THE FRITSMA FACTOR

Your Interactive Hemostasis Resource

Clumsy Clinical Communication
Let's Blame the Lab

2022 ASCLS Del-Mar-Va-DC Joint Spring Meeting

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Hemostasis Resource
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Bottom Line at the Start [BLAST]

What do Medical Laboratory Scientists Do to Prevent Diagnostic Errors? We…

- Review diagnostic assay utilization.
- Prevent specimen management errors.
- Interpret laboratory assay results.

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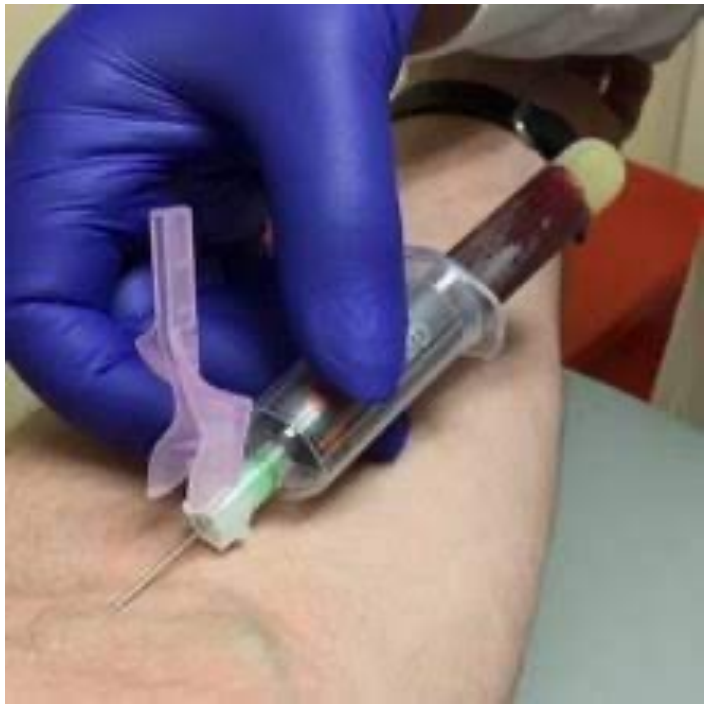
"Wellness Visit"

At your annual visit to your PCP…

- Does she order "routine" lab work every time?
- What labs? CBC, PT, PTT, CMP, Lipids, PSA, UA?
- Does she review the results with you?
- Anything important?



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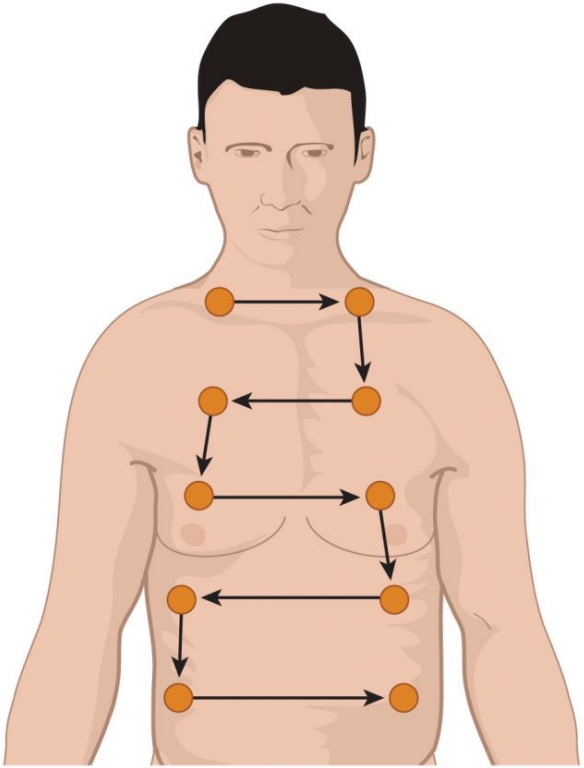
Chronic Cough with Chest Pain

- You see your PCP for a 7-day cough with mild chest pain. To diagnose, she…
  - Documents Hx, records vitals plus O_2 sat, performs physical exam with auscultation of chest and abdomen
  - Develops a preliminary Dx
  - Orders an ECG and chest x-ray
  - Orders "blood work"
  - Starts Rx while awaiting results
- 24-h diagnosis: bronchitis

Fig 4a. **Anterior chest auscultation**



Starting at the top of the chest (first intercostal space), use a 'stepladder' approach to listen to breath sounds on the anterior chest finishing at the seventh intercostal space

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What Tests Influence the Diagnosis?

