3rd Annual EMS Medical Directors' Conference

Indiana State Department of Health

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TXA

To Drink Or, Not To Drink

The Kool Aid

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Professor of Surgery
Indiana University School of Medicine
Medical Director, Surgical Field Response Team

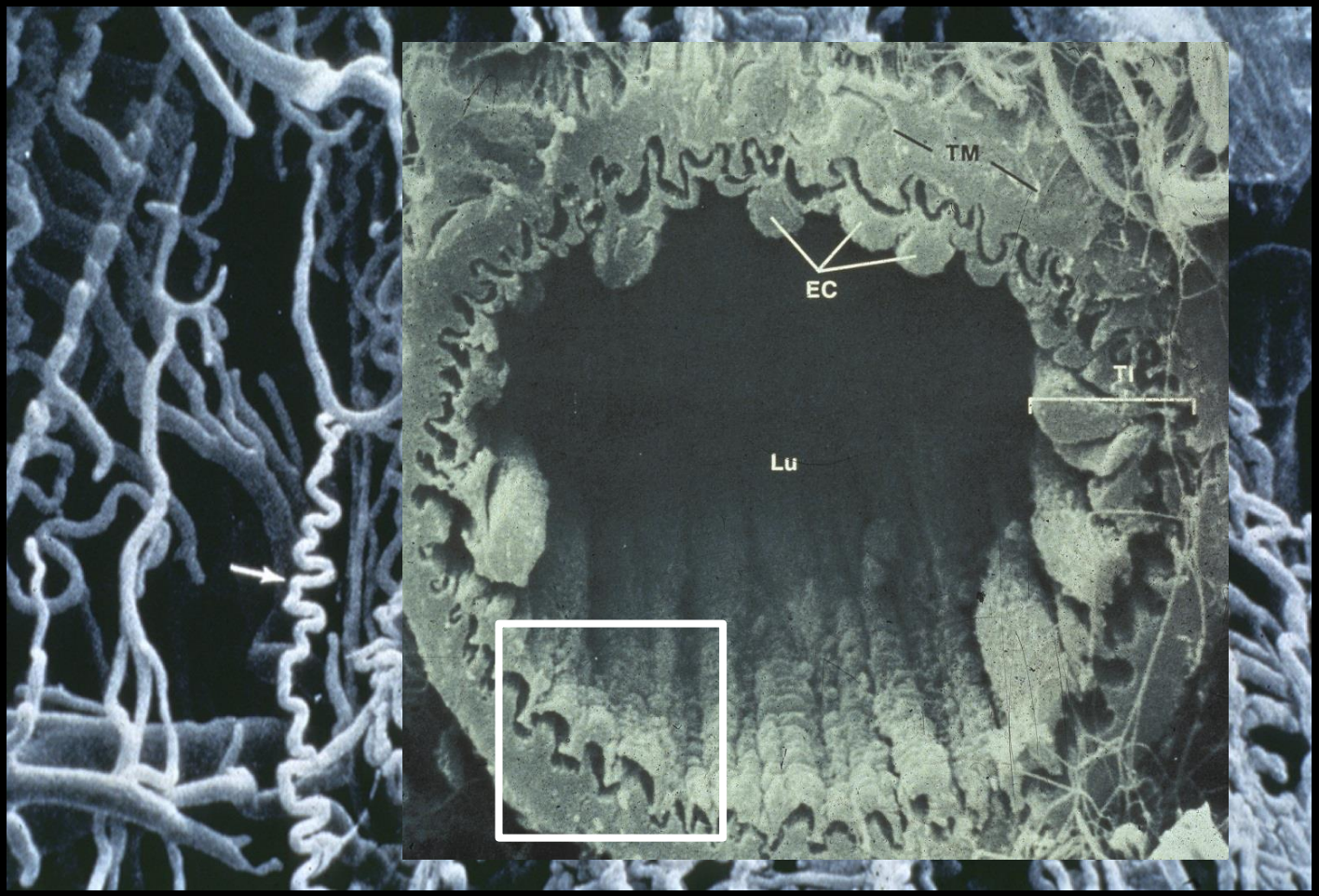
Financial Disclosure

- J&J DePuy Synthes
  - Consultant
  - Speaker
- Acute Innovations, Inc.
  - Consultant
- Zimmer Biomet
  - Consultant

(Nothing to do with TXA or any other aspect of hemorrhage control.)

