Antifibrinolytics</td>
<td>4  Spontaneous or traumatic requiring Surgical intervention or Blood transf</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cutaneous</th>
<th>Gl bleeding</th>
<th>Menorrhagia</th>
<th>Hemarthrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>0  No or trivial (&lt;1 cm)</td>
<td>0  No</td>
<td>0  No</td>
<td>0  Never</td>
</tr>
<tr>
<td>1  &gt;1 cm and no trauma</td>
<td>1  Associated with ulcer, portal hypertension, hemorrhoids, angiodysplasia</td>
<td>1  CONSULTATION ONLY</td>
<td>1  Post-trauma no therapy</td>
</tr>
<tr>
<td>2  CONSULTATION ONLY</td>
<td>2  Spontaneous</td>
<td>2  Antifibrinolytics or pill use</td>
<td>2  Spontaneous no therapy</td>
</tr>
<tr>
<td></td>
<td>3  Surgical hemostasis or Blood transfusion or Replacement therapy or Desmopressin</td>
<td>3  Curettage or Iron therapy</td>
<td>3  Spontaneous or traumatic requiring Desmopressin or Replacement therapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bleeding from minor wounds</th>
<th>Tooth extraction</th>
<th>Post-partum hemorrhage</th>
<th>CNS bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>0  No or trivial (less than 5)</td>
<td>1  No bleeding in at least 2 extractions</td>
<td>1  No bleeding in at least 2 deliveries</td>
<td>0  Never</td>
</tr>
<tr>
<td>1  &gt; 5 or more than 5’</td>
<td>0  Not done or no bleeding in 1 extraction</td>
<td>0  No deliveries or no bleeding in 1 delivery</td>
<td>1  -</td>
</tr>
<tr>
<td>2  CONSULTATION ONLY</td>
<td>1  Reported in &lt;25% of all procedures</td>
<td>1  CONSULTATION ONLY</td>
<td>2  -</td>
</tr>
<tr>
<td>3  Surgical hemostasis</td>
<td>2  Reported in &gt;25% of all procedures, no intervention</td>
<td>2  Curettage or Iron therapy or Antifibrinolytics</td>
<td>3  Subdural, any intervention</td>
</tr>
<tr>
<td>4  Blood transfusion or Replacement therapy or Desmopressin</td>
<td>3  Resuturing or Packing</td>
<td>3  Blood transfusion or Replacement therapy or Desmopressin</td>
<td>4  Intracerebral, any intervention</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th>Total assigned score:</th>
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<tbody>
<tr>
<td></td>
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©2012 by American Society of Hematology: Education Book
<table>
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<tr>
<th>Pattern Recognition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucocutaneous</td>
</tr>
<tr>
<td>Intraarticular, intramuscular</td>
</tr>
<tr>
<td>Spreading hematomas</td>
</tr>
<tr>
<td>Delayed bleeding</td>
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</tbody>
</table>
Mild unrecognized bleeding disorders

- Syndromes
  - mild or heterozygous hemophilia A or B
  - less common autosomal coagulation factor deficiencies
  - Von Willebrand’s disease
  - platelet function disorder
  - Acquired hemophilia
Most patients with congenital bleeding abnormalities give some history, either family or personal

- Inherited coagulation defects are rare [hemophilia A, 1 in 5,000; hemophilia B, 1 in 30,000]
- Rare clotting disorders are even rarer: 1 in 250,000-300,000
- Factor XI deficiency: 8% of Ashkenazi Jews
Common acquired causes of unexpected bleeding

- ITP
- Liver disease
- Uremia
- Drug-induced platelet dysfunction
- Drug interaction with warfarin
When should testing be done?

Testing should be considered in patients with conditions potentially associated with hemorrhage:

- known bleeding disorder
- emergency surgery without a history
- liver disease
- uremia
- sepsis
- diffuse intravascular coagulation
- preeclampsia
- cholestasis
- severe nutritional deficiency
- patients on anticoagulants (drug interaction)
Screening Hemostatic Testing

- Hemoglobin
- Platelet count
- Activated PTT
- Prothrombin time
- Thrombin time
- Fibrinogen
- Bleeding time or PFA-100
- Clot lysis time
- Factor XIII
Laboratory Investigation of Bleeding Disorders

Sample collection

- a. Non traumatic venipuncture
- b. Non-heparinized catheters
- c. Where possible 21 gauge needle

Anticoagulant

- a. One volume anticoagulant to nine volumes blood
- b. 3.2% sodium citrate
- c. Plastic or siliconized glass tube
Laboratory Evaluation of the Coagulation Pathways

**Partial thromboplastin time (aPTT)**
- Surface activating agent
- Phospholipid
- Calcium

**Prothrombin time (PT)**
- Thromboplastin
- Tissue factor
- Phospholipid
- Calcium

*Intrinsic pathway* → *Extrinsic pathway* → *Common pathway* → *Fibrin clot*
Principles of screening coagulation tests

- **Prothrombin time (PT)**
  - physiological coagulation activation, via VIIa-tissue factor
  - abnormality: factor deficiency (VII, X, V, II, I) or antagonist to factor or cofactor

- **INR**
  - derived from the PT, normalized for thromboplastin reagent
Principles of screening coagulation tests

- **aPTT**
  - surface-dependent coagulation, initiated by contact factors (XII, XI, HMWK)
  - abnormality: factor deficiency (except VII, XIII) or antagonist to factor or cofactor