- SARS-CoV2 PCR, R/O C19
- ECG, troponin: R/O acute myocardial infarction [AMI]
- D-dimer, spiral tomography: R/O pulmonary embolus
- Chest X-ray: R/O Ca, pneumonia
- CBC: R/O infection
- PT, PTT, UA, metabolic and liver profiles: no indication-based info, ran anyway

Li J, Dohm MR, Thomas J, et al. Why is there variation in test ordering practices for patients presenting to the emergency department with undifferentiated chest pain? A qualitative study. Emergency Med J 2021; 38: 820–4.

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Why PT, PTT, UA, Metabolic & Liver Profile?

- 1/3 of tests ordered in ED for chest pain are not indicated; why order?
  - "Locum" ED physicians—a new doc each week
  - Liability: avoid lawsuits
  - Multiple and inconsistent test selection guidelines
  - IT system offers ordering framework that favors overordering [profiles] with no restrictions [no hard stops]
  - Facilitate broader care continuum: admission/transfer

Li J, Dohm MR, Thomas J, et al. Why is there variation in test ordering practices for patients presenting to the emergency department with undifferentiated chest pain? A qualitative study. Emergency Med J 2021; 38: 820–4.

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Emergency Room "Rainbow Draw"

Cons

- Iatrogenic anemia
- Wasted resources
  - Oschner: 20,000 tubes/month

Pros

- Blood cultures needed before antibiotics
- Prevents subsequent re-draws for "add-ons"

Solutions

- Small volume tubes
- Pediatric tubes
- Monitor ordering patterns

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Collection Errors

- "Rogue" tubes
- Discard tubes and refrigeration for coag tests
- Wrong A/C: heparin or citrate for CBC
- "Topping off," combining short draws
- Tourniquet application >2 minutes
- Hemolysis and clots: poor collection methods
- Lengthy transport, pneumatic tube stresses

R. Marlar, PhD, D. Adcock, MD

Recommendations from the International Council for Standardization in Haematology: Kitchen S, et al. Int J Lab Hematol. 2021;43:571–80

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"Lab Results Are the Basis for 70% of Medical Decisions"

- Widely misquoted 1996 Forsman [Mayo] publication
  - It specified "critical" decisions
- Lab costs consume 5% of total medical costs
  - Accurate documentation from Medicare billing database
- Aurora Health Systems, Milwaukee, 2010
  - Lab data occupies 82% of EHR data bits
  - Does this prove Forsman's point?
- We don't know the real percentage
  - Depends on efficacy

Forsman RW. Why is laboratory an afterthought for managed care organizations? Clin Chem1996;37:1244–48.
Forsman RW. The electronic health record: implications for the laboratory. Clin Leadership Manag Rev 2000;14:292–5.

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The Effective Lab Test…

- Is selected to address clinical indications
- Confirms or rules out predicted outcomes as it…
  - Establishes diagnosis
  - Affects Rx
  - Improves outcome
- Causes no harm, for example…
  - Inappropriate test ordered
  - Appropriate test not ordered
  - Result is erroneous, delayed, lost, or misused

Hallworth M, et al. Current evidence and future perspectives on the effective practice of patient-centered laboratory medicine." Clin Chem 2015, 61, 589–99.
Hallworth M, "The '70 percent claim': what is the evidence base?" Ann Clin Biochem 2011; 48, 487–8.

