

# Patient Safety Tip of the Week

June 6, 2017

## NYS Mandate for Sepsis Protocol Works

In 2013 the New York State Department of Health mandated that hospitals begin using protocols to help with early identification and treatment of sepsis. Hospitals began implementing these protocols in 2014 and outcomes related to this project were reported in 2 recent publications ([NYSDOH 2017](#), [Seymour 2017](#)). By the third quarter of 2016, 84.7% of adult patients and 85.3% of pediatric patients with severe sepsis or septic shock were treated using protocols ([NYSDOH 2017](#)). Adult in-hospital mortality fell from 30.2% in early 2014 to 25.4% by late 2016. Pediatric mortality rates were more variable without clearcut trend. After adjusting for patient factors, the NYSDOH analysis of the data showed that the odds of dying were 21% less for adult patients who received protocol-driven treatments compared to patients who do not receive protocol-driven treatments. The time frame for management was also critical. After adjustment, the NYSDOH analysis showed that the odds of dying were 27% less for adult patients who received all of the recommended treatments within three hours compared to patients who did not receive all of the recommended treatments.

Seymour et al. dove deeper into the data in an article published in the New England Journal of Medicine ([Seymour 2017](#)). Protocols were required to include a 3-hour bundle consisting of receipt of the following care within 3 hours:

- obtaining of a blood culture before the administration of antibiotics
- measurement of the serum lactate level
- administration of broad-spectrum antibiotics

Protocols were also required to include a 6-hour bundle, consisting of:

- administration of a bolus of 30 ml of intravenous fluids per kilogram of body weight in patients with hypotension or a serum lactate level of 4.0 mmol or more per liter
- initiation of vasopressors for refractory hypotension
- remeasurement of the serum lactate level within 6 hours after the initiation of the protocol

Individual facilities could further customize the protocols as they wished.

Of over 49,000 eligible patients in the emergency department at 149 hospitals, 82.5% had the 3-hour bundle completed within 3 hours, with a median time to the completion of the

3-hour bundle of 1.30 hours. Median time to the administration of broad-spectrum antibiotics was 0.95 hours and median time to the completion of the initial bolus of intravenous fluids was 2.56 hours.

Supporting the importance of early treatment, they found that **each hour of time to the completion of the 3-hour bundle was associated with higher mortality** (odds ratio of death until completion of 3-hour bundle, **1.04 per hour**). Patients who had the bundle completed during hours 3 through 12 had 14% higher odds of dying in the hospital than those whose bundle was completed by 3 hours. Those same odds (1.04 per hour) were seen for time to administration of antibiotics and in-hospital mortality and patients who received first dose of antibiotics during hours 3 through 12 had 14% higher odds of dying in the hospital than those receiving antibiotics by 3 hours. However, the researchers found no association between the timing of the fluid bolus and mortality.

But the authors caution against concluding that early administration of a fluid bolus is not important. Early fluid resuscitation is likely important. In fact, another recent study on pediatric sepsis patients noted that the nature of fluid resuscitation in sepsis may be important. The Surviving Sepsis Campaign guidelines updated in 2016 ([Rhodes 2017](#)) did not consider the evidence strong enough to recommend balanced fluids over unbalanced fluids (“balanced” fluids are crystalloids such as lactated ringers, while chloride-rich fluids such as normal saline are not balanced). But Emrath and colleagues ([Emrath 2017](#)) recently compared outcomes in children with pediatric severe sepsis receiving balanced fluids for resuscitation in the first 24 and 72 hours of treatment to those receiving unbalanced fluids. After propensity matching, they found the 72-hour balanced fluids group had lower mortality (12.5% vs 15.9%), lower prevalence of acute kidney injury (16.0% vs 19.2%), and fewer vasoactive infusion days (3.0 vs 3.3 days) compared with the unbalanced fluids group.

