Rapid Time to Positivity of Cerebrospinal Fluid Culture with Coagulase-Negative *Staphylococcus* Is More Likely to Reflect a True Infection Than Contamination

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OBJECTIVE: **Cerebrospinal fluid (CSF) culture is the gold standard for diagnosing postoperative central nervous system infection. The time to positivity (TTP) of an automated continuous blood culture system may indicate the original concentration of the organism. Coagulase-negative *Staphylococcus* (CoNS), the common organism recovered in CSF, poses difficulty in differentiating infection from contamination. This study investigated the TTP of CSF culture with CoNS and its relationship to clinical parameters and prognosis.**

METHODS: **Adult neurosurgical patients with CoNS who recovered via the use of CSF culture in BacT/ALERT Pediatric FAN blood culture bottles and were admitted from September 2013 to July 2015 were enrolled. The demographics, clinical and microbiological data, and treatment were reviewed, and the TTP of each culture was retrieved.**

RESULTS: **Thirty-nine adult patients with CoNS recovered from CSF culture were included. The TTP ranged from 7.68 to 57.36 hours. A univariate logistic regression analysis indicated patients with rapid TTP (<21.5 hours) compared with those with longer TTP were more likely to be female, show an effective response to antibiotic therapy within 7 days, have clean-contaminated surgical incisions, and show CSF leak. A multivariate logistic regression analysis indicated that being female, an effective antibiotic therapy within 7 days, and clean-contaminated surgical incisions were independent predictors of rapid TTP.**

CONCLUSIONS: **Targeted antibiotic therapy was more likely to be beneficial to patients with a rapid TTP within 7 days, which suggested that CoNS with a rapid TTP represents the pathogen of central nervous system infection rather than contamination in neurosurgical patients.**

INTRODUCTION

Neurosurgical patients often have scalp wounds in which numerous normal flora, including coagulase-negative *Staphylococcus* (CoNS), are resident. Some neurosurgical procedures require a transphenoidal approach, and incisions might be contaminated by chance and even result in a central nervous system (CNS) infection. Cerebrospinal fluid (CSF) culture is the gold standard for the diagnosis of CNS infection. Moreover, the use of a continuous blood culture device enhances the sensitivity of the culture method. Although CoNS of the skin flora are the most frequent contaminants of blood culture, they are also common causative agents of infections.[1,2] The significance of CoNS in CSF culture remains obscure. Multisets of blood culture can help to differentiate CoNS as contamination or pathogen of the infection. Collection of a CSF specimen requires lumbar puncture; therefore, repeat CSF collection from 1 patient in a short period is not feasible. A single CSF culture with CoNS is often complicated and it is difficult to discriminate infection from contamination.

Although quantitative culture may be helpful for interpreting the controversy, this procedure has not been used routinely in

Key words
- Cerebrospinal fluid culture
- Clean-contaminated surgical incisions
- Coagulase-negative *Staphylococcus*
- Neurosurgery
- Time to positivity

Abbreviations and Acronyms
CI: Confidence interval
CNS: Central nervous system
CoNS: Coagulase-negative *Staphylococcus*
CSF: Cerebrospinal fluid
NICU: Neurosurgical intensive care unit
OR: Odds ratio
TTP: Time to positivity

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Citation: World Neurosurg. (2016) 93:330-335.
http://dx.doi.org/10.1016/j.wneu.2016.06.056

*Journal homepage: **www.WORLDNEUROSURGERY.org***

*Available online: **www.sciencedirect.com***

Table 1. Univariate Analysis: Risk Factors and Outcomes Associated with Time to Positivity (<21.5 hours or ≥21.5 hours) of Cerebrospinal Fluid Culture of 39 Adult Patients with Coagulase-Negative *Staphylococcus*

Variables	TTP <21.5 hours (n = 17)		TTP ≥21.5 hours (n = 2)		Odds Ratio	95% Confidence Interval	*P* Value
	Number	%	Number	%			
Demographic characteristic							
Female	12	70.59	8	36.36	4.220	1.081—16.324	0.038
Age group							
<40 years	5	29.41	7	31.82	0.893	0.226—3.535	0.872
40—60 years	9	52.94	11	50.00	1.125	0.317—3.994	0.855
>60 years	3	17.65	4	18.18	0.964	0.185—5.030	0.966
Severity of illness							
Neurosurgical intensive care unit stay	4	23.53	10	45.45	0.369	0.091—1.497	0.163
Pittsburgh Bacteremia Score, mean ± SD	0.88 ± 1.36	—	1.73 ± 2.05	—	0.748	0.501—1.118	0.157
Pittsburgh Bacteremia Score (except mental status), mean ± SD	0.29 ± 0.59		0.32 ± 0.57		0.926	0.298—2.876	0.895
Glasgow Coma Scale score <9	1	5.89	3	13.64	0.281	0.028—2.784	0.278
In-hospital mortality	2	11.76	1	4.55	2.800	0.232—33.779	0.418
14-day mortality	2	11.76	1	4.55	2.800	0.232—33.779	0.418
Antibiotic therapy							
Fever when CSF were collected	15	88.24	19	86.36	1.184	0.175—8.021	0.862
Antibiotic administered when CSF was collected	9	52.94	15	68.18	0.525	0.142—1.943	0.334
Effective antibiotic therapy within 48 hours	8	47.06	8	36.36	1.556	0.429—5.645	0.502
Effective antibiotic therapy within 7 days	14	82.35	12	54.55	3.889	0.865—17.482	0.077
Surgery treatment							
Patients with clean-contaminated surgical incision	6	35.29	1	4.55	11.455	1.220—107.506	0.033
CSF leak	5	29.41	1	4.55	8.750	0.912—83.949	0.060
Open head injury	1	5.88	1	4.55	1.312	0.076—22.624	0.852
Operation duration (hours), mean ± SD	4.99 ± 1.94	—	4.45 ± 2.18	—	1.141	0.830—1.568	0.417
CSF biochemical index							
CSF glucose, mean ± SD (mmol/L)	2.83 ± 1.18	—	3.54 ± 1.76	—	0.711	0.439—1.153	0.167
CSF L-lactate dehydrogenase, mean ± SD (U/L)	258.99 ± 497.68	—	199.76 ± 243.68	—	1.000	0.999—1.002	0.622
CSF chloride, mean ± SD (mmol/L)	116.86 ± 6.75	—	117.08 ± 6.69	—	0.995	0.903—1.096	0.918
CSF protein, mean ± SD (g/L)	1.09 ± 0.60	—	1.38 ± 0.88	—	0.591	0.242—1.441	0.247

CSF, cerebrospinal fluid; SD, standard deviation; TTP, time to positivity.

clinical laboratories. Automated continuous monitoring devices have been used worldwide, and the time to positivity (TTP) is defined as the time when the bottle is loaded into an automated system to the detection of a positive signal, which might provide some information regarding the original concentration of the organism. The TTP was inversely proportional to the initial *Staphylococcus epidermidis* concentration of blood culture bottles. Initial densities of <10 CFU/mL and ≥50 CFU/mL had a TTP of >20 hours and ≤15 hours, respectively.[3] Rogers and Oppenheim[4] also found that TTP was strongly related to the concentration of CoNS inoculated, and a decrease of 1.5 hours indicates a 10-fold increase in the initial bacteria concentration.

This study was a single-center, retrospective study in which 39 consecutive neurosurgical patients aged 18 years or older with 1 or more CSF cultures with CoNS were enrolled. The objective of this study was to assess the risk factors affecting the TTP of CoNS in