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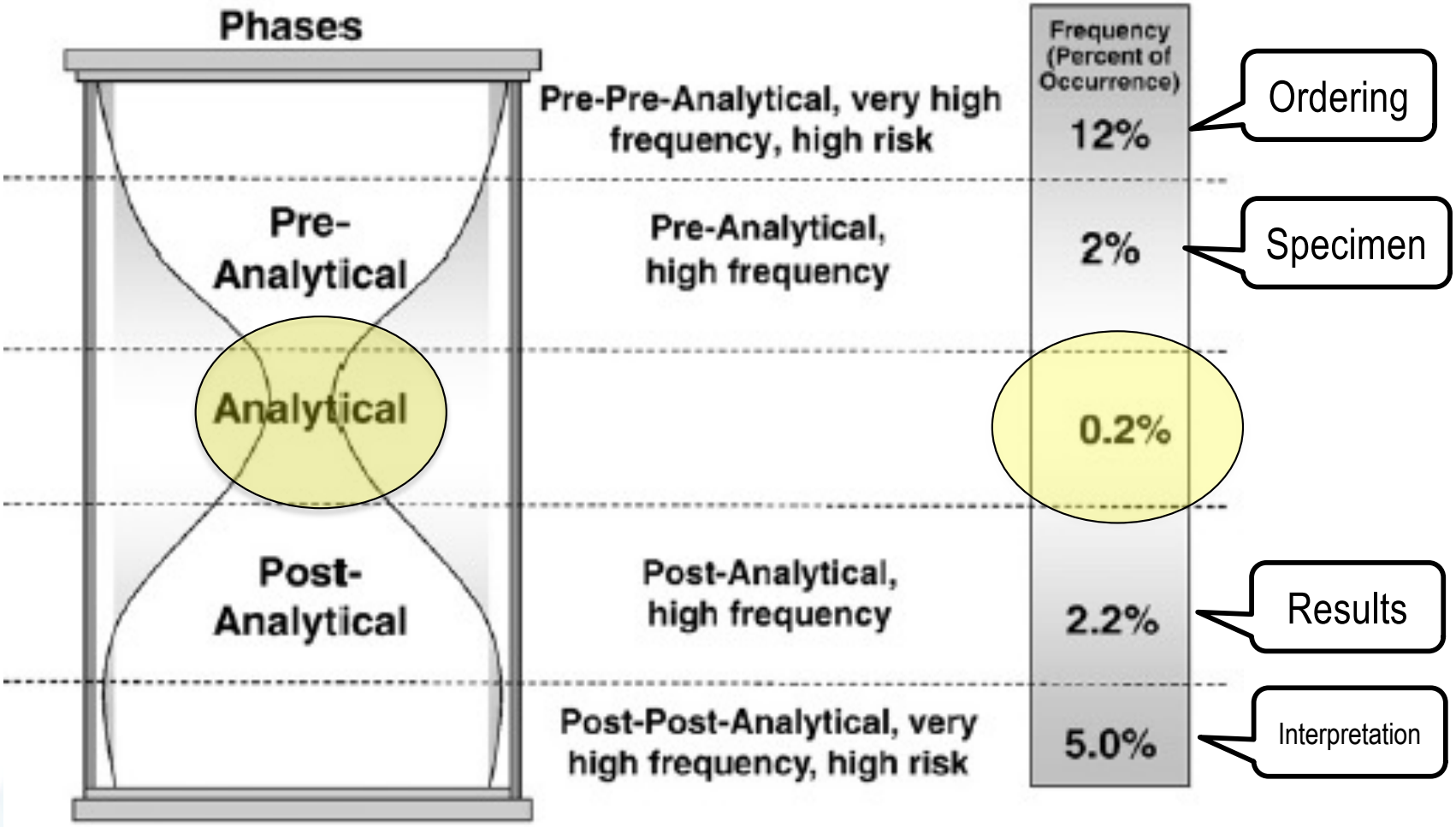
Where are the errors?



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.

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2014 Survey of Primary Care Physicians Pre-analytical Error?

- 1800 US PCPs surveyed, mean age 51; 21 years in practice; 81 avg patients seen per week
  - ~500,000,000 PCP patient visits/year
- Averaged 25 diagnostic lab tests/week, 31% of pts
- Uncertain about what test[s] to order: 14.7% of pts who needed diagnostic tests
- Uncertain about how to interpret results: 8.3%
- Potential 23,000,000 incorrectly ordered or interpreted tests/year

Marques MB, Hickner J, Thompson PJ, Taylor JR. Primary care physicians and the laboratory; now and the future. Am J Clin Pathol 2014;142:738–40.

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Post-analytical Diagnostic Errors

- Misdirected or lost results
- Errors that occur after results are delivered…
  - Incorrect interpretation, 37%; inappropriate or inadequate follow-up, 45%; failure to refer, 26%
- Factors contributing to errors
  - Erroneous judgment, 70%; lack of vigilance, 59%; knowledge, 48%; handoffs, 20%
  - Multifactorial: 54% of errors involve 3 process breakdowns
  - Multi-clinician: 43% of errors involve 2 or more physicians
- Wall Street Journal, 2013: "*Patients would be safer if doctors did not …diagnose alone. Physicians should…bring pathologists and radiologists into the loop to make sure the correct test is ordered and the right diagnosis is offered.*"

