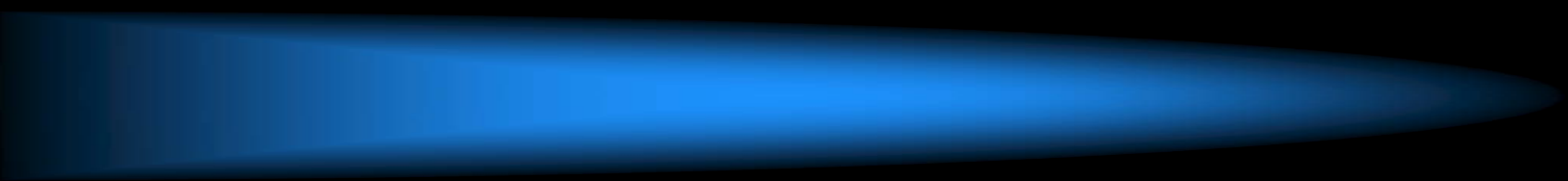


# *POC Hematology & Coagulation Tests for Optimizing Intraoperative Transfusion Decisions*



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# *Transfusion Decisions*

- Dilemma in the operating room
  - ◆ Rapid pace of bleeding
  - ◆ Rapid results often not available from the lab
  - ◆ Consumption of hemostatic components during bleeding exacerbates the problem
  - ◆ Massive transfusion and fluid resuscitation can lead to dilutional coagulopathies

# *Transfusion Decisions*

- Subjective

- ◆ Chest is dry – no transfusion needed
- ◆ Chest is wet – transfuse 6 units platelet concentrate, 2 units fresh frozen plasma

- Objective

- ◆ Hemoglobin/hematocrit often available for RBC decisions
- ◆ Tests to provide guidance for platelet, plasma, and cryoprecipitate transfusion

# *How Do We Provide Objective Evidence for Decisions?*

- Consider what tests will give useful information in a timely manner
- Determine transfusion triggers
- Build an algorithm
- Assess its effectiveness

# *What is Timely?*

- Time is blood loss
- Even 15 minutes is an eternity with brisk bleeding and hemodynamic instability
- Our goal: 5 minutes or less
  - ◆  $\Rightarrow$  Point of care testing

# *Post-Cardiopulmonary Bypass (CPB) Hemorrhage*

- Cardiac surgery has highest average transfusion utilization (Mayo data)
- 11% incidence rate (Mayo data)
- 4% incidence of surgical exploration
  - ◆ <50% have a surgical source of bleeding
  - ◆ Majority have hemostatic defects
    - Despotis, et al. Ann Thorac Surg 72:S1821, 2001

# *Pathophysiology of Post-CPB Hemorrhage*

## HEMODILUTION

CPB Prime

Cardioplegia  
solution

Extensive use of  
cell salvage  
systems

## ACTIVATION

Contact activation

Tissue factor  
activation

Fibrinolysis

## CONSUMPTION

Thrombin-  
mediated

Plasmin-  
mediated

Inflammation-  
mediated

Mechanical

Influenced by: heparin-protamine protocol,  
hypothermia, preoperative & operative medications,  
length of bypass, prior surgery

# *What Do We Need to Assess?*

- *Hemoglobin / hematocrit*
  - ◆ **Methods**
    - Spectrophotometric
    - Centrifugation
    - Cell counting
    - Conductivity
  - ◆ **Issues**
    - Comparability among methods
    - Effect of significant hemodilution

