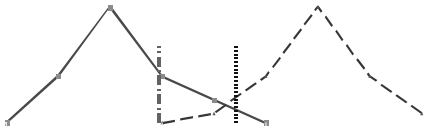
SCREENING COAGULATION STUDIES

When & when *NOT* to do them

SCREENING TESTS
Perfect Test

- Cheap
- Easy to do
- Perfectly discriminates positives from negatives

SCREENING TESTS



- Changing cutoff points changes sensitivity & specificity
- Unless you change the technology, cannot change sensitivity without also changing specificity

SCREENING TESTS

- No perfect test
- Most laboratory tests designed to be confirmatory rather than screening
- Most initial studies of laboratory tests done on populations with a high disease prevalence
- Assumes there is a screening process done prior to obtaining laboratory test

SCREENING TESTS
Prerequisites

- False negative rate virtually 0 (specificity virtually 100%), or
- Findings of positives need to trigger confirmatory workup
- Ideally, finding of positive, if confirmed should trigger change in therapy

COAGULATION TESTING
? Screening

- Clearly laboratory essential for diagnosis of coagulation abnormalities
- ? - Can laboratory pick out patients at risk for bleeding with procedures better than history/physical
- What tests are potentially useful as screening tests?

COAGULATION TESTING

Prerequisites for Screening Tests

- Cover broad range of potential abnormalities
- Sensitive to clinically significant problems of pro- & anti-coagulant proteins
- Can lead to other confirmatory tests to look for abnormalities
- Accurate at predicting who is at risk for problems

COAGULATION TESTING

Potential Screening Tests

- PT
- aPTT
- Fibrinogen
- Thrombin Time
- Bleeding Time
- Problems with hypercoagulation disorders
- All of above have been extensively used for screening purposes

COAGULATION TESTING

Screening Tests - Duplicate Tests

- Thrombin time dependent on fibrinogen, so this is duplicative
- Clinically significant hypofibrinogenemia picked up by PT & aPTT

COAGULATION TESTING

Screening Tests

- PT needed to measure extrinsic pathway
- aPTT needed to measure intrinsic pathway
- Bleeding time only true measure for platelet function
- It was assumed (based on no data) that these tests would predict who would bleed

COAGULATION TESTING

Screening - Bleeding Time

- Bioassay
- Make measured incision in forearm of skin, not over visible blood vessel, under constant hydrostatic pressure
- Blood *gently* aspirated from area every 30 seconds, via capillary action
- Measure time to stop bleeding
- Difficult to standardize
- Requires trained technician

COAGULATION TESTING

Bleeding Time

- Amount of pressure makes large difference in bleeding time (standard is 40 mm Hg; more reproducible at 80 mm Hg, but most cannot tolerate this)
- If platelet plug disrupted, results prolonged
- If incision not precise, results vary
- If incision horizontal rather than vertical, results vary
- If vein incised, results prolonged

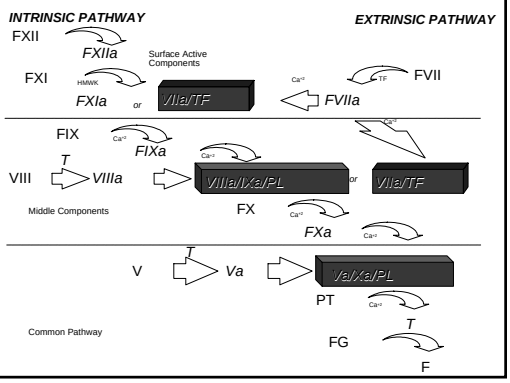
COAGULATION TESTING
Screening - Bleeding Time

- Useful for assessing platelet function in patients with bleeding disorders; however
- Even with trained technician, bleeding times NOT predictive of who will bleed at procedures, even when markedly prolonged, because false positive rate MUCH too high

BLEEDING TIME AS SCREENING TEST

DON'T USE IT!!!!

COAGULATION CASCADE



COAGULATION TESTING
Screening - PT/aPTT

- PT
  - Mix 2 parts patient's plasma (platelet poor), 1 part of Tissue factor/Phospholipid combination; then add calcium & measure time to clot
  - Measures extrinsic pathway
  - Very sensitive to factor VII levels

COAGULATION TESTING
Screening - PT/aPTT

- aPTT
  - Add 2 parts patient's platelet-poor plasma, 1 part of combination of phospholipid & negatively charged surface active agent; then add calcium & measure time to clot
  - Measures intrinsic pathway
  - Sensitive to upper factors (XII, XI,) more than lower factors
- Unlike bleeding time, these tests are sensitive to bleeding problems in the hemostatic range

COAGULATION TESTING
Screening - PT/aPTT

- These have continued to be extensively used to assess those at risk for bleeding, without testing whether they are useful for that purpose
- Became engrained that all patients having procedures, and eventually all hospital admissions, should have screening PT/aPTT measurements
- As assays became automated, this became trivial to do

COAGULATION TESTING
Screening PT/aPTT

- Pediatrics never adopted this practice, & they had little-no bleeding problems with procedures
- Who is at risk for bleeding?
  - Patients with congenital/acquired/familial bleeding disorders
  - Patients on anticoagulants
  - Patients with liver disease
- If these groups eliminated, the pickup rate for screening PT/aPTT studies drops to *< 0.5%!!!!*

COAGULATION TESTING
Screening PT/aPTT

- At this rate of prevalence, positive predictive value drops to minuscule levels
- Even though clotting assays are excellent measures of clotting process in general, there are falsely positive tests, & in populations with low disease prevalence, false positives overwhelm true positives

COAGULATION TESTING
Screening PT/aPTT

- Why is this important?
  - Screening tests trivial in price, but
    - Confirmatory tests are not
    - Time lost in chasing false positives is problematic
    - Delay in diagnosis/procedure often not worth the time to chase down results of tests

COAGULATION TESTING
Who should get screening coags?

- Those at risk of bleeding
  - Patients with congenital bleeding disorders
  - Patients with positive family history of bleeding
  - Patients on anticoagulants
  - Patients presenting with bleeding or thrombotic disorders
  - Patients being placed on anticoagulants
  - Patients with significant liver disease or alcoholism

COAGULATION TESTING
Who shouldn't get screening coags?

- Hospital admissions except as above
- Preoperative patients unless they fit one of the above categories
- Preprocedure patients unless they fit one of the above categories

COAGULATION TESTING
Historical assessment of those at risk

- History of bleeding problems in the family
- History of spontaneous bleeding
- History of heavy menses
- History of easy bruising
- History of prior blood transfusion
- History of prior tooth extractions
- History of prior surgery/pregnancy