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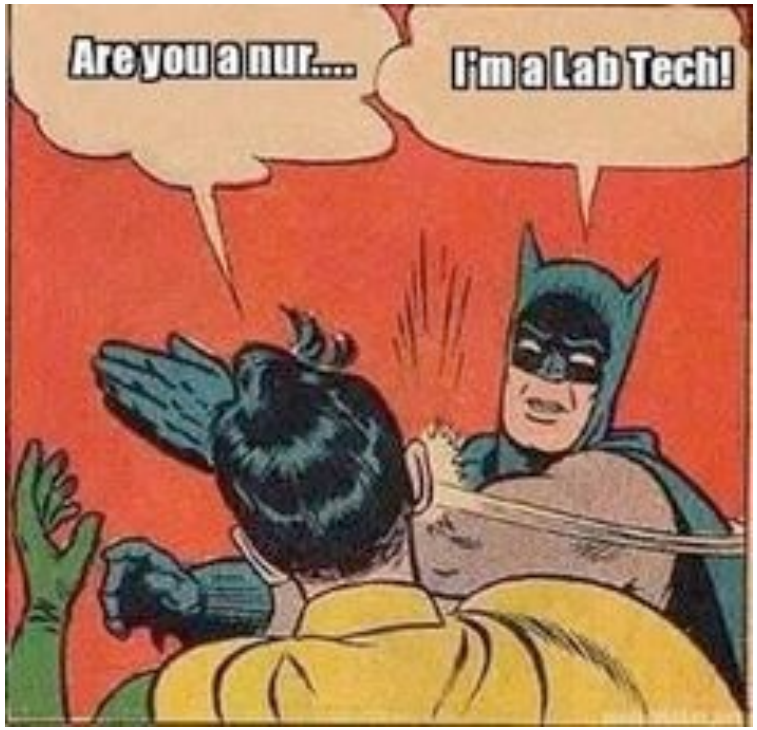
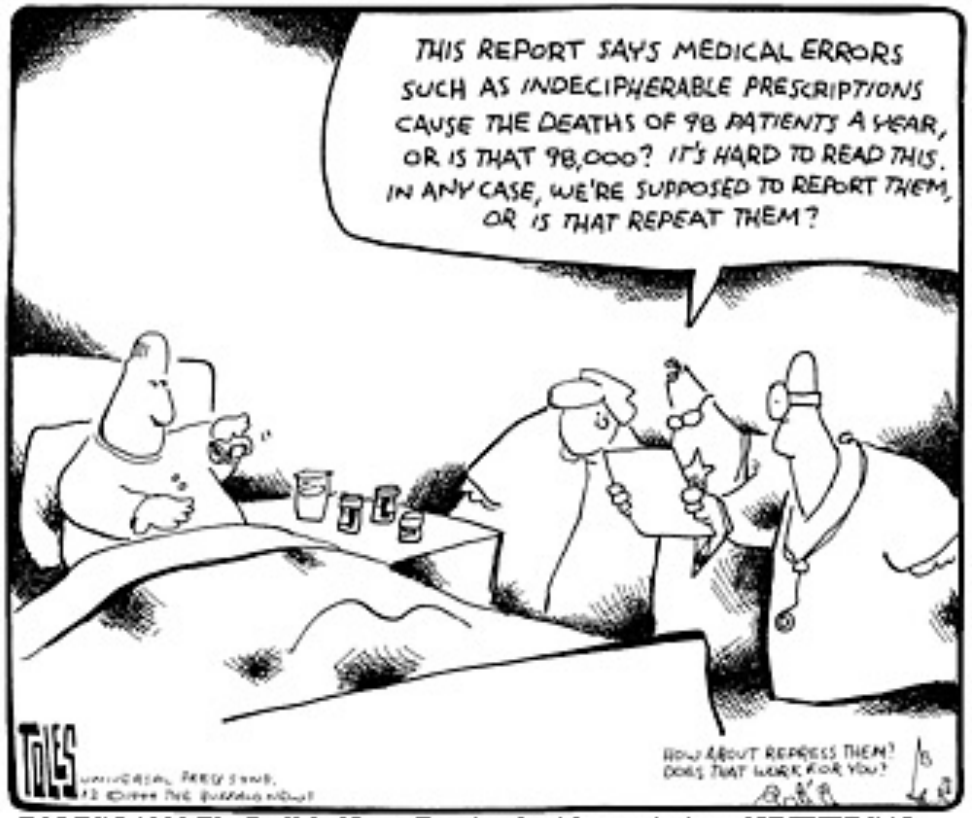
How do PCPs Deal with Lab Test Interpretation Uncertainty?



- Review patient history: 70%
- Follow up with patient: 66%
- Review references: 46%
- Order more lab tests: 34%
- Refer to a specialist: 29%
- Consult fellow PCP: 23%
- Check guidelines and references: 22%
- Repeat the same test: 19%
- Consult with lab professional: 6%
  - Helpful? 35%

Why don't PCPs contact the lab?

