

Emergency Department Sepsis Protocol does not Impact Time to Antibiotics

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Abstract: *Background:* Early goal directed therapy (EGDT) can reduce mortality in an Intensive Care Unit (ICU) population with severe sepsis. It is not clear whether EGDT can be effectively implemented in an Emergency Department (ED) with existing resources to achieve the same goals.

Objectives: To assess the impact of EGDT in our ED with existing resources on time to antibiotics (ABX) and patient outcomes.

Methods: We performed a before and after study of the effects of the EGDT protocol on patients over age 21 with severe sepsis admitted to the ICU. Time to ABX was the primary outcome, mortality and other care processes were secondary. Descriptive statistics, Fisher's exact chi-square, and Wilcoxon rank sum tests compared time periods. Multivariate analyses with logistic and Cox proportional hazard regression models were performed.

Results: 192 cases: 91 before and 101 after protocol. Groups were similar in demographics, co-morbidities, severity scores, and overall mortality of 17.7%. Patients with higher Mortality in ED scores (MEDS) received ABX sooner than patients with lower MEDS after adjusting for time period. There was no difference in time to ABX between time periods after adjusting for disease severity (Hazard Ratio: 0.88, 95% CI: 0.65-1.18; OR: 0.88, 95% CI: 0.49-1.57).

Conclusion: Our EGDT protocol did not change management, time to ABX, or mortality of septic patients admitted to the ICU, when relying on existing resources. Further study is needed to evaluate barriers to EGDT and feasibility of translating resource intensive protocols to the bedside in routine ED care.

Keywords: Sepsis, critical care, drug delivery.

INTRODUCTION

Severe sepsis is a devastating disease, with an estimated 28% in-hospital mortality [1]. Sepsis may result in 215,000 annual deaths and cost of \$16.7 billion nationwide [1]. In 2001, Rivers demonstrated that employing Early Goal Directed Therapy (EGDT), an aggressive strategy aimed to optimize patient hemodynamics, resulted in a 16% reduction in 28-day mortality when compared with standard care in an Intensive Care Unit (ICU) population [2]. This strategy was time and resource intensive, requiring placement of central venous catheters, invasive blood pressure monitoring, and dedicated physician and nurse teams allocated to the singular care of these patients for six hours. It remained to be seen whether sepsis protocols could be effectively implemented in an Emergency Department (ED) with existing resources to achieve the same goals.

The objective of this study was to determine whether implementation of EGDT with existing resources would result in decreased time to antibiotics and improved patient outcomes. Collaborative projects between ED and critical care departments can implement many elements of EGDT [3-5]. A two year implementation of the sepsis bundle increased adherence from zero to 51.2% and improved mortality from 39.5% to 20.8% [6].

We modelled our protocol on previous efforts to improve time to drug therapy for patients with critical illnesses, such as acute myocardial infarction [7-9]. We used time to administration of antibiotics as the primary outcome measure as each hour of delay in antibiotic administration during the first six hours of hypotension in septic patients has been associated with a 7.6% increase in mortality (range 3.6%-9.9%) [10]. Materials and Methods

Study Design

We performed a before and after study of the effects of EGDT protocol implementation on the treatment of patients

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with severe sepsis treated in the ED and admitted to the ICU. Our project was approved by the hospital Institutional Review Board.

Study Setting and Population

This study was performed in an urban, level one, academic ED with 128,000 annual patients. We care for a largely low-income population with high rates of homelessness, substance abuse and HIV/AIDS. At any time, there are 6-12 residents, 1-4 attending physicians and 12-18 nurses in the ED which is similar to other large academic centers. There is a dedicated ED staff pharmacist available for 10-14 hours a day to review orders and assist in rapidly delivering antibiotics. There is a focused team at all times in the ED dedicated to responding to critical care patients made up of two emergency medicine residents, two nurses and 1 attending physician. This team is triggered by the triage nurse and is not specific to septic patients, but is designed to respond rapidly to any critically ill patient, for example, patients requiring emergent intubation, blood products, trauma evaluation, etc. Most patients with sepsis who are stable at the time of triage are not cared for by this specialized team but are cared for in the general ED.