# *What Do We Need to Assess?*

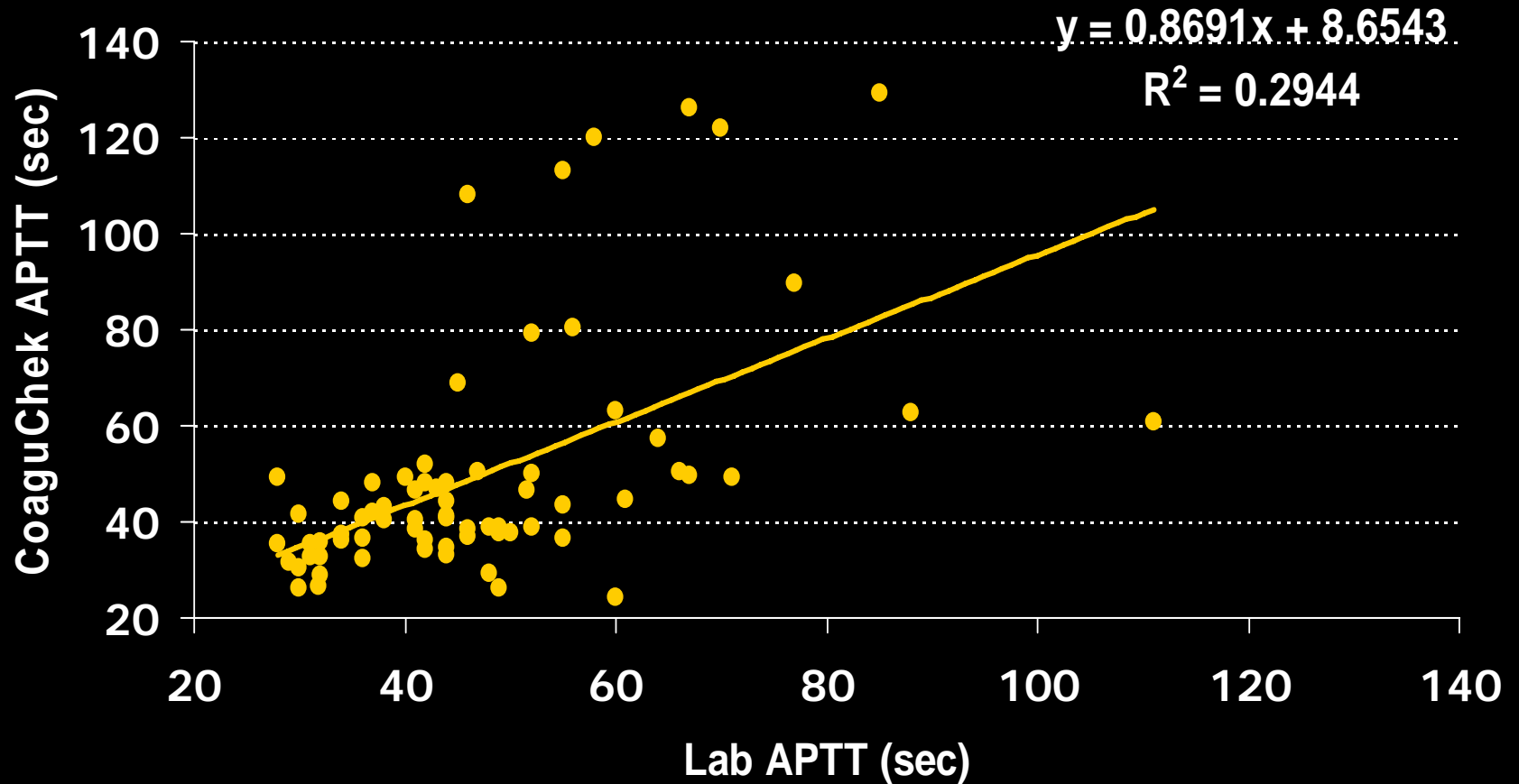
- *Coagulation factors*

- ◆ PT, APTT, fibrinogen

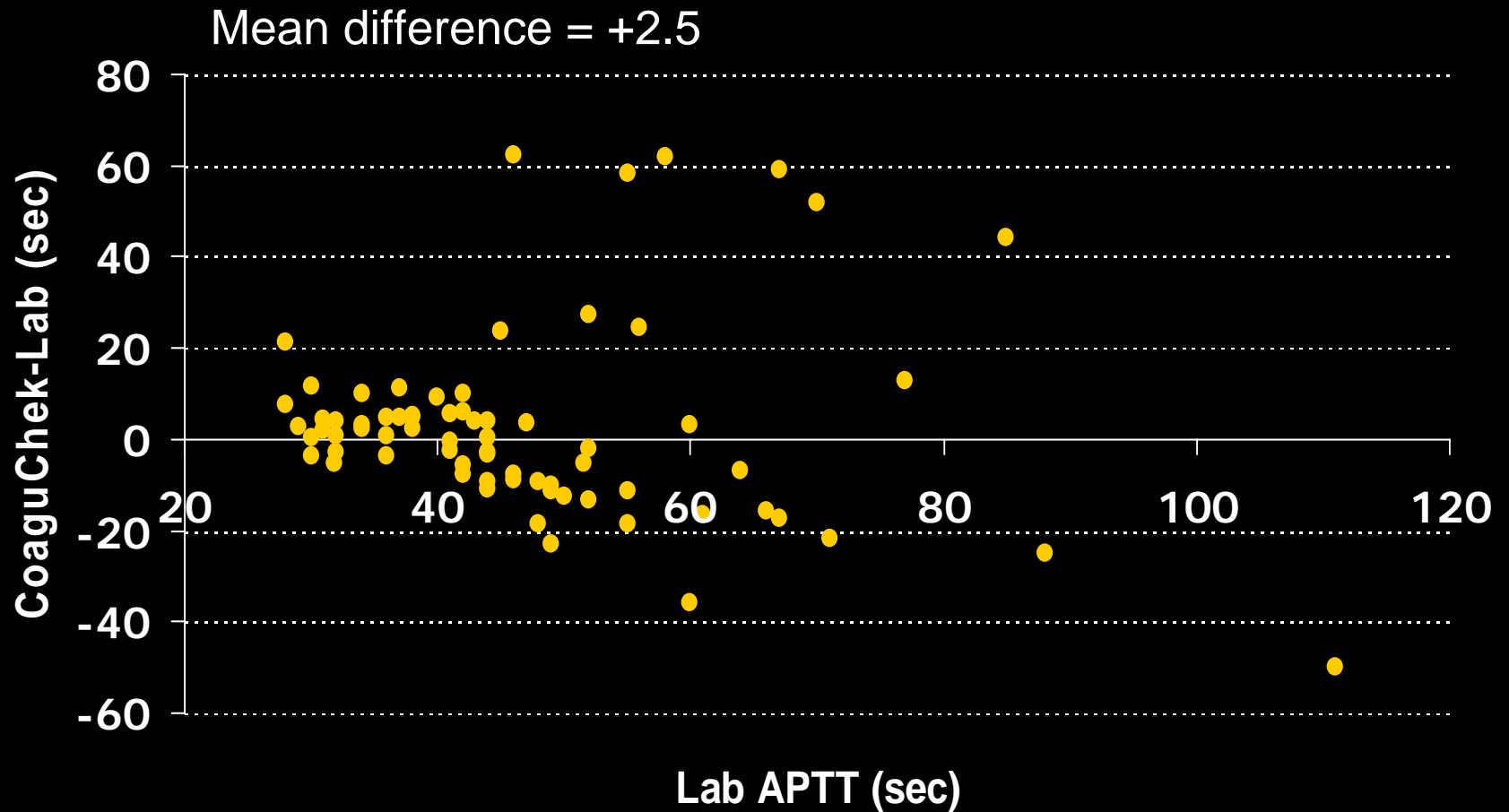
- ◆ Issues

- Availability of APTT and fibrinogen systems
- Comparability with the lab is problematic, particularly for the APTT
- INR not intended to be used as a transfusion trigger

# *Comparison of Lab and POCT for APTT*



# *Comparison of Lab and POCT for APTT*



# *What Do We Need to Assess?*

- *Platelet concentration*
  - ◆ Available POCT systems
    - Small cell counters from a variety of manufacturers
  - ◆ Issues
    - Process for dealing with “flags” on cell counters