- Confusing test names
- Slow turnaround time
- Reference interval variation: no harmony
- Report info and format variation
- Whom to call?



Clinical pathologist MB Marques, MD, "I know for certain that most of my relevance as a member of the medical staff stems from my direct relationships and collaboration with physicians from other departments."

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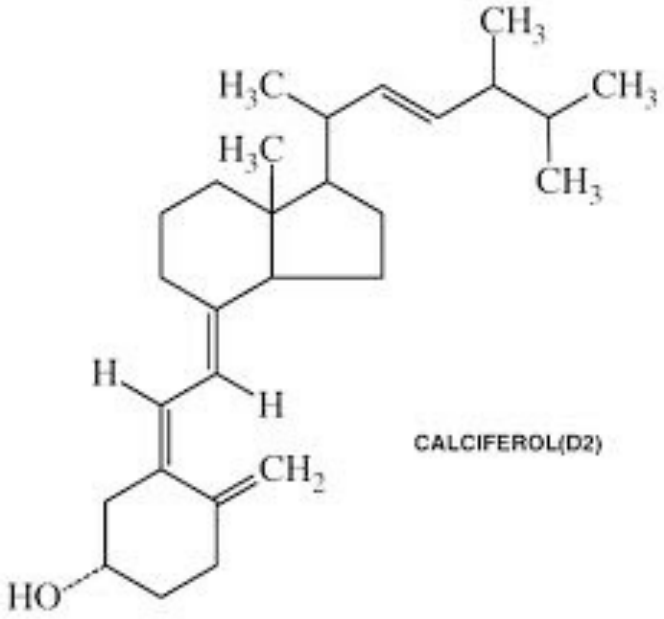
Lab Scientist–Clinician Communication

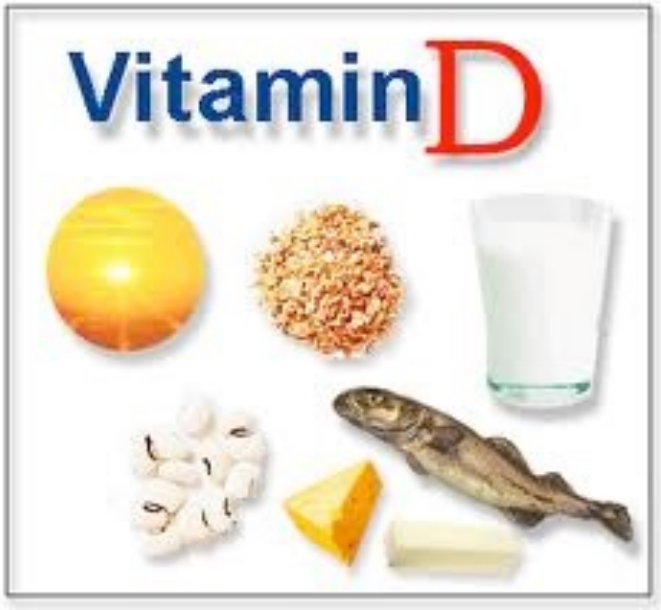
How does the lab scientist improve patient experience?

Passiment E, Meisel JL, Fontanisei J, Fritsma GA, Aleryani S, Marques, M. Decoding laboratory test names: a major challenge to appropriate patient care. J Gen Intern Med DOI 10.1007/s11606-012-2253-8.

Test Names

An order arrives with a serum-separator tube requesting “Vitamin D.” How do you log it?





- Kleerekoper M, Schleicher RL, Eisman J, et al. Clinical applications for vitamin D assays: what is known and what is wished for. Clin Chem 2011;57:1227–32.

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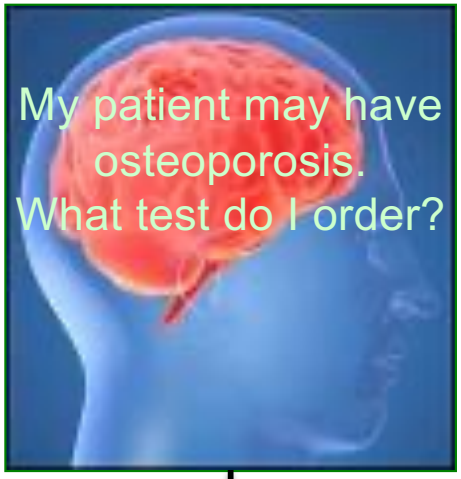
Test Names: The Vitamin D Puzzle