Adult patients (older than 21 years) admitted to the ICU with two or more systemic inflammatory response syndrome criteria were included: temperature less than 36°C (96.8°F) or greater than 38°C (100.4°F), heart rate greater than 90 bpm, respiratory rate greater than 20 or PaCO₂ less than 32 mm Hg, white blood count greater than 12,000/μL or less than 4,000/μL or greater than 10% bands, systolic blood pressure less than 90 mm Hg systolic, and lactate greater than 4 mmol/L. Patients who died in the ED or received intravenous (IV) antibiotics prior to arrival were excluded. Patients designated as comfort care only were excluded.

The EGDT protocol was implemented during January 2006. Septic patients in the ED who were admitted to the ICU between July 1, 2005 and December 31, 2005, constituted the before group and those admitted between February 1, 2006 and July 31, 2006 constituted the after group.

EGDT Protocol

The EGDT protocol was derived from evidence-based recommendations [11]. Our sepsis bundle was created in collaboration with members of our infectious disease, pharmacy, ICU and ED. It provided guidelines for antibiotic choices for presumed and empiric sources, encouraged early intubation with low tidal volumes, aggressive fluid resuscitation and reviewed indications for vasopressors and transfusion.

All laboratory, imaging and medications require computer orders in our institution. We created a computerized order set designed to help the clinician order appropriate laboratory, imaging and medications in accordance with the sepsis guidelines. We also created web-based resources and pocket cards for staff. The guidelines, computer order sets and pocket cards were introduced to nursing through in-services and to residents and faculty through three hours of case-based lectures and presentations. (Appendices: 1 Order Set, 2 Adult Antibiotics, 3 ED Pocket Card). The staff re-

ceived reminders about the guidelines through email, brief discussions before and after shifts, and during conference time. Due to lack of staff resources, we did not perform on-going case review or monitoring of adherence to the guidelines.

Study Protocol

Trained research assistants (RAs) screened charts of all ED patients 22 years of age or older who were admitted to the ICU with sepsis. Medical charts were abstracted onto structured data sheets. Six charts were abstracted three times by the RAs and the investigators and standard data abstraction rules were developed. Each chart was abstracted independently by two RAs and reviewed by the investigators; agreement among the multiple data abstractions was not estimated. It was not possible to blind the data abstractors to the study group, as many data points were time and date dependent.

Measurements

The main outcome measure was time to administration of antibiotics. We also examined the effect of the protocol on processes of care included in the sepsis bundle [11].

Data Analysis

Descriptive statistics (median, interquartile range) were used for age, severity scores, and length of stay (LOS). We used Fisher's exact chi-square test for categorical variables and Wilcoxon rank sum test for continuous variables to compare time periods. Multivariate analyses with logistic and Cox proportional hazards regression models were performed. For logistic regression, we dichotomized time to antibiotic administration as less than or equal to 2 hours and greater than 2 hours. For Cox proportional hazards analysis, we used a survival model of time to antibiotic administration with time of arrival in the ED censored at time of departure to the ICU. Variables significant at alpha = 0.20 were included in multivariate models and statistical significance was assessed at alpha=0.05 for the final analyses.

A priori sample size calculations were performed and the study was powered to detect an absolute 30% increase in antibiotic administration within two hours of arrival (50% to 80%). A sample size of 160 was considered adequate to examine the primary and secondary outcome measures with a power of 80% at an alpha level of 0.05. Data were analyzed using SAS version 9.1 (SAS Institute, Cary, NC)

RESULTS

Of the 1,607 cases admitted to the ICU during the study period, 229 had a diagnosis of sepsis. Of the 229 charts reviewed, 192 were included: 91 before and 101 after protocol (Fig. 1). Groups were similar in demographics, comorbidities and social history (Table 1).

Mortality did not change after protocol implementation (Table 2); 14.3% (n=13) died in the before group vs. 20.8% (n=21) in the after group (p=0.26) with an overall mortality of 17.7%. Both groups were critically ill, with similar hemodynamics and Glasgow Coma Scores (Table 1). The median