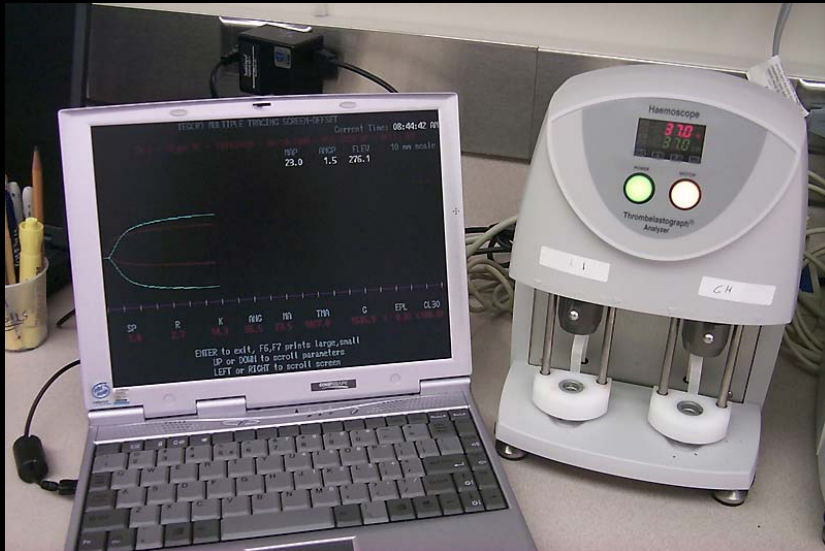
# *What Do We Need to Assess?*

- *Platelet function*

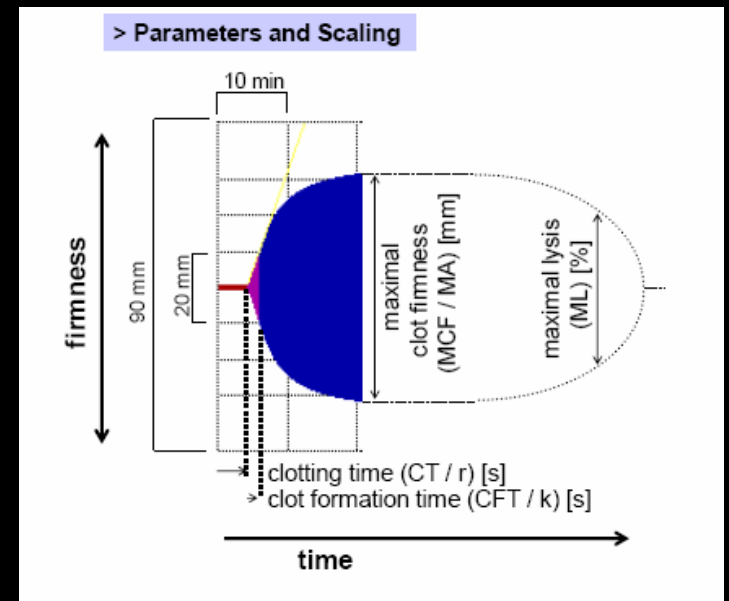
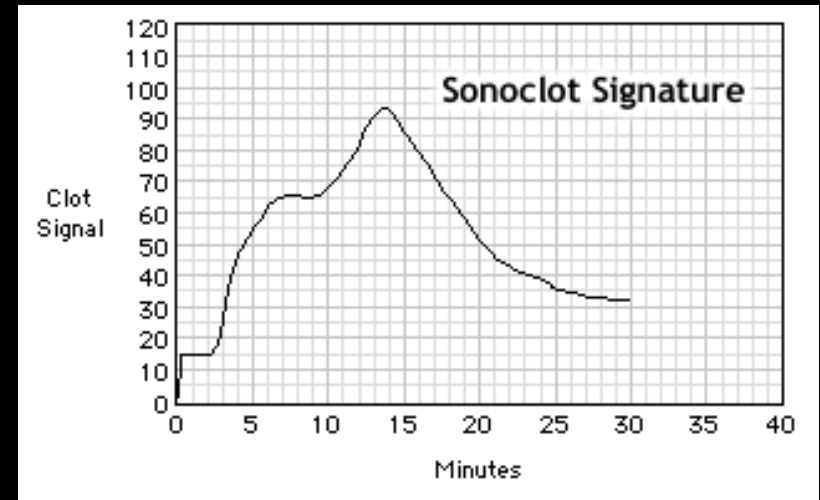
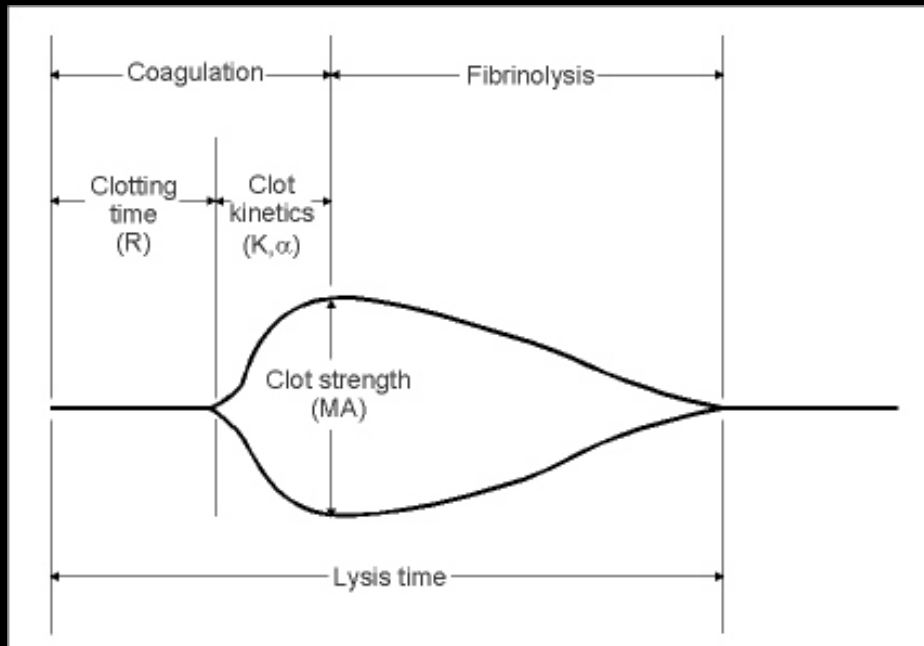
- ◆ Available POCT systems

- Helena Plateletworks (aggregation with ADP, collagen)
- Accumetrics Ultegra (inhibition of platelet aggregations due to presence of anti-platelet agents in patient's blood – ASA, clopidogrel, GP IIB/IIIa inhibitors)
- Dade PFA-100 (in vitro bleeding time with ADP, collagen as activators)
- Haemoscope Thromboelastograph (viscoelastic test of hemostasis)
- ROTEM (viscoelastic test of hemostasis)
- Sienco Sonoclot (viscoelastic test of hemostasis)

# Viscoelastic Tests of Coagulation



# Viscoelastic Tests of Coagulation



# *What Do We Need to Assess?*

- *Platelet function*

- ◆ Issues

- Platelet function is complex with many different facets
- Tests tend to focus on some aspect of platelet function which may not be relevant to the clinical situation
- Published correlation studies in post-CPB bleeding are very mixed

# *What Do We Need to Assess?*

- *Fibrinolysis*

- ◆ Available POCT systems

- Haemoscope Thromboelastograph (viscoelastic test of hemostasis)
- Sienco Sonoclot (viscoelastic test of hemostasis)
- ROTEM (viscoelastic test of hemostasis)

- ◆ Issues

- Rare occurrence in cardiac surgery – more useful during liver transplantation

# *What Do We Need to Assess?*

- *Residual heparin*

- ◆ Available POCT systems

- Activated clotting time (ACT)
- Heparinase ACT
- Heparinase TEG
- Heparin concentration (protamine titration)