Experts identify multiple vitamin D forms with no naming consensus:

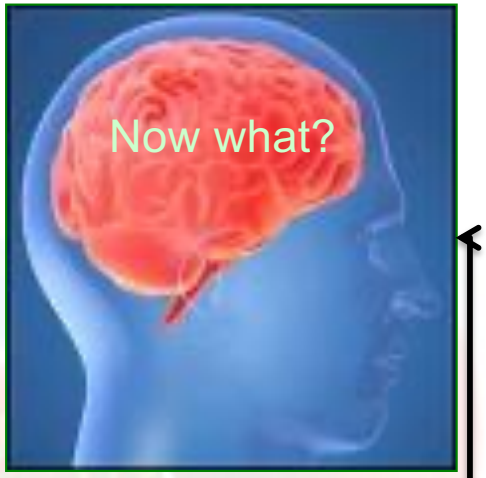
- calciferol, calcidiol, calcitriol
- cholecalciferol
- 1,25 dihydroxycholecalciferol
- ergosterol
- vitamin D
- vitamin D_2
- vitamin D_3
- 25-0H vitamin D [this one]
- 25-0H vitamin D_2
- 25-0H vitamin D_3
- 25 hydroxy vitamin D
- 25 hydroxy vitamin D_2
- 25 hydroxy vitamin D_3
- 1,25 $(OH)_2$ vitamin D
- 1,25 $(OH)_2$ vitamin D_2
- 1,25 $(OH)_2$ vitamin D_3
- 1,25 dihydroxy vitamin D
- 1,25 dihydroxy vitamin D_2
- 1,25 dihydroxy vitamin D_3

Which is correct?

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

- Vitamin D, VITD
- 25-0H vitamin D
- 25-OH VITD

Result: 60 ηg/mL



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What's in a name?

LAC

FX

PTT

AT

FV

PT

INR

PC

VWF

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More Pre-analytical Issues
What to Do?

- PTT ordered for LMWH, fondaparinux, rivaroxaban, apixaban, dabigatran, how to test for DOACs?
- Order PT and PTT when lupus anticoagulant present?
- LA, LAC, DRVVT screen, DRVVT confirm, Sta-Clot LA; PTT-LA; what does it all mean?
- What are VWF:Ag, VWF:Ac; VWF:RCo VWF:GPIbM, VWF:GPIbR, VWF:CB, VWF multimers, VWF:etc?

Assistive Algorithm

- IOM says, "*facilitate more effective teamwork in the diagnostic process among health care professionals, patients, and their families*"
- Form collaborative partnerships to produce robust laboratory test utilization algorithms
- Assistive algorithm: clinician selects or enters indications gathered from patient Hx and physical.
- Algorithm returns recommendations for tests and test profiles, from which physician makes choices.

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Indication-based Laboratory Utilization

- Team of clinical and technical practitioners establishes algorithms
- Hemostasis indication examples
  - Current complaint—swollen leg, chest pain, shortness of breath, bruising, hemorrhage
  - History of prior events, first-degree relatives
  - Refer to age, sex, BMI, race, habits
- List applicable hemostasis assays: D-D, PT, PTT, FBG, PC, PS, AT, factor assay, PLT count, PLT aggregometry
- List hemostasis assay profiles: thrombophilia, anatomic bleeding, systemic bleeding, arterial thrombosis
- Match selected lists of indications with hemostasis laboratory assays and profiles.

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Example: Thrombophilia Profile

Assay	Patient	RI
60 YOA male, DVT, 3 Weeks Coumadin		
Protein C activity	35%	>70%
Protein S activity	39%	>65%
Antithrombin activity	87%	78–126%
APCR	2.4	>1.8
Factor V Leiden	Wild-type	Wild-type
PTT-LA	39 s	30–40 s
Protein C & S are vitamin K-dependent coag control proteins.		

- Double heterozygote?
- Increase Coumadin?
- Start heparin?
- Consult with the lab?

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Thrombophilia Profile Narrative Report

Assay	Patient	RI
60 YOA male, DVT, 3 Weeks Coumadin		
Protein C activity	35%	>70%
Protein S activity	39%	>65%
Antithrombin activity	87%	78−126%
APCR	2.4	>1.8
Factor V Leiden	Wild-type	Wild-type
PTT-LA	39 s	30–40 s

Or: "*Protein C and S decreased, probable Coumadin interference. Reflex INR = 2.1 indicates Coumadin. Other thromobitc risk factor results are within reference interval. No evidence for thrombotic risk, repeat profile 2 weeks after discontinuing Coumadin*."