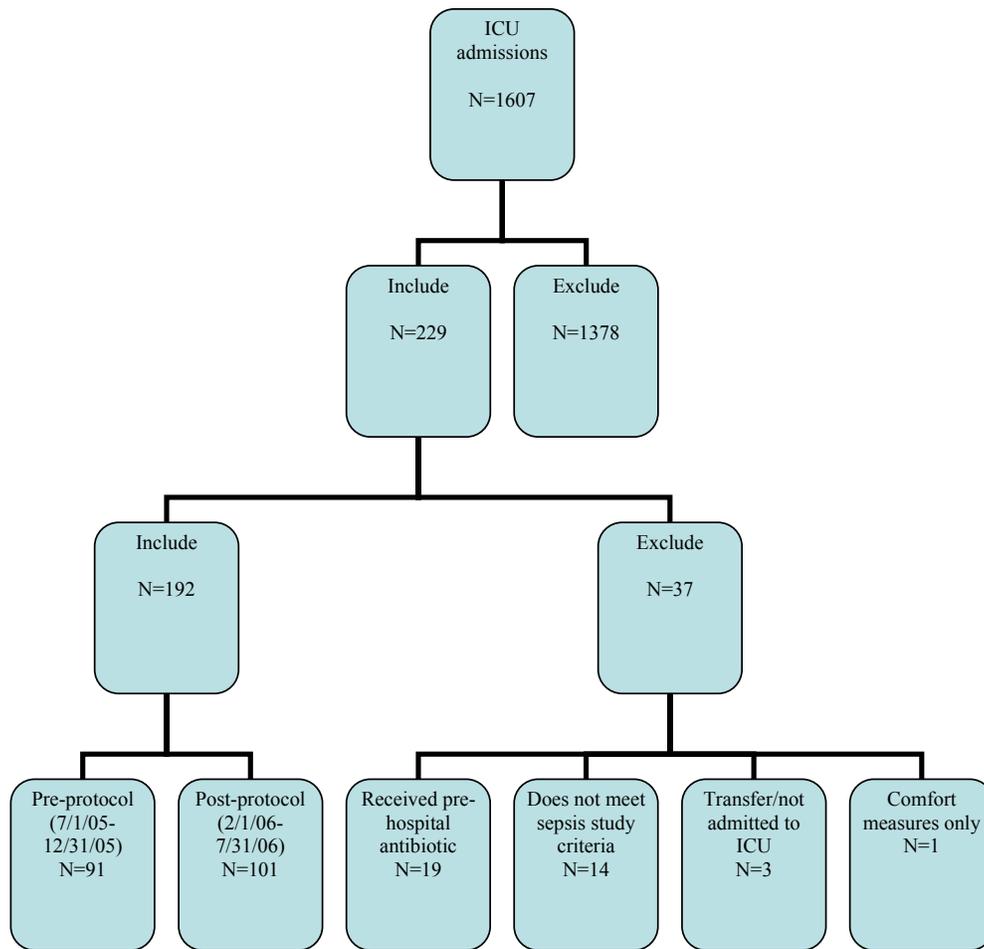


Fig. (1). Study Flow Chart.

Mortality in Emergency Department Sepsis (MEDS) score, as an indicator of illness severity, was 10 (IQR: 6-13). The median modified Rapid Emergency Medicine Score (REMS) was 8 (IQR: 6-10) on a scale of 0 to 23, with higher scores being more predictive of mortality. The median CURB-65 score was 3 (IQR: 1-3.5) on a scale of 0 to 5, with higher numbers being more predictive of mortality. Using CURB-65, 49 (25.5%) were in the low mortality group, 42 (21.9%) were in the intermediate mortality group, and 101 (52.6%) were in the high mortality group.

Our patients spent a relatively short time in the ED before going to the ICU (Table 2); the median ED length of stay (LOS) was 4.7 hours (IQR: 3.2- 6.5). The median ICU LOS was three days (IQR: 1.2-7.0). ED LOS and ICU LOS were not different before and after protocol implementation.

Management of sepsis did not change in the after group compared to the before group (Table 2). There was no difference in frequency of intubation, central line placement, volume of fluids, use of vasopressors, administration of steroids, or transfusion.

In multivariate analysis, there was no difference in time to antibiotics between the time periods (Table 3). Patients with higher mortality risk (indicated by increasing MEDS score) received antibiotics sooner than patients with lower MEDS scores, after adjusting for time period. There is a 6%

increased odds of receiving antibiotics for each increase in MEDS score, after adjusting for time period (Hazard Ratio: 1.06, 95% CI: 1.02-1.09), yet there was no statistically significant difference in time to antibiotics between the time periods after adjusting for MEDS score (Hazard Ratio: 0.88, 95% CI: 0.65-1.18). The after group was as likely as the before group to receive antibiotics within two hours, after adjusting for mortality risk (OR: 0.88, 95% CI: 0.49-1.57). In multivariate analysis, insurance, race/ethnicity, or gender did not impact time to antibiotics.

