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Vincent J-L et al. Critical Care: Advances and future perspectives. Lancet. 2010;376:1354-61. A very broad overview of the history of evidence-based Critical Care. The authors observe that results of most reported therapeutic RCTs in Critical Care Medicine have been negative – and some even harmed patients. Paradoxically, the main contribution of RCTs in Critical Care has been to show that overtreatment is harmful (e.g., high tidal volumes, excessive blood transfusions, oversedation, targeting supranormal oxygen delivery, etc.). Additionally, the authors point out inconsistency in clinical implementation of therapies supported by RCTs, compiling a table of positive RCTs that have failed to become part of bedside Critical Care. The example they provide regarding drotrecogin alpha is very enlightening, especially for those that didn't follow that story as it was unfolding. This review is well worth reading. It's uncommon that an editorial is published with this breath and depth of perspective.

Lee, et al. Probiotic prophylaxis of VAP. Am J Respir Crit Care medicine. 2010;182:1058-64. (Also - please see editorial on pages 993-4). This was a well-performed randomized controlled trial (RCT) that included 146 patients on mechanical ventilation, and showed that patients treated with the probiotic bacteria - *Lactobacillus rhamnosus* – instilled into their oropharynx and down their nasogastric tubes – had a significant reduction in the rate of VAP (19% vs. 40% $p<0.007$) compared to placebo. The theory behind therapeutic use of probiotic bacteria is that they compete with, and mitigate overgrowth of the upper respiratory tract by pathogenic bacteria. This study had several minor design flaws (e.g., misuse of intention-to-treat), and shared a problem that all such studies have – difficulty in firmly establishing the diagnosis of VAP. However, these shortcomings did not seem critical enough to overturn the author's conclusions. We feel that in general (and particularly in the area of VAP), RCTs that originally show positive results are often disproven by subsequent studies. Therefore, we wouldn't jump on this bandwagon yet with both feet. But the theory behind probiotics seems compelling and we await further studies with interest.

Guo Y-L, et al. Accuracy of BAL galactomannin in diagnosing invasive aspergillosis. Chest. 2010;138:817-24. This paper was of great interest because we often have difficulty diagnosing invasive pulmonary aspergillosis, especially in the bone marrow transplantation unit. Unfortunately, this paper was disappointing. The authors made a critical error in their study design. The "gold standard" they

used to calculate the operating characteristics did not allow patients to be firmly categorized as to whether or not they actually had invasive aspergillosis. This approach included patients with "possible" invasive aspergillosis in the category of "no disease". This is nonsensical. The concept of sensitivity is to describe how good a test is at ruling a disease out. Therefore the sensitivity of a test can't be calculated unless your gold standard firmly rules the disease out. This basic error propagated through much of the advanced statistics the authors provide (for instance the ROC curves, which are partially derived from sensitivity calculations). We used to call this technique "putting lipstick on a pig". No useful conclusions can be drawn from this study.

Benson AB, Austin GL et al, Transfusion-related acute lung injury in ICU patients admitted with gastrointestinal bleeding. Intensive Care Med. 2010 Oct;36(10):1710-7. Epub 2010 Jul 24. This paper was a retrospective cohort study that found the incidence of transfusion-related acute lung injury (TRALI) was 15% among 150 ICU patients who received transfusions for GI bleeds. Fresh frozen plasma (FFP), rather than packed red blood cells, were most likely to be temporally-related to TRALI onset. In patients with end stage liver disease (ESLD), each unit of FFP increased the risk of TRALI by 11%. Although we are unlikely to drastically change our approach to transfusion therapy based on this small retrospective study, we agree with the author's conclusion that we should carefully consider the risk of each unit of FFP we infuse – this may be another case in Critical Care of "less is better". Strangely, these authors found TRALI to occur almost exclusively in patients with ESLD (21 of 22 cases). This is not consistent with other trials, and doesn't have clear biological plausibility, since TRALI is thought to be due to the presence of anti-granulocyte antibodies, or granulocyte-activating cytokines in the *donor* plasma.

Summers, DM et al. Analysis of factors that affect outcome after transplantation of kidneys donated after cardiac death in the U.K.: a cohort study. Lancet. 2010;376:1303-11. This paper shows that organs harvested in patients who undergo controlled cardiac death are equivalent to organs harvested in patients who are declared brain dead (with essentially nil warm ischemic time). Briefly, controlled cardiac death may be considered in a patient on life support who is an organ donor, in whom an independent decision has been made to withdraw life support (based on the patient's wishes or best interests). Support can then be withdrawn in the OR, with the harvest team hovering to immediately

remove organs at the moment of death. The intensivist will usually be asked to determine this moment – typically after 5-minutes of asystole. This is a fascinating topic that focuses on a question that is surprisingly tough to answer – how can we define the exact moment of death? A significant number of physicians and ethicists feel that controlled cardiac death is unethical. A very good editorial in the NEJM discusses this: ***Truog RD***, ***Miller FG***. *The dead donor rule and organ transplantation.* ***N Engl J Med.*** *2008 Aug 14;359(7):674-5.*

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