# *Transfusion Triggers for POCT*

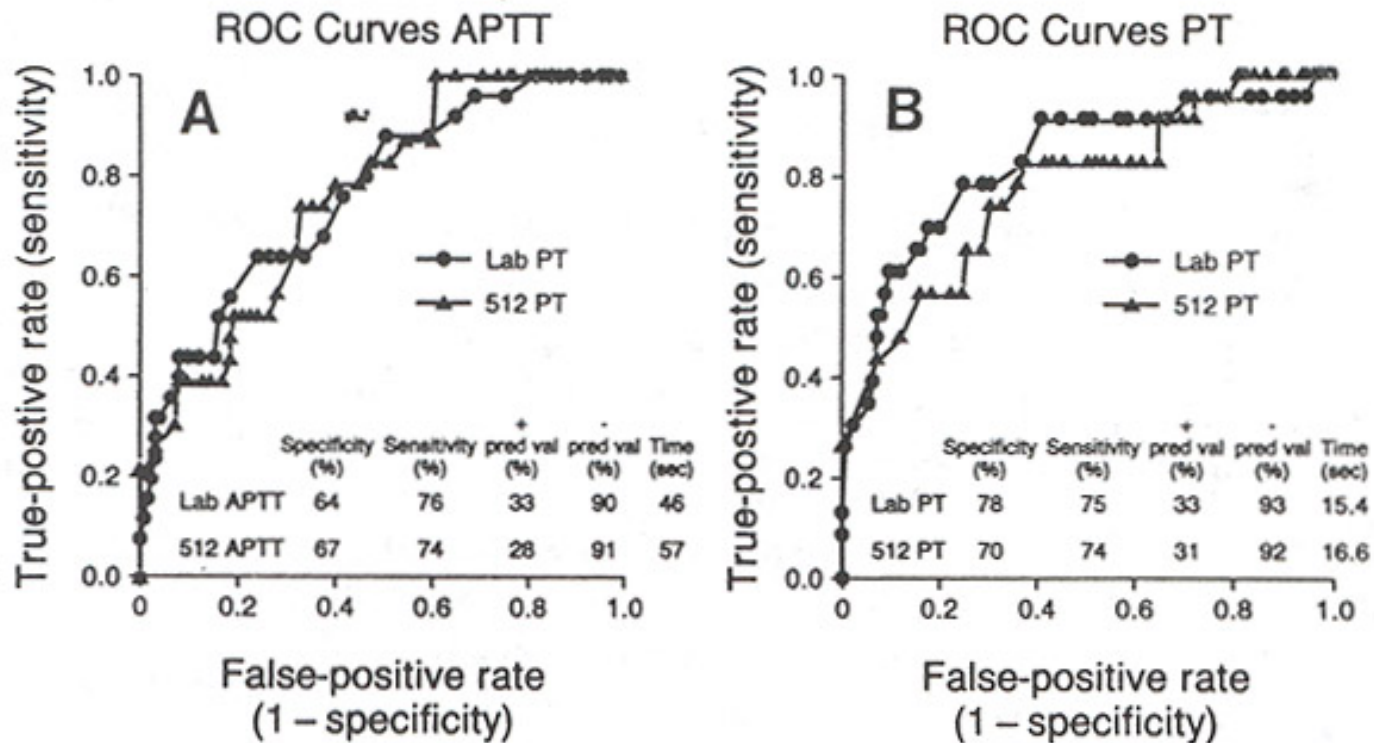
- Options
  - ◆ Reference range
  - ◆ Multiples of the upper limit of the reference range
  - ◆ Decision points provided by device manufacturer
  - ◆ Decision points from published studies
  - ◆ Do your own study
- Context: patient population of practice

# Transfusion Triggers for POCT

Table 4. Coagulation Values

	Bleeder (n = 23)	Nonbleeder (n = 125)	P Values
Baseline ACT (s)	152 ± 21	157 ± 32	P = 0.34
ACT during CPB (s)†	613 ± 159	585 ± 146	P = 0.577
ACT after protamine (s)	149 ± 22	144 ± 16	P = 0.093
Baseline lab PT (s)	12.8 ± 0.8	12.1 ± 1.2	P = 0.241
Lab PT after protamine (s)	17.0 ± 2.9	14.9 ± 1.2*	P = 0.000
512 PT after protamine (s)	17.8 ± 2.5	15.9 ± 2.0*	P = 0.049
Lab PT ICU <sub>1</sub> (s)	13.7 ± 0.8	13.7 ± 1.0	P = 0.615
Lab PT ICU <sub>12</sub> (s)	13.7 ± 2.8	12.3 ± 1.6*	P = 0.005
Baseline lab aPTT (s)	33.9 ± 4.8	31.9 ± 7.5	P = 0.161
Lab aPTT after protamine (s)	60.0 ± 31.5	42.5 ± 13.2*	P < 0.001
512 aPTT after protamine (s)	75.3 ± 30.8	54.6 ± 16.7*	P < 0.001
Lab aPTT ICU <sub>1</sub> (s)	46.0 ± 15.1	39.7 ± 11.4	P = 0.198
Lab aPTT ICU <sub>12</sub> (s)	36.8 ± 10.9	32.9 ± 7.7	P = 0.097

