Less Epi, More Brain

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Credit to Jeff Jarvis, who graciously allowed me to steal many of his slides

Resuscitation of the out-of-hospital cardiac arrest patient is OWNED by EMS

- 79 US and international studies
  142,000 patients
- Best prognosis: witness arrest, VF/VT rhythm
- Bystander CPR doubles odds of survival
- Most powerful predictor of survival to hospital discharge is ***ROSC in the field***

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- “The battle to save victims of OHCA is won or lost at the scene.”
- “Hospital-based measures are important, but they cannot compensate for a failed out-of-hospital resuscitation.”

Evidence for Epinephrine in OHCA

Study	Year	Outcome
Holmberg M et al	2002	Increased Mortality
Stiell IG et al	2004	Increased ROSC; No Diff Survival
Ong ME et al	2007	No Diff Survival
Olasveengen TM et al	2009	Increased ROSC; No Diff Survival
Jacobs IG et al	2011	Increased ROSC; No Diff Survival
Hagihara A et al	2012	Increased ROSC; No Diff Survival
Nakahara S et al	2013	No Diff Neuro Intact Survival
Sanghavi P et al	2015	Increased Mortality
PARAMEDIC-2	2018	Increased ROSC; Increased Severe Neuro Disabilities in Survivors

R.E.B.E.L.em

ROSC ≠ Neuro Intact Survival

https://rebelem.com/rebel-cast-ep56-paramedic-2-time-to-abandon-epinephrine-in-ohca/

- Crile, Doley 1906
- An Experimental Research into the Resuscitation of Dogs Killed by Anesthetics and Asphyxia

Hagihara A, Hasegawa M, Abe T, Nagata T, Wakata Y, Miyazaki S. Prehospital epinephrine use and survival among patients with out-of-hospital cardiac arrest. JAMA. 2012 Mar 21; 307: 1161-1168.

Outcome	Epinephrine	No Epinephrine
ROSC propensity match	2,446/13,401 (**18.3%**)	1,400/13,401 (**10.5%**)
Functional Survival	173/13,401 (**1.3%**)	413/13,401 (**3.1%**)

aOR (95%CI)	ROSC	1 month Survival	Functional Survival
Epi (vs no epi)	**2.36** (2.22-2.50)	0.46 (0.42-0.51)	**0.31** (0.26-0.36)

- Higher ROSC
- Lower 1 month survival and functional survival

Hagihara A, Hasegawa M, Abe T, Nagata T, Wakata Y, Miyazaki S. Prehospital epinephrine use and survival among patients with out-of-hospital cardiac arrest. JAMA. 2012 Mar 21; 307: 1161-1168.

6 RCTs of Standard Dose Epinephrine vs High Dose Epinephrine:

Outcome	aOR (95% CI)
ROSC	0.85 (0.75 – 0.97)
Survival to Hospital Admission	0.87 (0.76 – 1.00)
Survival to Hospital Discharge	1.04 (0.76 – 1.42)
Functional Survival	1.20 (0.74 – 1.96)

Lin S, Callaway CW, Shah PS et al. Adrenaline for out-of-hospital cardiac arrest resuscitation: a systematic review and meta-analysis of randomized controlled trials. Resuscitation. 2014 Jun; 85: 732-740.

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PARAMEDIC-2 Trial

- "In adult patients (>16) with all-cause, all-rhythm OOCHA, not caused by conditions known to respond to epinephrine (anaphylaxis and asthma), does the use of epinephrine 1 mg IV every 3-5 minutes compared with placebo improve 30 day survival?"
- Double-blind randomized control trial, **8000 patients**
- Placebo controlled, similar to our EMS system, all rhythms… *but time to 1st epi 21 minutes, and questionable CPR quality*
- Excluded: pregnant, epi PTA, anaphylaxis/asthma

Perkins GD, Ji C, Deakin CD et al. A Randomized Trial of Epinephrine in Out-of-Hospital Cardiac Arrest. N Engl J Med. 2018 Jul 18;

Trial drug pack:

Either:
1) 1 mg epi in 3 ml syringe X 10
2) 3 ml 0.9% NS syringe X 10

1:1 RANDOMIZATION BY PATIENT

Outcome	Epi	Placebo	aOR (95%CI)
30 day survival	**3.2%**	**2.4%**	**1.47 (1.09-1.97)**
Survival to Hospital Admission	23.8%	8.0%	3.83 (3.30-4.43)
Survival to Hospital Discharge	3.2%	2.3%	1.48 (1.10-2.00)
Good Neuro Status at 90 days	2.1%	1.6%	1.39 (0.97-2.01)

Perkins GD, Ji C, Deakin CD et al. A Randomized Trial of Epinephrine in Out-of-Hospital Cardiac Arrest. N Engl J Med. 2018 Jul 18;

PARAMEDIC-2 Trial

NNT (30 day mortality)

Epinephrine: 112

Bystander CPR: 15
Early recognition: 11
Early defibrillation: 5

NNH (neuro devastation among survivors)

Epinephrine: 8

- Odds of there being at least 1% better survival with epi: 37%
- Odds of there being at least 2% better survival with epi: 0.2%
- Odds of there being at least 1% better functional survival at dc with epi: 1.9%
- Odds of there being at least 2% better functional survival at dc with epi: 0%

PARAMEDIC-2 Trial

31% of patients were neuro devastated with epi

18% of patients were neuro devastated with placebo

OHCA **Epi** administration resulted in a **higher rate of 30-day survival**, but bad neuro outcomes.