DISCUSSION

Our EGDT protocol failed to demonstrate a change in management, time to antibiotics, or mortality of septic patients admitted to the ICU. Our study demonstrates the complexity of translating the EGDT guidelines into actual clinical practice. Each of the proposed actions in the sepsis bundle may have specific barriers that should be analyzed and addressed [12-14].

It was reasonable to hypothesize that the multifaceted approach we used could improve time to treatment with antibiotics since previous approaches have been successful in achieving recommended times for delivery of other critical drugs in the ED. However, we observed that only 43.8% of our patients received antibiotics within the first two hours

Table 1. Clinical and Demographics Characteristics of Subjects

	Total (N=192) N (%)	Pre-protocol (n=91) n (%)	Post-protocol (n=101) n (%)	P-value
Age yrs (median (IQR))	61.5 (49-73.5)	62.0 (47-75)	61.0 (50-73)	0.96*
Male gender	93 (48.4%)	46 (50.6%)	47 (46.5%)	0.66**
Race				
African American/black	74 (40.0%)	38 (43.2%)	36 (37.1%)	
White, non-Hispanic	83 (44.9%)	33 (37.5%)	50 (51.6%)	
Latino/Hispanic	22 (11.9%)	15 (17.1%)	7 (7.2%)	
Other	6 (3.2%)	2 (2.3%)	4 (4.1%)	0.08**
Insurance status				
Uninsured & free care	21 (11.7%)	12 (13.3%)	9 (10.0%)	
Public insurance	138 (76.7%)	73 (81.1%)	66 (72.2%)	
Private insurance	21 (11.7%)	5 (5.6%)	16 (17.8%)	0.04**
Temperature				
<36°C (96.8 °F)	24 (12.8%)	7 (7.7%)	17 (17.5%)	
36°C- 38°C (96.8 – 100.4 °F)	74 (39.4%)	35 (38.5%)	39 (40.2%)	
> 38°C (100.4 °F)	90 (47.9%)	49 (53.9%)	41 (42.3%)	0.09**
Heart rate > 90 bpm+	171 (89.1%)	82 (90.1%)	89 (88.1%)	0.82**
BP systolic < 90 mm Hg	103 (53.7%)	51 (56.0%)	52 (51.5%)	0.56**
Respiratory rate >20 breaths/ min	127 (66.2%)	62 (68.1%)	65 (64.4%)	0.65**
WBC				
< 4,000 /μL	17 (9.0%)	11 (12.1%)	6 (6.1%)	
4,000 - 12,000 /μL	78 (41.1%)	32 (35.2%)	47 (47.5%)	
> 12,000 /μL	95 (50.0%)	48 (52.8%)	46 (46.5%)	0.16**
Lactic acid > 4 mmol/L	20 (23.5%)	8 (20.5%)	12 (26.1%)	0.61**
GCS < 11	40 (33.1%)	22 (44.0%)	18 (25.4%)	0.05**
MEDS score (median (IQR))	10.0 (6-13)	10.0 (6-13)	10.0 (6-13)	0.81*
CURB-65 > 1	143 (74.5%)	71 (78.0%)	72 (71.3%)	0.32**
nREMS (median (IQR))	8.0 (6-10)	8.0 (5-10)	8.0 (6-10)	0.46*
History of CAD	46 (25.0%)	21 (23.9%)	25 (26.0%)	0.86**
History of CHF	25 (13.7%)	13 (14.8%)	12 (12.6%)	0.83**
History of diabetes	56 (30.4%)	27 (30.7%)	29 (30.2%)	1.00**
COPD	29 (15.9%)	14 (15.9%)	15 (15.8%)	1.00**
HIV or AIDS	21 (11.5%)	11 (12.5%)	10 (10.5%)	0.82**
Cancer	31 (16.9%)	16 (18.2%)	15 (15.8%)	0.70**
Nursing home resident	57 (29.7%)	24 (26.4%)	33 (32.7%)	0.35**
Heavy alcohol use	18 (14.6%)	7 (12.1%)	11 (16.9%)	0.61**
Drug use	19 (19.2%)	11 (25.6%)	8 (14.3%)	0.08**
Tobacco use	32 (28.1%)	18 (33.3%)	14 (23.3%)	0.30**

bpm+ = beats per minute.