- **Thrombin time**
  - clottability of fibrinogen by added thrombin
  - abnormality: deficient or abnormal fibrinogen or antagonist to thrombin or to fibrin assembly (heparin)
- The aPTT is used to monitor unfractionated heparin, lepirudin, bivalirudin and agatroban
- INR is used to monitor coumadin anticoagulants
- aPTT and PT are insensitive to low molecular weight heparin, fondaparinux and danaparainoid – anti-Xa measurements should be used
**New anticoagulants:**

- Apixaban
- Rivaroxaban
  - Measure Xa, PT and aPTT
- Dabigatran
  - Measure Hemaclot (TT too sensitive, but if normal indicates no or little drug present)
Prolonged aPTT without bleeding

- **Factor XII deficiency**
  - prolonged aPTT without bleeding history
  - confirm with activity assay

- **Lupus anticoagulant**
  - prolonged aPTT without bleeding history
  - diagnosed with screening and confirmatory testing

- **Artifactual**
  - suspect heparin contamination or inadequate sample volume in citrate tube
Prolonged aPTT: Is it heparin?

- **Clues**
  - very long aPTT, normal or slightly long PT
  - no suspicion of congenital abnormality
  - no other acquired cause for prolonged aPTT

- **Confirmation**
  - prolonged thrombin time
  - normal Reptilase time
  - correction of aPTT by Hepasorb or protamine
  - heparin assay positive
Thrombin Time

- Bypasses factors II-XII
- Measures rate of fibrinogen conversion to fibrin

Procedure:
- add thrombin with patient plasma
- measure time to clot

Variables:
- source and quantity of thrombin
Causes of Prolonged Thrombin Time

- Heparin – heparin -- heparin !!!
- Hypofibrinogenemia
- Dysfibrinogenemia
- Elevated FDPs or paraprotein
- Thrombin inhibitors
- Thrombin antibodies
Avoiding bleeding: bridging anticoagulation

- **Low risk**
  - stop Coumadin 4 days pre-operatively
  - check INR 1 day preop; if > 1.5 give Vitamin K 2 mg po

- **High risk**
  - Stop Coumadin 5 days pre-operatively and do INR
  - if INR >3 start LMW heparin 2 days later; if INR<3 start 1 day later
  - give last dose of LMW heparin the morning before OR, and do INR the same morning
  - if INR is too high, give vitamin K
  - PCCs to be used in emergency situations only
Platelet disorders in surgical patients

- Thrombocytopenia
  - drug-induced (various causes)
  - immune: primary, secondary, drug-induced
  - hypersplenism
  - consumption in DIC

- Platelet function disorders
  - uremia
  - drug-induced
  - cardiopulmonary bypass
  - Von Willebrand’s disease (a plasma protein deficiency which impairs platelet function)
Thrombocytopenia without bleeding

- Antiphospholipid syndrome
  - thrombosis may be part of syndrome, but primary thromboprophylaxis is not indicated

- Heparin-induced thrombocytopenia
  - thrombosis is part of syndrome, and primary thromboprophylaxis is indicated
Drug-induced thrombocytopenia

Some drugs used in surgical or critical care patients:

- abciximab
- acyclovir
- amiodarone
- amphotericin
- atorvastatin
- clopidogrel
- digoxin
- famotidine
- hydrochlorothiazide

- furosemide
- octreotide
- penicillin
- ranitidine
- rifampin
- cotrimoxazole
- sulfasalazine
- valproic acid
- vancomycin
## Avoiding bleeding: when to stop NSAIDs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pre-op stopping time</th>
</tr>
</thead>
<tbody>
<tr>
<td>aspirin</td>
<td>7 days (minimum 2)</td>
</tr>
<tr>
<td>clopidogrel (Plavix)</td>
<td>7 days (minimum 5)</td>
</tr>
<tr>
<td>diclofenac (Arthrotec)</td>
<td>1 day</td>
</tr>
<tr>
<td>ibuprofen (Advil, Motrin)</td>
<td>1 day</td>
</tr>
<tr>
<td>meloxicam (Mobicox)</td>
<td>4 days</td>
</tr>
<tr>
<td>naproxen (Naprosyn)</td>
<td>3 days</td>
</tr>
</tbody>
</table>
Adult ITP – “safe” platelet counts

- Dentistry $\geq 10 \times 10^9$/L
- Extractions $\geq 30 \times 10^9$/L
- Regional dental block $\geq 30 \times 10^9$/L
- Minor surgery $\geq 50 \times 10^9$/L
- Major surgery $\geq 80 \times 10^9$/L
Antiplatelet agents:

- There is new interest in possibility of perioperative monitoring of antplatelet agents such as aspirin or clopidogrel.

- Point of care agents are currently felt to be insensitive and are not recommended
Platelet function analyzer (PFA)-100®

One
Pipette 800 µL blood

Two
Insert cassette
(collagen/epinephrin
ADP/collagen)

Three
Start the test
Platelet Function Analyzer (PFA-100)

Measures time to form platelet plug across aperture of a capillary tube (normal 60-120 s)
Avoiding post-operative bleeding

- Screening for congenital or acquired coagulation disorder
  - by history and laboratory testing if necessary

- Withdrawal of drugs causing impaired coagulation

- Intra-operative surgical and anesthetic management
  - meticulous surgical technique, reversal of anticoagulants, maintenance of metabolic homeostasis, replacement of blood/component losses