THE FRITSMA FACTOR
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Laboratory Statistics and Quality Control Hematology and Hemostasis Concepts

Session 9: Postanalytical Variables

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Factors Driving Complexity

- Health Care Reform
  - Additional health care consumers
  - Focus on value: benefit/cost
- Laboratory provides best benefit/cost
  - Laboratory supports 70% of medical decisions
  - Laboratory occupies 2% of CMS charges
- Information explosion
  - 20,000 medical journals, thousands of DRGs
  - Increasing number of drugs
- McGlynn study
  - 6712 adults in 12 metropolitan areas
  - 439 quality care indicators
  - 61% had the correct laboratory test ordered
  - 55% received recommended care

Mcglynn EA, et al. N Eng J Med 2003; 348:2635

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Cleveland Clinic Test Utilization Committee
Annual Order Duplication

- Of 4,326,387 selected inpatient tests, 27,549 (0.64%) were ordered more than once per day
- Created list of tests that shouldn't be ordered more
- than once per day, vetted with medical staff
- Implemented "hard stops" for attempted order of duplicate test
- Means for the caregiver to still order the test, but with documentation and lab approval

Marchant C, Procop G; Test Utilization Committee

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"Hard Stop" Assays

- Quantitative transplant viruses: CMV, EBV, BKV
- Molecular thrombosis markers: FVL, FII 20210
- Hypercoagulation panel
- *Clostridium difficile* EIA
- Hepatitis panel
- Iron plus TIBC
- TC, HDL, LDL, triglyceride
- Reticulocyte count
- CRP, HGB A1C
- Will expand list and extend time interval

Modified Slides, Here to End

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Post-post: Thrombophilia Report

Assay	Patient	RI
Protein C activity	35%	>70%
Protein S activity	39%	>65%
Antithrombin activity	57%	78–126%
Factor VIII	125%	50–186%
APCR	2.4	>1.8
Factor II 20210	Wild-type	Wild-type
PTT-LA	39 s	30–40 s
Homocysteine	3.9 ηmol/L	<4.3 ηmol/L

- Triple heterozygote?
- Terminate pregnancies?
- Increase Coumadin?
- Start heparin?
- Consult with the lab?

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Or: "*Protein C, S, and AT appear deficient, probably Coumadin interference, reflex INR = 2.1, suggesting Coumadin is present. Other risk factor assay results are within reference interval. No evidence for thrombotic risk, repeat profile 2 weeks after discontinuing Coumadin.*"

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Post-post Issue: Pre-op Screen

Assay	Patient	RI
HGB	14.2 g/dL	13.5–15.6 g/dL
PTT	59 s	25–35 s
PT	12.4 s	9.8–12.6 s
TT	18.2 s	<21 s
PLT count	310,000/µL	250–450,000/µL
Fibrinogen	270 mg/dL	150–400 mg/dL
No bleeding Hx, surgeon postpones procedure		

- Heparin present?
- Risk: bleeding? Thrombosis?
- Repeat PTT until negative?
- Consult with laboratory?
- Laboratory immediate reflex to…

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Post-post Issue: How About This?

Assay	Patient	RI
HGB	14.2 g/dL	13.5–15.6 g/dL
PTT	59 s	25–35 s
PT	12.4 s	9.8–12.6 s
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PLT count	310,000/µL	250–450,000/µL
Fibrinogen	270 mg/dL	150–400 mg/dL
No bleeding Hx, surgeon postpones procedure		

"*Isolated prolonged PTT may indicate coagulation factor deficiency, coagulation factor inhibitor, or lupus anticoagulant. Normal TT indicates no heparin present. Laboratory reflex to PTT mixing study, results follow.*"

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Mixing Study: New Specimen, Next Day

Assay	Result	RI	Comment
PTT	57 s	25–35 s	Confirms previous PTT
PTT/control 1:1 immediate mix	38.5 s	Control value 27.5 s	Commercial platelet-free normal control plasma

- Uncorrected?
- Should lab have done incubated mix?
- Do you send this result to the surgeon?
- Continue to delay surgery?
- Consult with laboratory?
- Laboratory immediate reflex to…

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Mixing Study: How About This?

Assay	Result	RI	Comment
PTT	57 s	25–35 s	Confirms previous PTT
PTT/control 1:1 immediate mix	38.5 s	Control value 27.5 s	Commercial platelet-free normal control plasma

Interim report: "*Patient plasma mixed 1:1 with normal plasma, PTT performed immediately after mix remains prolonged (uncorrected). Presumptive evidence of lupus anticoagulant. LA profile follows.*"

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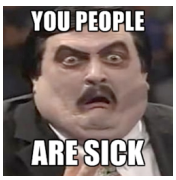
LA Profile: Third Day of Hospital Stay

Assay	Result	RI	Comment
PTT-LA	47.9 s	30–40 s	Confirms previous PTT
PTT-LA /control 1:1	38.5 s	Control value 34.5 s	Possible LA
Staclot LA kit	12 s correction	> 8s correction	Confirms LA
DRVVT	52.5 s	35–45 s	Possible LA
DRVVT Confirm	1.4 ratio	> 1.2 correction	Confirms LA

- Send this result to the surgeon w/o comment?
- Delay surgery?
- Consult with laboratory?