WBC= white blood cells.

GCS= Glasgow Coma Scale.

MEDS Score = Mortality in Emergency Department Sepsis Score.

CURB-65 = Confusion, Urea >7 mmol/l, Respiratory rate ≥30/min, low systolic(<90 mm Hg) or diastolic (≤60 mm Hg) Blood pressure), age ≥65 years.

nREMS = non Rapid Eye Movement in Sleep.

CAD = Coronary Artery Disease.

CHF = Congestive Heart Failure.

COPD = Chronic Obstructive Pulmonary Disease.

HIV = Human Immunodeficiency Virus.

AIDS = Acquired Immune Deficiency Syndrome.

*P values calculated using Wilcoxon rank sum test.

**P values calculated using chi square or Fisher's exact test.

Table 2. Comparison of Treatment and Outcomes Pre and Post Implementation of the Sepsis Protocol

	Total (N=192) N (%)	Pre-protocol (n=91) n (%)	Post-protocol (n=101) n (%)	P-value
Intubated in ED	61 (31.8%)	26 (28.6%)	35 (34.7%)	0.44**
Urine culture sent	130 (67.7%)	65 (71.4%)	65 (64.4%)	0.35**
Blood culture sent	169 (88.0%)	80 (87.9%)	89 (88.1%)	1.00**
Sputum culture sent	25 (13.0%)	13 (14.3%)	12 (11.9%)	0.67**
Central line placed	50 (26.0%)	26 (28.6%)	24 (23.8%)	0.51**
Volume of fluids administered				
< 2 L	48 (29.3%)	22 (29.0%)	26 (29.6%)	
2 – 4 L	82 (50.0%)	38 (50.0%)	44 (50.0%)	
> 4 L	34 (20.7%)	16 (21.1%)	18 (20.5%)	0.99**
Transfused red blood cells	10 (5.2%)	5 (5.5%)	5 (5.0%)	1.00**
Vasopressor administered	36 (18.8%)	22 (24.2%)	14 (13.9%)	0.09**
Antibiotics in ED				
Received no antibiotics in ED	11 (5.7%)	3 (3.3%)	8 (7.9%)	
Antibiotics ordered but not given	8 (4.2%)	3 (3.3%)	5 (5.0%)	
Antibiotics ordered and given	173 (90.1%)	85 (93.4%)	88 (87.1%)	0.32**
Received 1st dose antibiotic within 2 hours	84 (43.8%)	41 (45.1%)	43 (42.6%)	0.77**
Received 1st dose antibiotic within 6 hours	167 (87.0%)	82 (90.1%)	85 (84.2%)	0.28**
Received steroids	36 (18.8%)	19 (20.9%)	17 (16.8%)	0.58**
ED LOS, hours (median (IQR))	4.7 (3.2-6.5)	4.8 (3.2-6.4)	4.7 (3.2-6.7)	0.76*
Hospital LOS, days (median (IQR))	7.8 (4.3-14.5)	7.8 (4.2-12.8)	7.9 (4.4-17.3)	0.29*
ICU LOS, days (median (IQR))	3.0 (1.2-7.0)	2.6 (1.2-5.8)	3.6 (1.4-7.9)	0.16*
Died in hospital	34 (17.7%)	13 (14.3%)	21 (20.8%)	0.26**

ED LOS = Emergency Department Length of Stay.

ICU LOS= Intensive Care Unit Length of Stay.

*P values calculated using Wilcoxon rank sum test.

**P values calculated using chi square or Fisher's exact test.

Table 3. Multivariable Analyses of Time to Antibiotic Administration Adjusting for Protocol Time Period and Sepsis Severity

Model	Factor	Risk Ratio	95% CI	P-value
Logistic	Time period	0.88	0.49, 1.57	0.5804
	MEDS score	1.86	1.01, 3.43	0.0454
Cox PH	Time period	0.88	0.65, 1.18	0.3879
	MEDS score	1.06	1.02, 1.09	0.0010

MEDS Score= Mortality in Emergency Department Sepsis Score.

Cox PH= Cox Proportional Hazard.

only 87% of patients received antibiotics within the first six hours. Although this proportion compares favorably to other trials, it does not meet our goals. Micek found that standardized order sets resulted in a larger proportion of patients receiving initial antibiotic treatment earlier and reduced in-hospital mortality [15]. Our order sets were nearly identical in content but produced dissimilar results. This result highlights the need to examine the effectiveness of strategies to

achieve the goals of the sepsis campaign in diverse practice settings.