“Drinking the Kool Aid”

Used ironically, or humorously, to refer to anyone who blindly accepts an idea, or changes the way they do things due solely to peer pressure, or heavy persuasion.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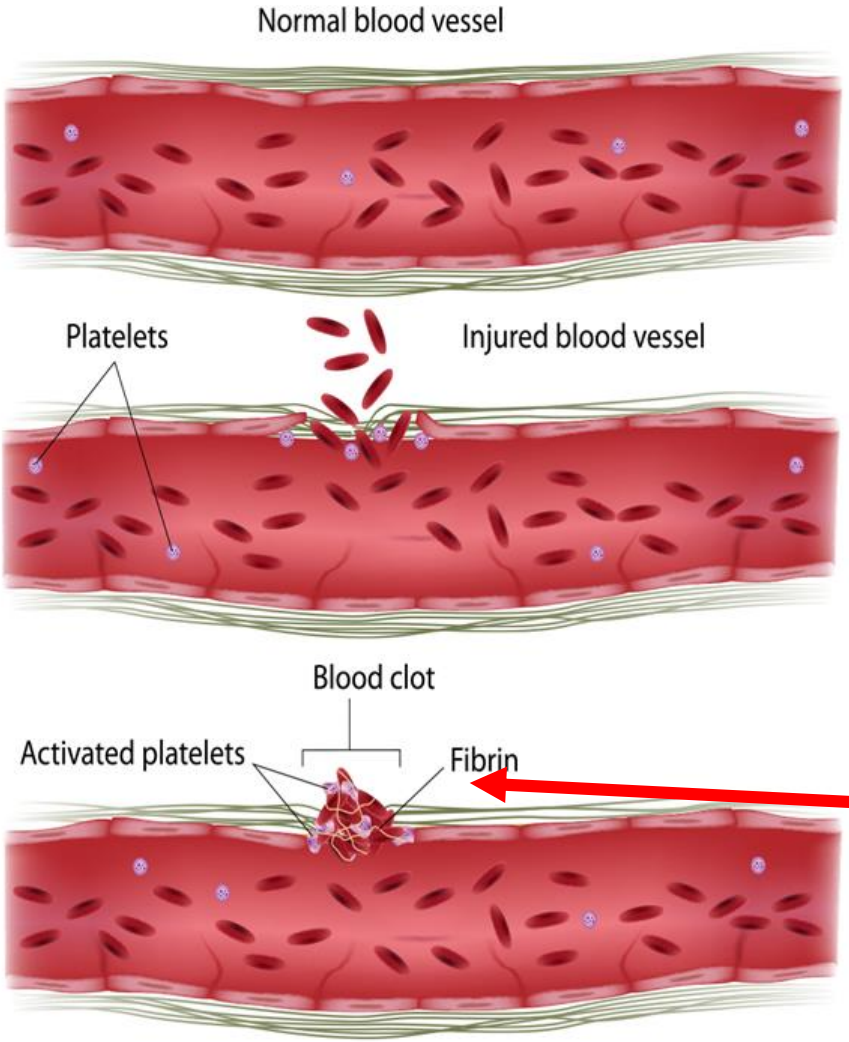
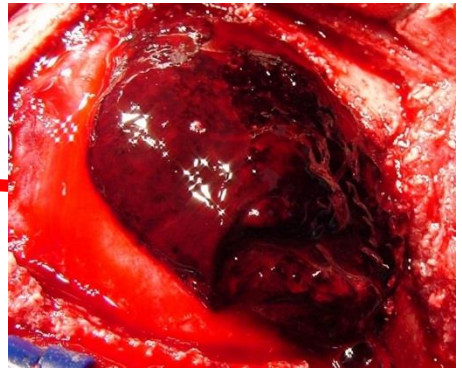