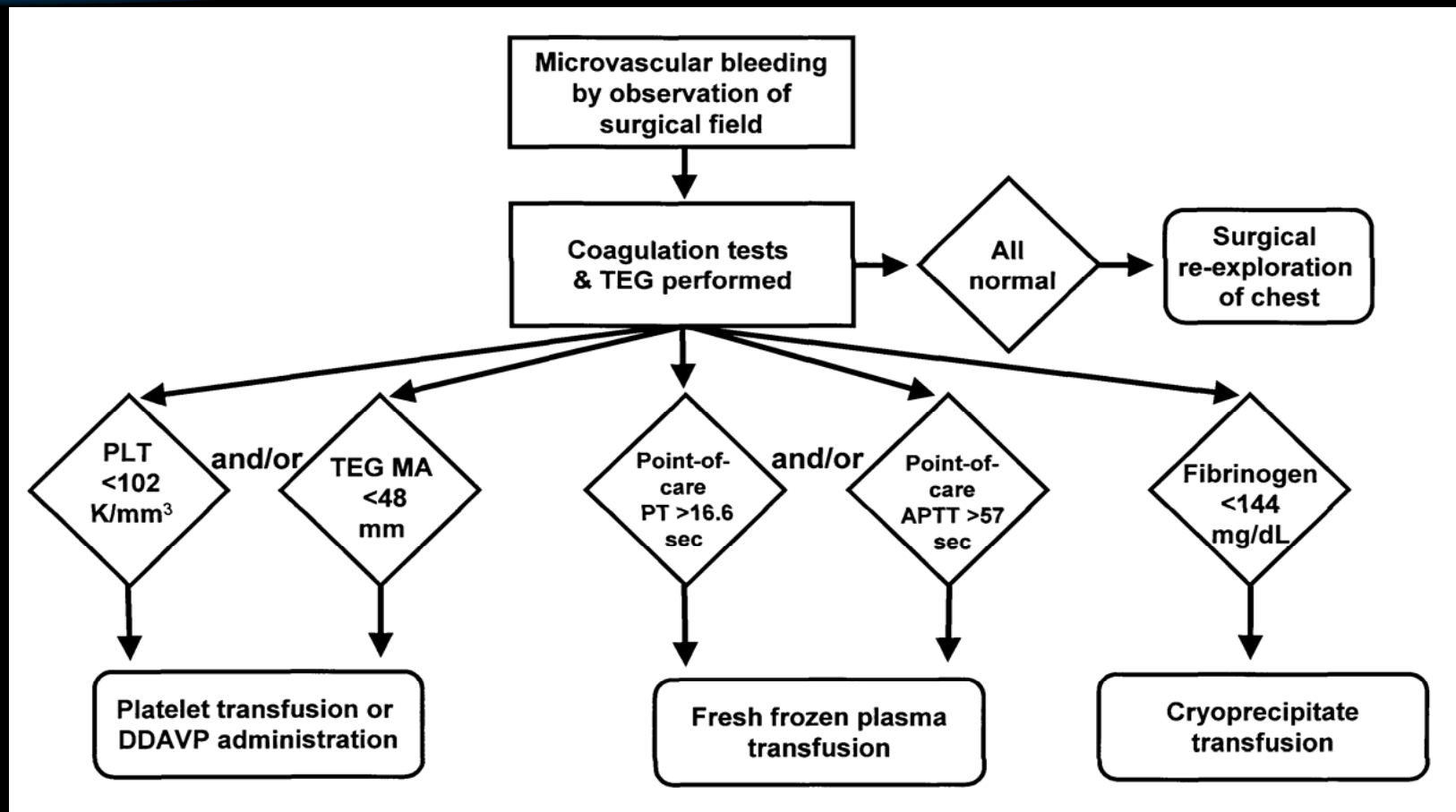
# Transfusion Triggers for POCT



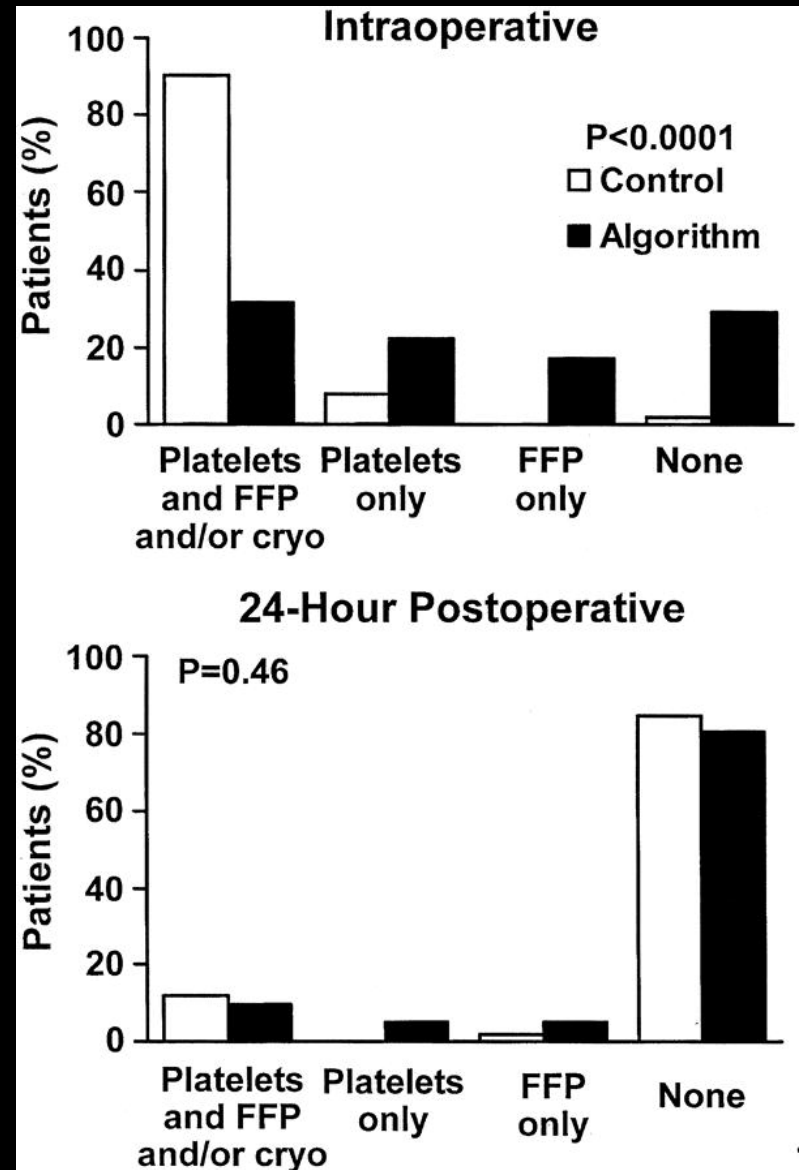
# *POCT Algorithm Outcome Studies*

<b>Author</b>	<b>Surg proc</b>	<b>Study type</b>	<b>Patients</b>	<b>Outcome</b>
Despotis	Card	Pro	362	Algorithm decreased trx & bleeding
Spieß	Card	Retro	1079	TEG use decreased trx
Shore-Lesserson	Card	Pro	102	TEG algorithm decreased trx
Nuttall	Card	Pro	836	Algorithm decreased trx & bleeding
Capraro	Card	Pro	1412	Algorithm increased platelet trx, no difference in bleeding
Royston	Card & Heart tx	Pro	60	TEG algorithm decreased trx
Avidan	Card	Pro	102	2 algorithms decreased trx
Anderson	Card	Retro	990	ROTEM algorithm decreased trx

# Mayo Transfusion Algorithm



# Mayo Transfusion Algorithm Effectiveness



Nuttall, et al. Anesthesiology 94:773, 2001

# *Mayo Transfusion Algorithm*

## *Effectiveness*

- Reduced transfusions in operating room, median (range)
  - ◆ FFP 0 (0,7) units vs 3 (0, 10) units ( $p = 0.0002$ )
  - ◆ platelets 4 (0, 12) units vs 6 (0, 18) units ( $p = 0.0001$ )
- Significant differences in total hospital transfusions
- Reduced chest-tube drainage at 4, 12 and 24 hours (all  $p < 0.03$ ) and reoperation for bleeding rate ( $p = 0.032$ ) in algorithm group
- No difference in ICU transfusions except RBCs
  - ◆ RBCs 0 (0,6) units vs 1 (0, 6) units ( $p = 0.0028$ )