We found that sicker patients received antibiotics sooner in both the before and after protocol implementation periods. However, some patients received no antibiotics at all in the ED. We found 85% of antibiotics ordered but not administered in the ED required either special approval from the

infectious disease department or hand-written orders to the pharmacy. This observation suggests that the implementation of a satellite pharmacy or pre-approved antibiotic orders could reduce treatment delays.

Finally, we relied on existing departmental resources for this project. We did not have dedicated sepsis teams or specialized equipment, as have been employed elsewhere, and we relied on staff already performing their existing duties to implement EGDT [5]. Our implementation phase provided staff education similar in intensity and quality to that described in previous studies [5]. However, we did not provide similar ongoing feedback to clinicians. It is likely that having a dedicated, on-going monitoring system in place would result in better implementation [4,5]. Shapiro has reported that “substantial contribution of time and effort” went into maintaining their protocol, others have reported that dedicated study teams and monitoring systems are needed to ensure compliance [5,15].

Our observed in-hospital mortality rate for sepsis of 17.7% is lower than mortality rates published elsewhere, even after implementation of EGDT. Specifically, the lowest mortality rate reported after implementing EGDT is 18.2% and others found rates of 20-30% [2,4,5,15]. We used the same enrolment criteria as other investigators and all of our patients were critically ill and admitted to the ICU. Our median age was 61.5 years, which is younger than the mean age in other studies. Our median MEDS score was 10, which is also lower than the mean MEDS score of 11 reported by Shapiro [5]. It is possible that our sample represented a healthier cohort of sepsis patients which is reflected in our lower mortality rates, or that standard care can achieve mortality rates similar to EGDT.

Following completion of this project, we implemented changes to the ordering system based on these results. Antibiotics formerly requiring specialist approval and hand-

written orders to the pharmacy were moved to the PYXIS medication distribution machine in the ED and nurses were authorized to administer the first dose without awaiting specialist approval. Staff were informed of these results and encouraged to prioritize antibiotic delivery to patients. Residents and nurses were instructed that patients should not be

moved to the intensive care unit until antibiotics were ordered and administration had begun.

LIMITATIONS

Our study was limited by the retrospective design. This design was chosen as we did not feel we could withhold EGDT protocol from a control group. Given that we demonstrated no change in management after our protocol, and a lower than expected mortality rate, it may be appropriate to conduct a prospective randomized trial comparing EGDT with standard care.

Our patients also spent a relatively short time in our ED (less than five hours) as compared to 7.5-13.9 hours reported by others [2,4,5,15]. While this short time in the ED may have impacted mortality, it should not have affected our ability to reduce the time to antibiotic administration, the primary outcome measure of this study.

CONCLUSION

We were unable to demonstrate successful implementation of an EGDT sepsis protocol in our ED utilizing existing resources. Our baseline mortality rate was lower than that reported by others, but no improvement in time to antibiotics or mortality was found after introduction of the protocol. Further study is needed to evaluate barriers to EGDT and feasibility of translating resource intensive research protocols to the bedside.

ACKNOWLEDGEMENTS

There was no external funding source for this study. Thanks for assistance with data gathering, data entry, and manuscript preparation: H. N. Bullock, J. M. Donovan, K. Shea. This was a poster presentation at the American College of Emergency Physicians Research Forum, October 2008.

CONFLICTS OF INTEREST

No conflict of interest.

APPENDIX 1: COMPUTERIZED ORDER SET FOR SEPSIS

*Adult- Sepsis Order Set – Appendix 1	
Select/Deselect All	
Custom Order	
<input type="text"/>	
Blood Bank	
Type/Screen/Crossmatch Workup - MENINO ONLY	
Lab- Chemistry: General	
<input type="checkbox"/> Amylase	<input type="checkbox"/> Magnesium
<input type="checkbox"/> Hepatic Function Panel	<input type="checkbox"/> Metabolic Panel - Basic