Tissue injury

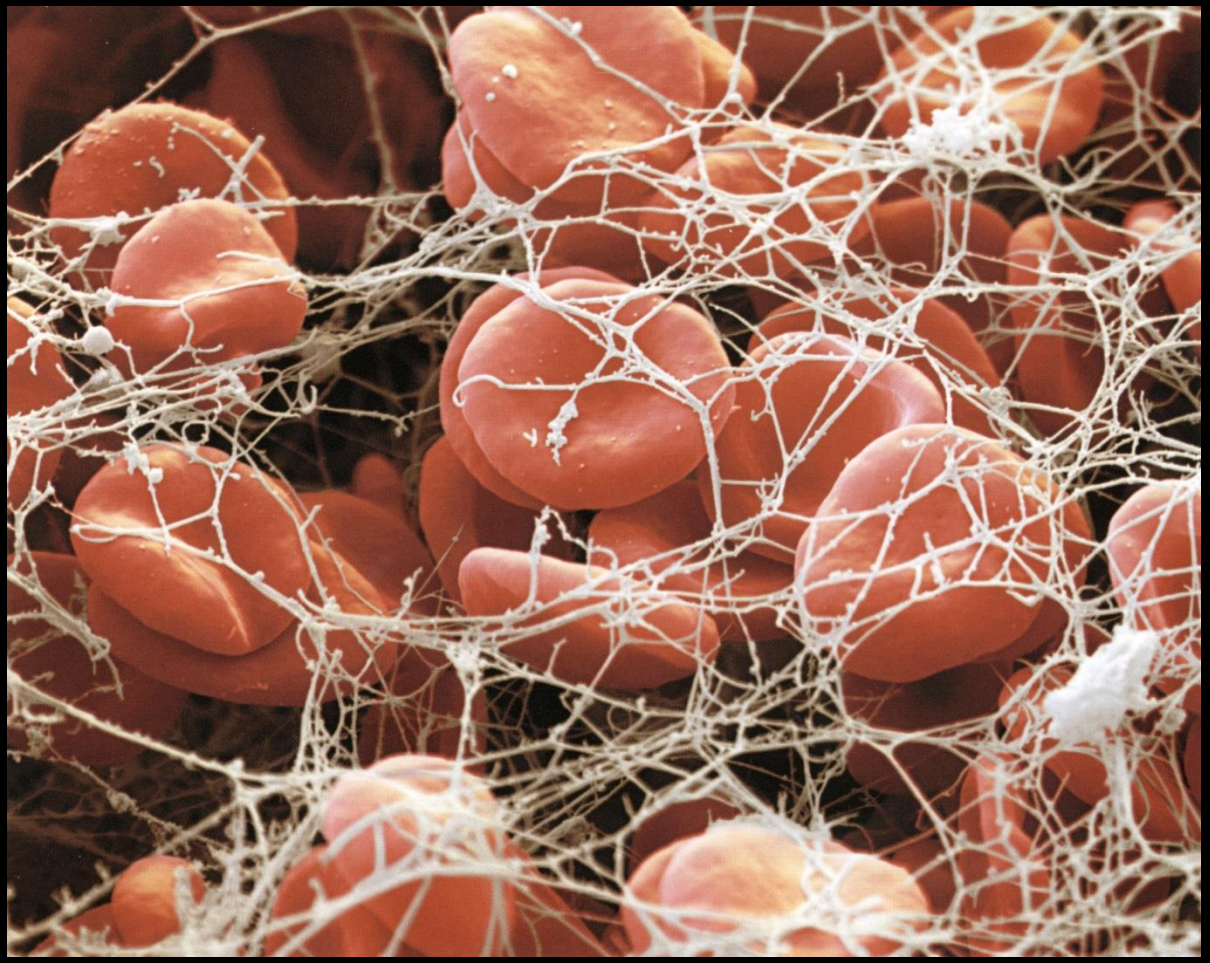
Exposure of blood to anything outside a blood vessel