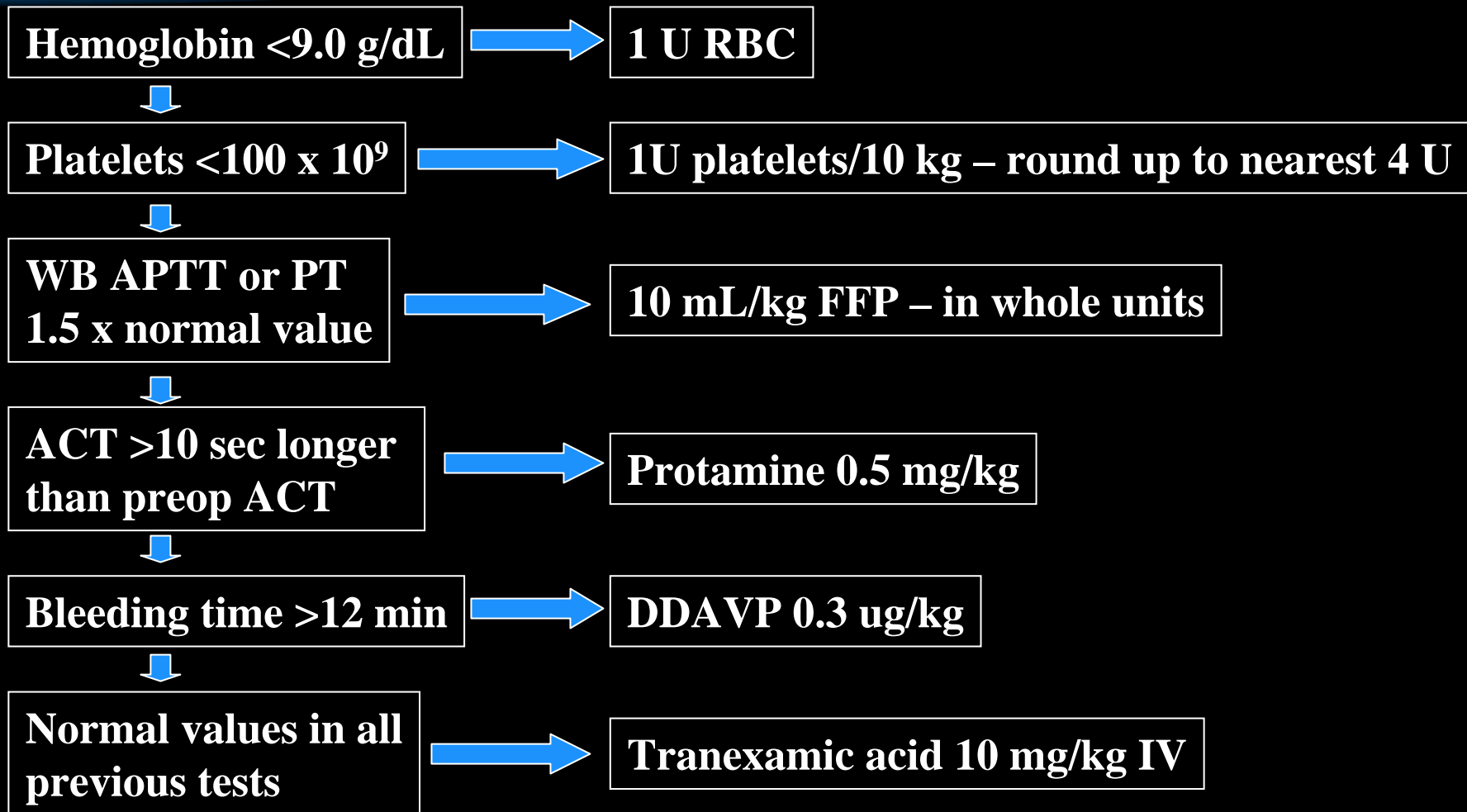
# TEG-Based Transfusion Algorithm

Intraop TEG variable	Implication	Therapy
R >14 & <21 mm	↓ clotting factors	1 FFP
R >21 & <28 mm	↓↓ clotting factors	2 FFP
R >28 mm	↓↓↓ clotting factors	4 FFP
MA <48 mm	↓↓ platelet no/fxn	1 plt pool
MA <40 mm	↓↓↓ platelet no/fxn	2 plt pools
Lys30 >7.5%	Increased lysis	Aprotinin

# *TEG-Based Transfusion Algorithm Effectiveness*

	Control	Algorithm	
Patients (no.)	30	30	
Patients transfused (no.)	10 (33%)	5 (17%)	
FFP transfused (units)	16	5	} <b>P&lt;0.005 compared to control</b>
Platelets transfused (pools)	9	1	
Median blood loss postop (mL)	390	470	

# Capraro Transfusion Algorithm



# Capraro Transfusion Algorithm Effectiveness

No. patients treated during immediate recovery period			
Treatment	Group A (n=28)	Group B (n=30)	P
Platelets	14	3	0.001
Protamine	8	9	NS
FFP	3	7	NS
DDAVP	8	2	0.04
Tranexamic acid	10	13	NS

# Capraro Transfusion Algorithm Effectiveness

Transfusion requirements during hospitalization			
	Group A (n=28)	Group B (n=30)	P
RBC units	6.5 ± 5.6	5.7 ± 5.6	0.5
FFP units	2.0 ± 2.6	2.3 ± 2.3	0.5
Platelet units	8.7 ± 10.1	6.5 ± 7.5	0.3
Total donor exposures	17.2 ± 17.2	14.4 ± 14.0	0.5

# *Capraro Transfusion Algorithm Effectiveness*

- Caveats

- ◆ Imbalance in groups

- More combined operations in algorithm group

- ◆ Already very conservative in transfusion decisions

- ◆ Re-exploration rate >20% in both groups

- ◆ Testing done in first hour postoperatively

- What about immediate post-pump time frame?

# Conclusions

- Algorithms are useful for transfusion decisions in the perioperative period, but need:
  - ◆ Focus on the correct hemostatic problems
  - ◆ Rapid results
  - ◆ Carefully selected transfusion triggers
- Remaining questions
  - ◆ Assessment of platelet function
  - ◆ Impact of preoperative platelet inhibition therapy
  - ◆ How do we get consistent use of the algorithm?
  - ◆ How do we translate this beyond cardiac surgery?

# Resources

- References for transfusion algorithm studies
  - ◆ Despotis, et al. J Thorac Cardiovasc Surg 107:271, 1994.
  - ◆ Speiss, et al. J Cardiothorac Vasc Anesth 9:168, 1995
  - ◆ Shore-Lesserson, et al. Anesth Analg 88:312, 1999
  - ◆ Nuttall, et al. Anesthesiology 94:773, 2001
  - ◆ Royston, et al. Br J Anaesth 86:575, 2001
  - ◆ Capraro, et al. Acta Anaesthesiol Scand 45:200, 2001
  - ◆ Avidan, et al. Br J Anaesth 92:178, 2004
  - ◆ Anderson, et al. Transfusion Med 16:31, 2006