Lipase	
Lab- Chemistry: Hormones - Blood	
Cortisol	HCG Pregnancy
Lab- Chemistry: Thyroid Tests	
TSH	
Lab- Hematology: Coagulation	
INR(PT) & PTT	
Lab- Hematology: Routine	
CBC with Differential	
Lab- Micro: Bacteriology	
Culture, Blood	Urine Culture - Routine
Culture, Urine SPTAP/Cysto (Aerobic)	
Lab- Urinalysis	
Urinalysis	
Rad- X-ray: Chest & Ribs	
Chest Portable X-Ray	
.General Nursing Orders	
Foley Cath	Saline Lock
Obtain IV Access	
.EKG	
ECG	
.IV Therapy	
Normal Saline 0.9%	Normal Saline 0.9% Bolus:
.Oxygen Therapy	
Oxygen	
.Monitors	
Cardiac Monitor	Pulse-Ox Monitor- 1 time
Non-Invasive Blood Pressure Monitor	Pulse-Ox Monitor- continuous
.Point of Care Tests	
UHCG Test (Point of Care)	

Lab- Chemistry: Blood Gases	
Arterial Blood Gas w/ Lytes and CR	Venous Blood Gas w/ Lytes and CR
Lactic Acid (Green Tube on Ice)	
.IV Pressors and Inotropes	
Dobutamine __ug/kg/minute, keep SBP>__	Norepinephrine __ug/minute, keep SBP>__
Dopamine __ug/kg/minute, keep SBP>__	Phenylephrine __ug/minute, keep SBP>__
Previous order exists for this service	

APPENDIX 2: COMPUTERIZED ORDER SET FOR ANTIBIOTICS FOR PATIENTS WITH SEPSIS

Adult- Sepsis Antibiotics – Appendix 2				
	Route	Time	Dosage	
<u>Ampicillin (Ampicillin Sodium)</u> :  	IV		2000	mg
<u>Azithromycin</u> :  	IV		500	mg
<u>Ceftriaxone Sodium</u> :  	IV			mg
<u>Ciprofloxacin Hydrochloride</u> :  	IV		400	mg
<u>Clindamycin Phosphate</u> :  	IV		600	mg
<u>Gentamicin Sulfate, Injectable (Gentamicin Sulfate)</u> : 	IV			mg
<u>Levaquin (Levofloxacin)</u> :  	IV		750	mg
<u>Maxipime ADD-Vantage (Cefepime Hydrochloride)</u> :  	IV		2000	mg
<u>Metronidazole</u> :  	IV		500	mg
<u>Solu-Cortef (Hydrocortisone Sodium Succinate)</u> :  	IV		100	mg

<u>Vancomycin Hydrochloride</u> : 	IV			G
<u>Zosyn (Piperacillin Sodium/Tazobactam Sodium)</u> : 	IV		2.25	G
<u>Zosyn (Piperacillin Sodium/Tazobactam Sodium)</u> : 	IV		3.375	G

APPENDIX 3: POCKET REFERENCE CARD FOR SEPSIS PROTOCOL

ED Sepsis Card 2008 – Appendix 3

BMC ED Adult Sepsis Guidelines 2008

- Untreated sepsis mortality rate 30-50%
- Early aggressive therapy can reduce mortality by 16%

Step 1: Recognize septic shock early

- Temperature < 96.8F (36 C) or > 100.4 F (38 C)
- HR > 90 beats/min
- BP < 90 systolic
- RR > 20 or PaCo2 < 32
- WBC > 12,000 or < 4000 or > 10% bands
- Lactate > 4
- Neuro: lethargy, change in mental status
- Respiratory: hypoxia, SOB, cough
- Renal: low urine output, elevated Cr
- Metabolic: acidosis, elevated lactate, hyperglycemia

Step 2: Consider differential diagnoses of shock

- Alcohol withdrawal, thyroid storm, GI bleed, occult trauma, toxic ingestion, DKA/AKA, MI

Step 3: Work-up, move unstable patients to Trauma 1

- Rectal temp
- Portable CXR
- EKG
- Comprehensive Metabolic
- CBC with differential
- Venous blood gas (ABG if shock or resp compromise)
- Lactate (on VBG or ABG)
- UA, urine culture
- Blood cultures (2 sets)
- Sputum culture (esp. if intubated)
- Type & cross
- Random cortisol & TSH

Step 4: Aggressive resuscitation

- 2 large peripheral IVs or subclavian or IJ central line
- 2nd choice femoral (incr risk of DVT & infection)
- Large volume NS (may need 4-10 L) titrate to SBP > 90 and urine output
- Early intubation or non-invasive BiPAP/CPAP
- Low tidal vol (6 ml/kg of ideal body wt) in ARDS/ALI
- Elevate head of bed
- Follow urine output