Thrombin (Coagulation)

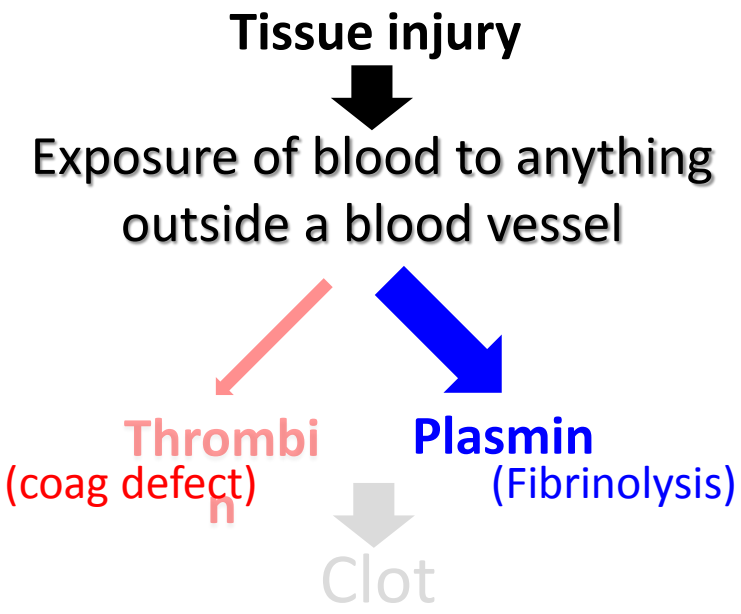
Plasmin (Fibrinolysis)