Overall, the New York State experience re-emphasizes the importance of early recognition and treatment of sepsis in reducing mortality. We have one additional comment on the New York State studies. They used the Sepsis-2 consensus criteria for diagnosis. Those include use of the SIRS criteria in making a diagnosis of sepsis. We’ve done numerous columns on the pitfalls of the SIRS criteria and have praised the newer criteria for sepsis that do not use the SIRS criteria (see our What’s New in the Patient Safety World columns for March 2016 “[Finally...A More Rationale Definition for Sepsis](#)” and February 2017 “[Yes, the New Sepsis Criteria Fit the Bill](#)”). We doubt, however, that the key conclusions reached in the NYS studies would be altered if the newer Sepsis-3 criteria ([Singer 2016](#)) had been used.

In a “Perspective” accompanying the Seymour article, Hershey and Kahn ([Hershey 2017](#)) note that, even though 82.5% of hospitals in the New York State experience did complete the 3-hour bundle within 3 hours, there was still considerable variation across hospitals. There are several potential reasons.

One possible reason may relate to how busy the emergency departments are. In a study just presented in abstract form ([Peltan 2017](#)), researchers found that patients received

antibiotics within three hours in 83 percent of cases in uncrowded ERs, but only 72 percent of the time when the ER was crowded (exceeded the ERs' licensed beds).

The New York State studies reported only the relationship of mortality to the timing of the first dose of antibiotics. But subsequent administration of antibiotics may also be important. Another recent study ([Leisman 2017](#)) found that **major second antibiotic dose delays** were common, especially for patients given shorter half-life pharmacotherapies and who boarded in the emergency department. They also observed an **association between major second dose delay and increased mortality, length of stay, and mechanical ventilation requirement**. In fact, in their multivariable analysis, major delay was associated with a **61% increased odds of hospital mortality**. Interestingly, they found that major delays in second doses were paradoxically more frequent for patients receiving compliant initial care. So the moral of this study is that we can't pat ourselves on the back when we meet the first 3 hours goals.

Those second dose delays should not be surprising. In our January 29, 2013 Patient Safety Tip of the Week "[A Flurry of Activity on Handoffs](#)" we noted that back in the 1990's we realized that patients with community-acquired pneumonia at some renowned organizations were not getting their first dose of antibiotics for up to 18 hours. That, of course, was related to bottlenecks in moving patients from the ED to the floor and problems with handoffs (relating to both information transfer and transfer of responsibility for managing the patients). Fortunately, we had performance improvement projects that focused on ensuring timely administration of the antibiotics regardless of physical location of the patient. But we likely still see ambiguities of coordination and responsibility that occur in between-unit transfers that need to be resolved in the handoff. The finding in the Leisman study that delays in a second antibiotic dose were paradoxically more frequent in those patients who had received a first antibiotic dose in a timely fashion suggests problems in that coordination of care.

Some of the nuances of CPOE and standardized medication administration times may also contribute to such delays in antibiotic administration once the patient reaches the inpatient unit. For example, some facilities consider an order for "drug X q6hours" will be given at the facility's standard times of 6AM, 12PM, 6PM, and 12AM. If the patient arrives on that inpatient unit at 12:01 PM, he/she may not get that next dose until 6PM even when the intent of the ordering physician was for earlier administration of the next dose.

Given the magnitude of the increase in in-hospital mortality (61%) seen with major delays in second dose of antibiotics in the Leisman study we would wholeheartedly endorse adding the timing of the second antibiotic dose as a quality parameter to be measured in patients with sepsis.

#### **Our other columns on sepsis:**

- March 15, 2011 "[Early Warnings for Sepsis](#)"

- April 1, 2014 “[Expensive Aspects of Sepsis Protocol Debunked](#)”
- September 8, 2015 “[TREWScore for Early Recognition of Sepsis](#)”
- October 2015 “[Even Earlier Recognition of Severe Sepsis](#)”
- February 2, 2016 “[Success Against Sepsis](#)”
- March 2016 “[Finally...A More Rationale Definition for Sepsis](#)”
- February 2017 “[Yes, the New Sepsis Criteria Fit the Bill](#)”

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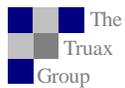
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