1st Line Pressors: if BP refractory to fluids, titrate to MAP > 65 or systolic > 90

- Dopamine 5-20 mcg/kg/min
- Norepinephrine (Levophed) 2-30 mcg/min

2nd Line Pressors:

- Vasopressin 0.04 units/min gtt
- Phenylephrine (Neosynephrine) 100-300 mcg/min
- Dobutamine 5-20 mcg/kg/min

Consider:

- Transfuse RBCs for Hb < 8
- Xigris (needs APACHE-2 > 25, discuss with MICU)
- Hydrocortisone 100 mg IV (only if known adrenal insufficiency, random cortisol < 15)
- Avoid Na Bicarb unless pH < 7.15

Guidelines created by: Meg McGrath MD, Tamar Barlam MD, Dana Whitney PharmD, Phil Grgurich PharmD, Art Theodore MD

7/2008 3rd edition

ED Adult Sepsis: Early Antibiotics (goal in 1st hour)

- Clarify PCN/Ceph “allergy” - if not significant, use 1st line antibiotics
- Consult ID (pager 8902 HAC, 8903 ENC) or Antibiotic Management Team (pager 8523)
- ER pharmacy 4-5609 Phil Grgurich, PharmD: pager 8321 Central Pharmacy 4-7687

Source	1 st line antibiotic	PCN/Ceph allergic
Unknown source (Empiric)	Cefepime 2 G IV + Vancomycin 15 mg/kg IV <i>If risk for multi-drug resistance:</i> + Gentamicin 6 mg/kg IV (high dose, good for 24 hrs, 2 mg/kg x 1 dose if renal failure)	Ciprofloxacin 400 mg IV + Vancomycin 15 mg/kg IV + Gentamicin 6 mg/kg IV (high dose, good for 24 hrs, 2 mg/kg x 1 dose if renal failure)
Intra-abdominal Sepsis Consult surgery early & consider CT scan	Zosyn 3.375 G IV (1 st dose in ED does NOT need ID approval)	Vancomycin 15 mg/kg IV + Flagyl 500 mg IV + Gentamicin 6 mg/kg IV (high dose, good for 24 hrs, 2 mg/kg x 1 dose if renal failure)
Urosepsis	Ceftriaxone 1 G IV <i>Chronic foley catheter pt:</i> + Gentamicin 6 mg/kg IV (high dose, good for 24 hrs, 2 mg/kg x 1 dose if renal failure)	Ciprofloxacin 400 mg IV + Gentamicin 6 mg/kg IV (high dose, good for 24 hrs, 2 mg/kg x 1 dose if renal failure)
Respiratory	Ceftriaxone 1 G IV + Azithromycin 500 mg IV <i>If risk for multi-drug resistance:</i> Cefepime 2 G IV + Vancomycin 15 mg/kg IV + Azithromycin 500 mg IV + Gentamicin 6 mg/kg IV (high dose, good for 24 hrs, 2 mg/kg x 1 dose if	Levofloxacin 750 mg IV <i>If risk for multi-drug resistance:</i> Levofloxacin 750 mg IV + Vancomycin 15 mg/kg IV + Gentamicin 6 mg/kg IV (high dose, good for 24 hrs, 2

	renal failure)	mg/kg x 1 dose if renal failure)
Skin/soft tissue	Toxic shock: Vancomycin 15 mg/kg IV + Clindamycin 600 mg IV Necrotizing fasciitis: Vanc + Clinda + Zosyn 3.375 G IV	Toxic shock: Vancomycin 15 mg/kg IV +/- Clindamycin 600 mg IV Necrotizing fasciitis: Vanc + Clinda + Gentamicin 2 mg/kg IV
Catheter/IVDU/ endocarditis	Vancomycin 15 mg/kg IV +Gentamicin 2 mg/kg IV	Vancomycin 15 mg/kg IV + Gentamicin 2mg/kg IV
CNS	Ceftriaxone 2 G IV + Vancomycin 15-20 mg/kg IV +/- Ampicillin 2 G IV (if suspect Listeria)	Page ID if CNS infxn and true PCN allergy

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Received: October 04, 2011

Revised: November 17, 2011

Accepted: November 21, 2011

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