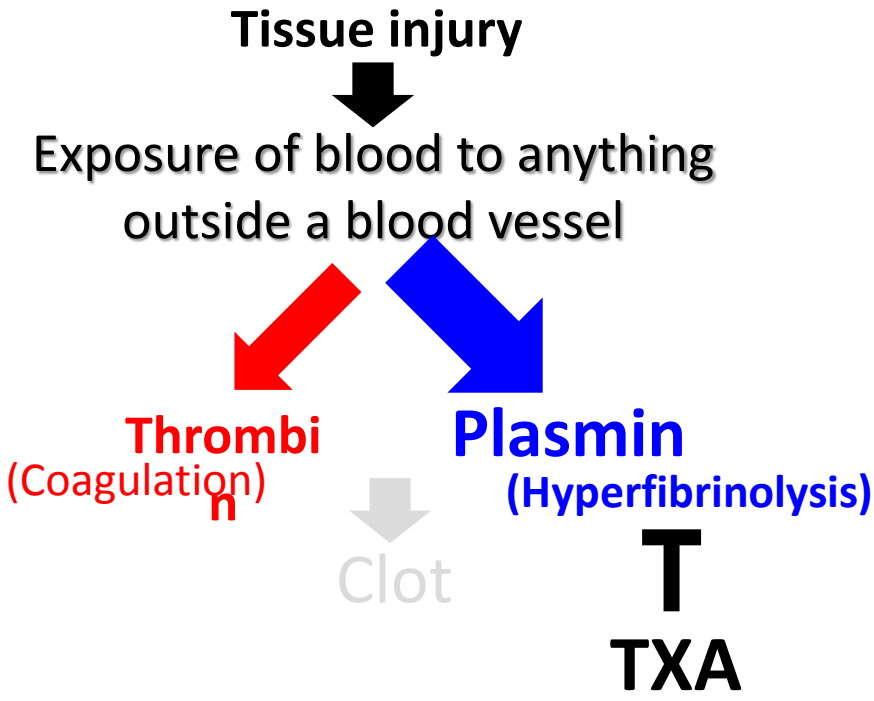


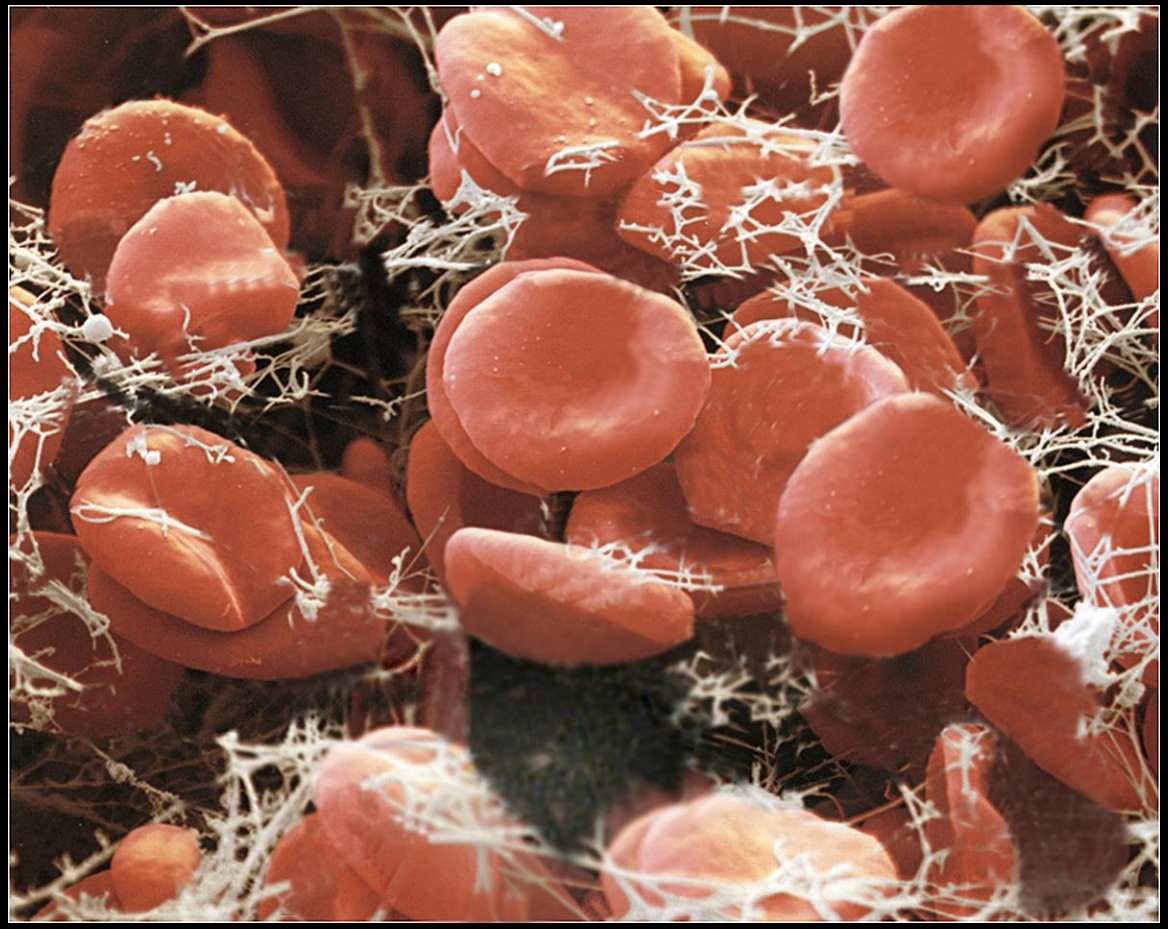
Clot



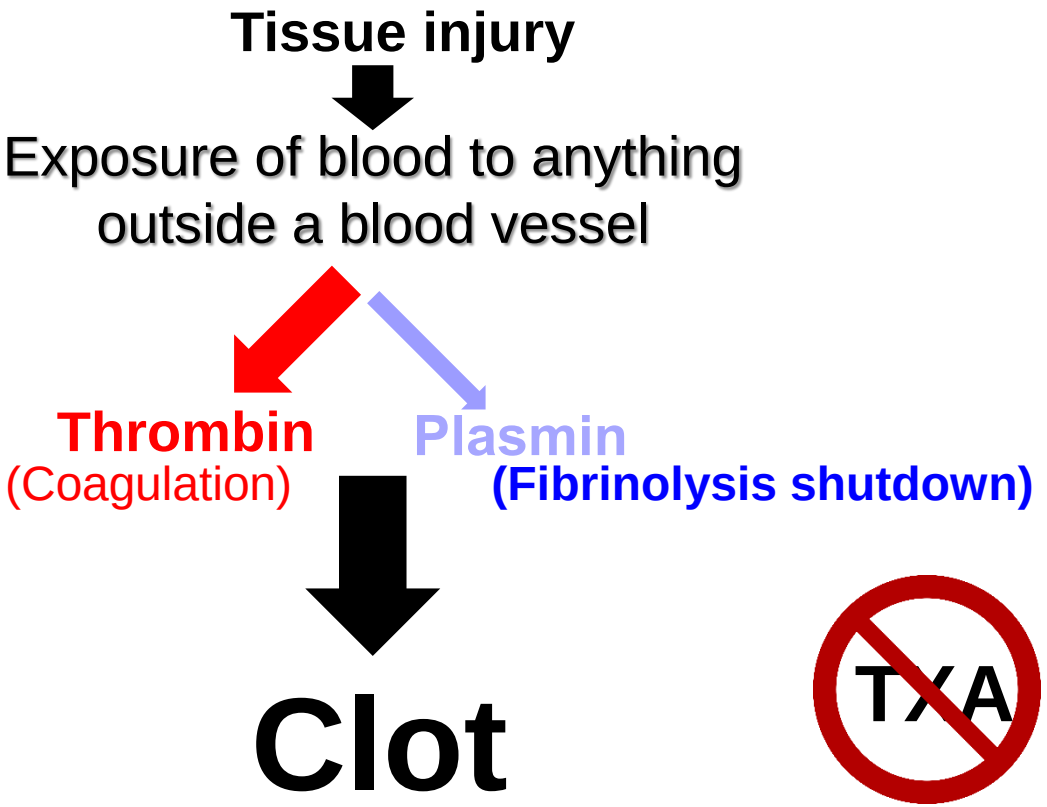
Coagulopathy in Trauma







Hypercoagulability in Trauma Patients



REVIEW ARTICLE

Postinjury fibrinolysis shutdown: Rationale for selective tranexamic acid

Ernest E. Moore, MD, Hunter B. Moore, MD, Eduardo Gonzalez, MD, Michael P. Chapman, MD, Kirk C. Hansen, PhD, Angela Sauaia, MD, PhD, Christopher C. Silliman, MD, PhD, *and* **Anirban Banerjee, PhD,** *Denver, Colorado*

Postinjury systemic fibrinolysis has been recognized as a biologic process for more than 200 years, but the mechanisms of regulation and their clinical implications remain unclear. In 1794, John Hunter from Edinburgh observed that the last blood exiting from fatal gunshot wounds did not clot.[1] Albert Dastre from Paris proposed the term *fibrinolysis* in 1893 (*Archives de Physiologie*) based on experimental work demonstrating digestion of fibrin. In 1927, interest in fibrinolysis was piqued by a Russian report that victims of sudden death were preferred as blood donors because their blood "reliquified" within a few hours, permitting transfusion without an anticoagulant. Scientific knowledge of physiologic fibrinolysis improved rapidly during the ensuing two decades and, by the 1950s, the plasminogen (PLG)-plasmin-antiplasmin system