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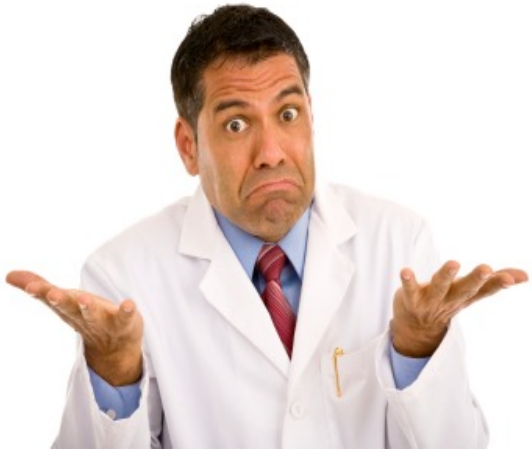
Example 2: Pre-op Screen

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		

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



Pre-op Screen: 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
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		

"*Isolated prolonged PTT may indicate coagulation factor deficiency, coagulation factor inhibitor, or lupus anticoagulant. Normal TT indicates no heparin. 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 prior PTT
PTT/NP 1:1 immediate mix	38.5 s	NP 27.5 s	Mix is >10% prolonged over the normal plasma

- Uncorrected?
- Do you send this result to the surgeon?
- Continue to delay surgery?
- Consult with laboratory?
- Narrative report?
- Laboratory immediate reflex to…

Mixing Study: How About This?

Assay	Result	RI	Comment
PTT	57 s	25–35 s	Confirms prior PTT
PTT/NP 1:1 immediate mix	38.5 s	NP 27.5 s	Mix is >10% prolonged over the normal 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 PTT
PTT-LA /control 1:1	38.5 s	Control 34.5 s	Possible LA
Staclot LA kit	12 s	> 8 s 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?
- Continue to delay surgery?
- Consult with laboratory?
- Narrative report?

LA Profile: How About This?

Assay	Result	RI	Comment
PTT-LA	47.9 s	30–40 s	Confirms PTT
PTT-LA /control 1:1	38.5 s	Control 34.5 s	Possible LA
Staclot LA kit	12 s	> 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*."

Quesada AE, Jabcuga CE, Nguyen A, et al. Interpretation of coagulation test results using a web-based reporting system. Lab Medicine 2014;45:343–56.

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My Portal: 3-2-22

- Creatine kinase: 90 U/L
  - Narrative: “A creatine kinase (CK) test checks the level of the enzyme creatine kinase, which is found in heart tissue and skeletal muscles. This enzyme also can be found in smaller amounts in the brain. A blood test to check the level of CK can show if there has been damage to the heart, skeletal muscles, brain, and sometimes...” [end of narrative]
  - My note: CK replaced by troponin for sensitivity
- ESR: 8 mm/h
  - Narrative: “The sedimentation rate (sed rate) blood test measures how quickly red blood cells (erythrocytes) settle in a test tube in one hour. The more red cells that fall to the bottom of the test tube in one hour, the higher the sed rate. When inflammation is present in the body, certain proteins cause red blood cells to stick...” [end of narrative]
  - My note: ESR is obsolete, use CRP

Association for the Advancement of Blood and Biotherapies [American Association of Blood Banks]

- Don't transfuse red blood cells for iron deficiency without hemodynamic instability.
- Don't routinely use blood products to reverse warfarin.
- Don't perform serial blood counts on clinically stable patients.

Choosing Wisely®
An initiative of the ABIM Foundation

American Society for Clinical Laboratory Science

- Don't order a factor V Leiden (FVL) mutation assay as the initial test to identify a congenital cause for a thrombotic event. First, order a phenotypic activated protein C resistance (APCR) ratio assay.
- Avoid using hemoglobin to evaluate patients for iron deficiency in susceptible populations. Instead use ferritin.
- Do not transfuse red blood cells as the sole intervention for expansion of circulatory volume unless deemed necessary for patients experiencing severe hemorrhage.

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- Avoid routine prothrombin time (PT) and partial thromboplastin time (PTT, APTT) pre-operative screens on asymptomatic patients, use instead a history-based bleeding assessment test.
- Do not order a homocysteine assay as part of the thrombophilia work up.
- Do not use viscoelastic testing to determine blood product transfusions in trauma patient resuscitation without an established, institutional treatment algorithm in place.

