

THE FRITSMFACTOR
Your Interactive Hemostasis Resource

Laboratory Statistics and Quality Control Hematology and Hemostasis Concepts

Session 1: Preanalytical Variables

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Total Testing Process

“Pre-pre” Analytical	Pre-Analytical	Analytical	Post-analytical	“Post-post” Analytical
Patient visit	Specimen collection	Assay performed	Assay result published and delivered	Doctor interprets result
Dr. writes lab order; correct test selection	Tube selection, fill, mix, ID, specimen management	Validation, lot-to-lot, internal & external QC	Written report to chart, electronic delivery	Doctor treats patient

• Ward-Cook KM, Lehmann CA, Schoeff LE, Williams RH. Clinical Diagnostic Technology—The Total Testing Process, 2004, AACC Press
• Laposata M. Clin Chem Lab Med 2007;45:712

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“Extra-analytical” Error

Phases	Frequency (Percent of Occurrence)
Pre-Pre-Analytical, very high frequency, high risk	12%
Pre-Analytical, high frequency	2%
Analytical	0.2%
Post-Analytical, high frequency	2.2%
Post-Post-Analytical, very high frequency, high risk	5.0%

Stroobants AK, Goldschmidt HM, Piebani M. Error budget calculations in laboratory medicine: linking the concepts of biological variation and allowable medical errors. Clin Chim Acta 2003;333:169-76.
Hickner J, Graham DG, Elder NC, et al. Testing practices: a study of the American Academy of Family Physicians National Research Network. Qual Saf Health Care 2008;17:194-200

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“Pre-pre” Analytical Error: Test Selection

My patient has osteoporosis. What test do I order?

Now what?

Experts identify multiple vitamin D forms with no naming consensus:

- calciferol
- cholecalciferol
- 1,25 dihydroxycholecalciferol
- ergosterol
- vitamin D
- vitamin D2
- vitamin D3
- 25-OH vitamin D
- 25-OH vitamin D2
- 25-OH vitamin D3
- 25 hydroxy vitamin D
- 25 hydroxy vitamin D2
- 25 hydroxy vitamin D3
- 1,25 (OH)₂ vitamin D
- 1,25 (OH)₂ vitamin D2
- 1,25 (OH)₂ vitamin D3
- 1,25 dihydroxy vitamin D
- 1,25 dihydroxy vitamin D2
- 1,25 dihydroxy vitamin D3

Which is correct?

Lab director coins arbitrary assay names, IT director creates arbitrary LIS mnemonics:

- Vitamin D, VITD
- 25-OH vitamin D, 25-OH VITD

Courtesy of Elissa Passiment, EVP, ASCLS and Julie Taylor, CDC

Result: 60 ng/mL

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More Name Problems What’s in a name?

You’re going to call me WHAT!?

FX FV FVIII PT INR PC

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Wrong Anticoagulant?

Assay	Citrate	EDTA	Heparin	Serum
PTT	29s ¹	68s	>180s	>180s
PT	12.4s	23s	>60s	>60s
FVII:Act	115%	116%	77%	308%
FVIII:Act	141%	4.5%	<1%	4.5%
FIX:Act	122%	115%	<1%	350%
VWF:Ag	122%	143%	70%	101%
VWF:RCo	114%	131%	37%	74%
PC:Act	111%	152%	<1%	<1%
PS:Act	96%	30%	<1%	21.6%

¹Means

Data courtesy of Dorothy Funk, MD, Esoterix Coagulation

Adcock, DM, Hoefner DM, Kottke-Marchant K. Collection, transport, and processing of blood specimens for testing plasma-based coagulation assays and molecular hemostasis assays; Approved Guideline—5th Edition, CLSI H21-A5, 2008.