MORE survivors in the **Epinephrine** group

had **SEVERE NEURO** Impairment

Why Epinephrine?

Alpha Effects

- Increased systemic vascular resistance
- Increased aortic diastolic pressure
- Increased coronary perfusion pressure
- Increased cerebral perfusion pressure

Why **Not** Epinephrine?

Beta Effects

- Increases oxygen demand
- Produces tachydysrhythmias
- **Decreases microcirculatory flow**
- **Increases cerebral vasoconstriction**

Epi drip in Cardiac Arrest

- 1 mg loading dose, 100 mcg/min in PEA/asystole
- No loading dose, 50 mcg/min in VF/VT

Low Dose Epinephrine Infusion

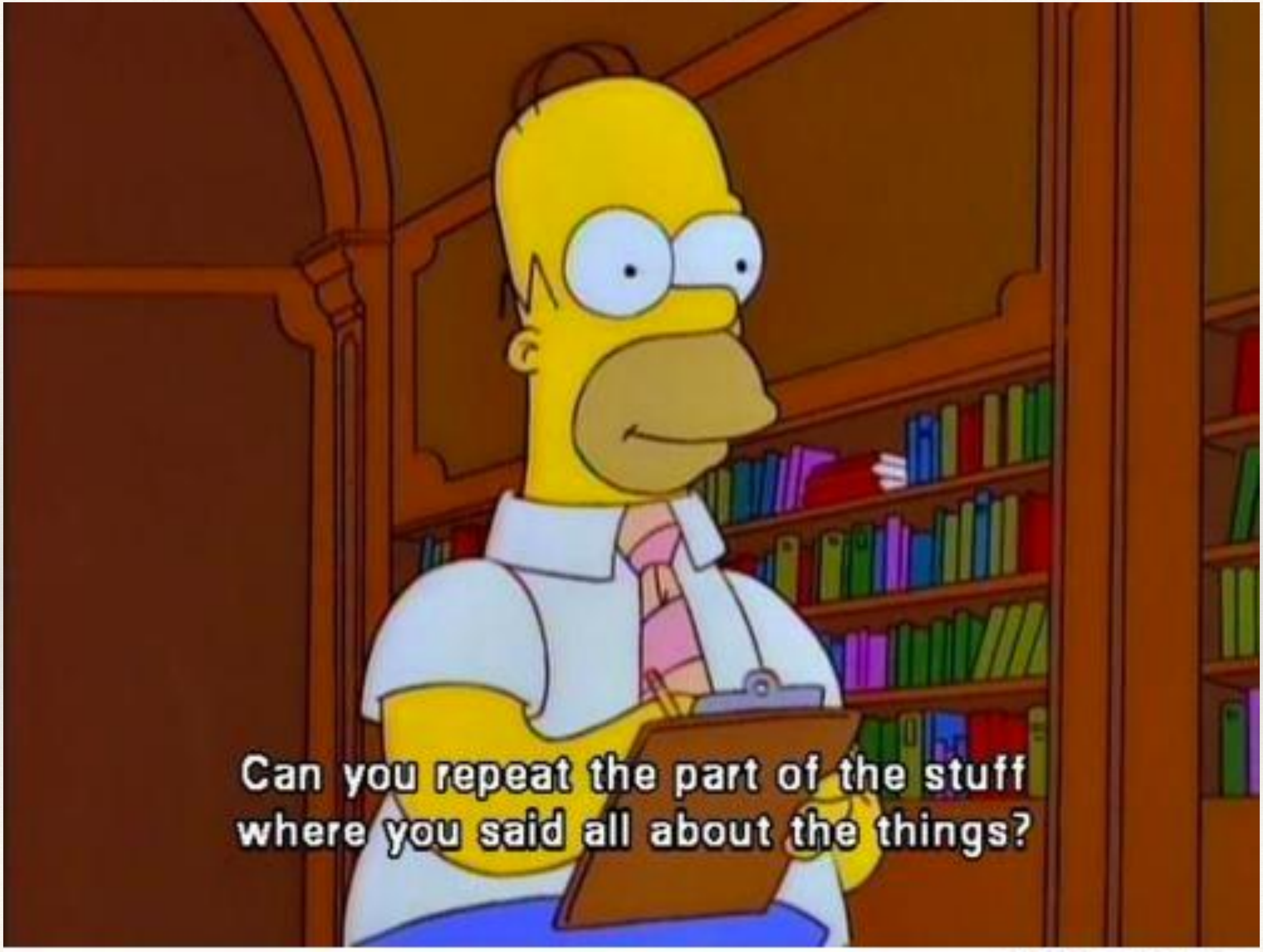
- Mixing the medication
  - 4 mg 1:10,000 Epi in 250 mL (16 mcg/mL)
- Steps to mixing:
  - Inject four (4) 10 mL pre-filled epi syringes into the bag for a total of 290 mL
  - Lightly mix the bag (do not shake)

Epi in ROSC

- Automatically half dose with ROSC
- Switch to levophed as soon as possible

Next steps

- Join us
- Collect data
- Change the world


Can you repeat the part of the stuff
where you said all about the things?