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- Don't screen for 25-OH-vitamin D deficiency.
- Avoid routine preoperative testing for low-risk surgeries without a clinical indication.
- Don't use the bleeding time test to guide patient care.
- Don't use ESR, use C-reactive protein (CRP) for acute inflammation in patients with undiagnosed conditions.
- Don't test vitamin K levels unless the patient has an abnormal INR and doesn't respond to VK therapy.
- Use only troponin I or T in the diagnosis of acute myocardial infarction (AMI).

ASCP

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American Society of Hematology

- Don’t transfuse more than the minimum RBC units necessary to relieve symptoms of anemia or to return a patient to a safe HGB range: 7–8 g/dL in stable, non-cardiac in-patients.
- Don’t test for thrombophilia in adult patients with VTE who have major transient risk factors—surgery, trauma, immobility.
- Don’t test or treat for heparin-induced thrombocytopenia (HIT) in patients with a low pre-test probability of HIT.

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AMERICAN SOCIETY OF HEMATOLOGY®

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SWMC, Dallas, 2009: Appropriate Thrombophilia Testing Profile Indications

Retrospective observational study of consecutive unselected patients undergoing thrombophilia testing

- Pregnancy morbidity: pre-eclampsia, intrauterine growth retardation
- Recurrent pregnancy loss, three or more instances
- Unprovoked arterial or venous thrombosis

- Department of Pathology, University of Texas Southwestern Medical Center, Dallas, TX,
- Shen YM, Tsai J, Taiwo E, et al. Analysis of thrombophilia test ordering practices at an academic center: a proposal for appropriate testing to reduce harm and cost. Plos ONE 11: e0155326. doi:10.1371/journal.pone.0155326

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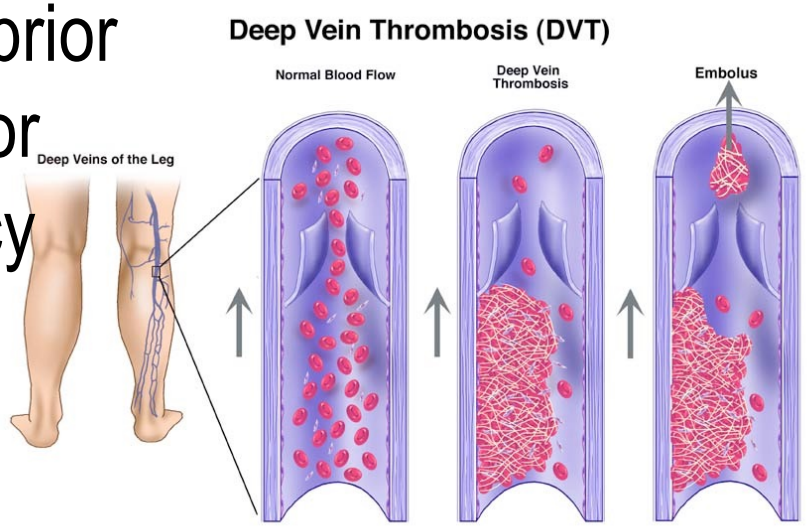
Thrombophilia Testing Non-Indications

- One or two pregnancy losses
- *Provoked* venous thrombosis: immobilization, surgery, trauma, and malignancy prior to or at the time of the event
- *Provoked* arterial thrombosis: hypertension, dyslipidemia, diabetes, atherosclerotic disease
- Screen without a prior thrombotic event or adverse pregnancy outcome



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The Dallas Intervention

- Investigate as outpatients if they met the criteria (young age, unprovoked event) ≥2 weeks following D/C of anticoagulation.
- Hemostasis service communicated with clinicians to cancel testing that was deemed inappropriate.
- Intervention reduced total orders from 87/m to 5/m.
  - Reduced inpatient orders by 90%

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Electronic Best Practice Alert: Stanford

- In 2016, every thrombophilia order generated an *interruptive [no hard stop] BPA* highlighting the CW thrombophilia recommendation.
- 12m pre-BPA versus 7m post-BPA orders
- Inpatients
  - Pre-BPA: 101.1 tests/m; post-BPA: 73.3 tests/m, p = 0.03
- Outpatients
  - Pre-BPA: 471.5 tests/m; post-BPA: 471.6 test/m, p = 1.0

Jun T, Kwang H, You E, et al. Using electronic best practice alerts to improve thrombophilia testing based on ASH choosing wisely guidelines. ASH Poster, Atlanta, 12-10-17, 6–8 PM

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Bottom Line at the End [BLEAT]

What do Medical Laboratory Scientists Do to Prevent Diagnostic Errors? We…

- Review diagnostic assay utilization.
- Prevent specimen management errors.
- Interpret laboratory assay results.