Sarah Bohn
Block 5 CAT

Clinical Question: IS EGDT for pts with Sepsis really all that and a bag of chips? Or are the chips extra?
Citation: The PROCESS Investigators. A Randomized Trial of **Pro**tocol-BASED **C**are for **E**arly **S**eptic **S**hock. NEJM 204 May; 370(18):1683-1693.
Introduction: EGDT was a single-center study with patients presenting to ED in Severe sepsis and Septic shock in 2001 by Rivers, et al. which included early fluids, CVP monitoring, use of pressors and blood as you recall. The PROCESS trial evaluated if all parts of the EGDT "protocol were necessary."
Methods: in 31 ED in US, 1341 patients in septic shock were randomly assigned to one of 3 groups

1. Protocol based EGDT (like original paper in 2001) 439 pts
2. Protocol based standard therapy (didn't require CVP, inotropes, blood transfusions) 446 pts
3. Usual care (doctor picks tx with no prompts) 456 pts

Primary endpoint: 60 day in hospital mortality
Secondary endpoints: long term mortality and need for organ support
DESIGN: Randomized 1:1:1 ratio
STUDY POPULATION:

1. Sites were academic hospitals with >40K ED visits/year
2. Sites had to use serum lactate and to adhere to Surviving Sepsis Campaign guidelines for non-resuscitation portions of care, have no routine resusc protocols, not routinely use continuous $SCVO_2$ monitors.
3. Pts: at least 18 yo sepsis suspected, met at least 2 SIRS criteria, had refractory hypotension SBP <90 despite fluids (20 ml/kg, initially then changed to 1L or more) or needed pressors to keep 90) or lactate 4 mmol/L, enrolled within 2 hours of recognition of shock and within 12 hours after arrival – no measured baseline differences across the 3 groups.
4. Average age 60-62, 52-58% male, 14-16% from nursing home

STUDY intervention:

1. EGDT: mimics Rivers, et al 2001 but didn't require A-line
2. Protocol based std therapy: specified amount and timing of resusc fluid, thresholds for pressor use, adequate peripheral access, pRBCs only if Hgb <7.5, prompts for specific goals q 2 hours in first 6 hours.
3. Usual care: beside providers directed all care, no prompts

Results:

- **60 day mortality** was 92 (21%), 81 (18.2%), 86 (18.9%) in the groups respectively (as listed in intervention section) p Value 0.83 **= NO DIFFERENCE!**
- **90 day mortality** was 129 (31.9%), 28 (30.8%), 139 (33.7%) P value 0.66 **= NO DIFFERENCE**
- **1 year mortality was about 40 % across the board** (actual number not given in paper, maybe in Supplemental Appendix) **READ AGAIN: NO DIFFERENCE**
- AKI with need for RRT was ***higher*** in group 2 (6%) vs 3.1% in group 1 and 2.8% in group 3
- Among the groups -- Similar discharge status profiles, LOS, LOS-ICU, duration of organ support

Discussion:
There's no doubt that the 2001 EGDT paper changed the way we practice, and the write up of this trial doesn't account for the actual doings of the "protocol based standard therapy" and "usual care" groups in the primary paper – it may be in the supplemental appendix, but after reading 10 pages, how many are really going to go for the supplement? Having listened to EMRAP, I do realize that at least the fluid resusc volumes were similar across the 3 groups (4.5-5 liters), but this is not accounted for in the primary paper as noted. Other changes in practice since the EGDT paper include changes after the resuscitation – protecting the lungs with lower volumes on vents, tighter glucose control, and lower HGb thresholds – and are difficult to ascertain those effects on the outcomes in this paper. The PROCESS trial poses the thought that need for CVP/SVO_2 monitoring and giving

blood for hgb < 10 rather than 7.5 does not improve mortality outcomes, at least when comparing EGDT care to standardized protocolized care without the extra monitoring. I'm not as convinced that it says anything about "usual care" as I've already argued the "usual care" has changed as a result of the 2001 EGDT paper and other changes in critical care. Should this hold up, it's likely a good thing, because it's not as feasible to do across the board *outside* the academic centers who, in my experience, don't all have CVP monitors and SvO_2 monitors in their EDs – validating the care that I see and have seen done without the extra bells and whistles of expensive machines and extra blood, and unnecessary central lines which are not without risk.