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Pre-Analytical: Specimens

Images courtesy of Dorothy (Adcock) Funk, MD, Esoterix Coagulation

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Adjusting for HCT >55%

- $C = 1.85 \times 10^{-3} (100 - \text{HCT}\%) V$
- Where...
 - C = final volume of anticoagulant in tube
 - HCT% = hematocrit in percent
 - V = desired total volume of blood and anticoagulant
- Example, how much anticoagulant should be used to collect a 3 mL specimen from a patient with HCT of 70%?
 - $C = 1.85 \times 10^{-3} (30)3 = 0.17 \text{ mL}$

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Adjusting for HCT >55%

Anticoagulant solution (mL)

Percentage Packed Cell Volume

Reagents

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Specimen Transport: No Ice

Samples with >50% VWF:RCo: 4°C, 6h		
Assay	Sample 1	Sample 2
VWF:Ag	42%	128%
VWF:RCo	38%	30%
VWF:CB	12%	28%

Sample 1: false diagnosis of VWD type 1 in a normal subject
Sample 2: false diagnosis of VWD type 2 in a type 1 VWD patient

- Also cold activates platelets and coagulation factor VII
- Refrigerate EDTA tubes up to 24 h for hematology to stabilize platelet count and hematocrit
- In clot tubes for clinical chemistry, cold raises serum K⁺

Favoloro E. Thromb Haemost 2001;86:1589-90
Young D. Effects of preanalytical variables on clinical laboratory tests. AACCPress, 1997

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Specimen Storage

PPP stored 24h at 1-4°C			
Factor	Fresh	12h	24h
VIII	110%	102%	71%
VIII	60%	47%	39%
VIII	51%	50%	33%
V	94%	93%	87%
PS	93%	97%	63%

Adcock D, Kressin D, Marlar RA. The effect of time and temperature variables on routine coagulation tests. Blood Coagul Fibrinolysis 1998;9:463-70.

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Pseudothrombocytopenia

What to do?

Zandacki M, Genevieve F, Gerard J, Godon A. Spurious counts and spurious results on haematology analysers: a review. Part II: white blood cells, red blood cells, haemoglobin, red cell indices and reticulocytes. Int J Lab Hematol 2007;29:21-41.


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Pre-pre Issues, Not Name-related

- PTT ordered for LMWH or fondaparinux
- PTT interpretation in UFH Rx: 1.5–2.5 X MRI
- INR for coagulopathy, do you want a PT?
- Interpret PT and PTT when LA present
- What is in a thrombophilia profile?
- Lupus anticoagulant: what is it, what do you do?
- What is in a VWD profile?

First of 6 Add-on Slides



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Pre-pre: Pre-op Screen

Assay	Patient	RI
HGB	14.2 g/dL	13.5–15.6 g/dL
PTT	29 s	25–35 s
PT	12.4 s	9.8–12.6 s
BT	16.5 m	2–9 m
PLT count	310,000/μL	250–450,000/μL
Fibrinogen	270 mg/dL	150–400 mg/dL
D-dimer	190 ng/mL	110–240 ng/mL

No bleeding Hx, surgeon postpones procedure

What do you recommend?

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Pre-pre Issue: Pre-op Screen

Assay	Patient	RI
HGB	10.2 g/dL	13.5–15.6 g/dL
PTT	29 s	25–35 s
PT	12.4 s	9.8–12.6 s
PLT count	310,000/μL	250–450,000/μL
Fibrinogen	270 mg/dL	150–400 mg/dL
D-dimer	160 ng/mL	110–240 ng/mL

Hx: Easy bruising, chronic epistaxis, prolonged bleeding after shaving. Surgeon decides to go ahead with procedure.

What do you recommend?

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Pre-pre 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
PLT count	310,000/μL	250–450,000/μL
Fibrinogen	270 mg/dL	150–400 mg/dL

No bleeding Hx, surgeon postpones procedure

What do you recommend?

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Pre-pre: Thrombophilia Screen

Assay	Patient	RI
Protein C Activity	61%	>70%
Protein S activity	69%	>65%
Antithrombin activity	27%	78–126%
Factor VIII	125%	50–186%
APCR	2.4	>1.8
Factor II 20210	Wild-type	Wild-type
PTT-LA	34 s	30–40 s
Homocysteine	9 ηmol/L	>18 ηmol/L

50-YO man with DVT on UFH 4 days, physician orders thrombophilia profile.

What do you recommend?

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Pre-pre: Thrombophilia Screen

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

60-YO woman, DVT on Coumadin 3 w, physician orders thrombophilia profile.

What do you recommend?

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