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LA Profile: How About This?

Assay	Result	RI	Comment
PTT-LA	47.9 s	30–40 s	Confirms previous PTT
PTT-LA /control 1:1	38.5 s	Control value 34.5 s	Possible LA
Staclot LA kit	12 s correction	> 8s correction	Confirms LA
DRVVT	52.5 s	35–45 s	Possible LA
DRVVT Confirm	1.4 ratio	> 1.2 correction	Confirms LA

Or: "*Patient plasma tested using LA-sensitive PTT reagent and dilute Russell viper venom reagent, both prolonged, both corrected by high phospholipid neutralization reagent, confirming LA. No bleeding risk, may indicate thrombosis risk if LA is chronic. Repeat after 12 weeks to determine persistence.*"

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Pre-op Coags Look the Same as Before "Will This Never End?"

Assay	Result	RI
PT	14.2 s	12.6–14.6 s
PTT	42.5 s	25–35 s
TT	17.5 s	< 21 s
PLT	245,000/µL	150–450,000/µL

- Heparin present?
- Risk: bleeding? Thrombosis?
- Repeat PTT until negative?
- Consult with laboratory?
- Laboratory reflex to…

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Pre-op Coags Look the Same as Before How About This?

Assay	Result	RI
PT	14.2 s	12.6–14.6 s
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PLT	245,000/µL	150–450,000/µL

Or: "*Isolated prolonged PTT may indicate coagulation factor deficiency, coagulation factor inhibitor, or lupus anticoagulant. Normal TT indicates no heparin present. Laboratory reflex to PTT mixing study, results follow.*"

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Mixing Study: How About This?

Assay	Result	RI	Comment
PTT	42.5 s	25–35 s	Confirms previous PTT
PTT/control 1:1 Mix immediate	31.1 s	Control value 27.5 s	Commercial platelet-free normal control plasma
PTT/control 1:1 Mix 2 h at 37°C	33.4 s	Control value 31.3 s	Control is incubated alone and with mix

- Corrected?
- Send results to surgeon w/o comment?
- Delay surgery?
- Consult with laboratory?
- Laboratory reflex to…

Or: "*Patient plasma was mixed 1:1 with normal plasma, PTT within 10% of control immediately and after incubation. (corrected). Presumptive evidence of factor deficiency, factor assays follow.*"

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VWD Profile

Assay	Result	RI	Comment
FVIII	40%	50–150%	Mildly decreased
VWF:Ag	37%	50–150%	VWD Type 1
VWF:RCo	45%	50–150%	
VWF:Act	48%	50–150%	
VWF:CBA	37%	50–150%	

- Send this result to the surgeon w/o comment?
- Delay surgery?
- Consult with laboratory?

Or: "*Results indicate von Willebrand disease type 1, risk of mucocutaneous bleeding may require pre-operative corrective therapy.*"

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Consultative Lab Testing

- "Goal-oriented" ordering: assays keyed to condition
- Assess causes for long PT or PTT: Hx of bleeding or thrombosis, interfering drugs, summarize results
- Initial profile with algorithm-based reflex additions
- Reduce cost by selecting correct assays
- Fewer repeat samples, less blood volume
- Conclude on abnormalities efficiently
- Shortened TAT and stay
- Interpret results, indicating cause and significance of the coagulation abnormality, bleeding and thrombotic risk, recommendations for therapy

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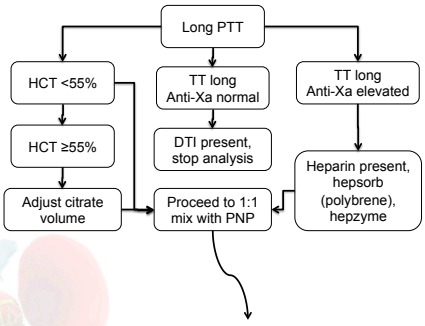
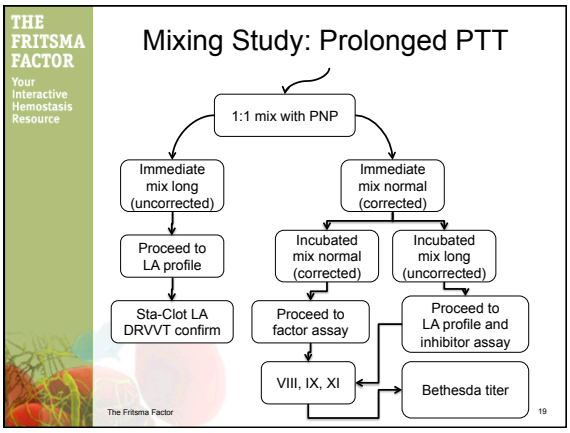
Prolonged PTT Workup

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Mixing Study: Prolonged PTT
1:1 mix with PNP
Immediate mix long (uncorrected)
Immediate mix normal (corrected)
Proceed to LA profile
Incubated mix normal (corrected)
Incubated mix long (uncorrected)
Sta-Clot LA DRVVT confirm
Proceed to factor assay
Proceed to LA profile and inhibitor assay
VIII, IX, XI
Bethesda titer
The Fritsma Factor
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