PLG activator (tPA) became the fibrinolytic of choice. On the other side, with the widespread availability of TEG, excessive fibrinolysis was incriminated in post–coronary artery bypass grafting mediastinal bleeding presumably because of contact activation. But the enthusiasm for antifibrinolytics was dampened after the BART (Blood Conservation using Antifibrinolytics in a Randomized Trial) indicated increased renal failure, myocardial infarction, and mortality after coronary artery bypass grafting when a plasmin inhibitor (aprotinin) was given.[6]

ENTHUSIASM FOR TRANEXAMIC ACID IN TRAUMA MANAGEMENT

Acknowledging the potential role of the PLG-plasmin

J Trauma Acute Care Surg 2015;78(6Suppl1):S65-9

CRASH-2

The Crash-2 collaborators. *Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial*. ***Lancet*** 2010;376(9734):23-32.

- A very large pragmatic international randomized placebo-controlled trial of the effects of the early administration of TXA on 28-day hospital mortality, vascular events, and transfusions in adult trauma patients*
- The trial enrolled 20,211 patients with, or at risk of, significant bleeding from 274 hospitals across 40 countries.
  - 20,225 patients were screened, and 20,211 patients were randomized, leaving only 14 patients who were excluded.
- Results
  - Mortality was **1,463** (14.5%) in TXA group vs **1,613** (16.0%) in placebo group
  - Relative risk [RR], 0.91; 95% confidence interval [CI], 0.85-0.97; $p = 0.0035$).
  - All-cause mortality reduction was 1.5%
  - Number needed to treat (NNT) = 67 to save one life over 28 days.

*1 g i.v. over 10 minutes, then 1 g i.v. over 8 hours

Review Article

CRASH-2 Study of Tranexamic Acid to Treat Bleeding in Trauma Patients: A Controversy Fueled by Science and Social Media

Sophia Binz,[1] Jonathon McCollester,[2] Scott Thomas,[3] Joseph Miller,[1] Timothy Pohlman,[4] Dan Waxman,[5] Faisal Shariff,[3,6] Rebecca Tracy,[3] and Mark Walsh[3,7]

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CRASH-2 STUDY LIMITATIONS

Limitation	Comment
Meaningful finding?	.....**Only a 0.8% reduction in death**
No injury severity data	.....Unable to compare cohorts
No assessment of shock (lactate, pH, -BE)	.....Unable to compare cohorts
Number of hypotensive patients small (31%) ..	.....Majority of patients were not bleeding
No tests of fibrinolysis or other coagulopathy	.....Fibrinolysis in U.S. Trauma Centers ≤ 5%
Majority of deaths not due to bleeding	.....TBI most common cause of death
TXA did not reduce blood transfusions	.....Only 50% of TXA group got blood
Patient follow-up reported as 100%	.....Difficult to believe
No adverse outcomes reported	.....Really?

CRASH-2 STUDY LIMITATIONS

TXA INFUSION (Time from Injury)	**DEATHS**		**RR (95% CI)**
	TXA	**PLACEBO**	
< 1 hr	198/3,747(5.3%)	286/3,704(7.7%)	0.68 (0.57-0.82)
1-3 hrs	147/3,037(4.8%)	184/2,996(6.1%)	0.79 (0.64-0.97)
> 3 hrs	144/3,272(4.4%)	103/3,362(3.1%)	1.44 (1.12-1.84)

Conclusion: Slight improvement in mortality if you give less than one hour after injury; slight increase in mortality if you give it 3 hrs after injury

Recommendations

- Give TXA to trauma patients with evidence of severe hemorrhagic shock (Shock Index > 1.5), who are likely to require MT, or who demonstrate fibrinolysis by TEG (LY30 > 3%)
- Infuse 1 g over 10 mins, followed by 1 g over 8 hrs.
- Only infuse TXA if < 3hrs of injury

Questions?

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