Determinants of antibiotic tailoring in Pediatric Intensive Care: a survey

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Infection, antibiotics, procalcitonin, child, critical care, survey, clinical reasoning

Short title

Determinants of antibiotic use in PICUs

Version

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OVERVIEW

Antibiotics are commonly used in pediatric intensive care units (PICUs) for suspected or proven ***severe bacterial infections (sepsis, pneumonia, central nervous system, and intra-abdominal)***.[1] The frequent use of antibiotics is associated with adverse events and the development of resistant strains, such as methicillin-resistant *Staphylococcus aureus* (MRSA).[2-4] Reducing unnecessary exposure to antibiotics is considered the optimal strategy to deal with these important problems.

While initiating antibiotic therapy in PICU patients hospitalised with suspected severe bacterial infections cannot be avoided, it may be possible to shorten antibiotic treatment duration according to individual patient needs and/or to stop it for patients who do not have bacterial infections. Currently, there are many infections markers, including fever, white blood cell (WBC) count, and C-reactive protein (CRP) that could be used to assess when antibiotics can be stopped.[5,6] In addition, different research groups have recently proposed the use of procalcitonin, a biomarker with good specificity for bacterial infections, to guide the duration of antibiotic therapy with promising results.[7-13]

However, it is not clear which infection markers are used in PICUs to tailor antibiotic treatment for children with severe bacterial infections, as such a study has never been performed. The answer to this question is crucial to better understand how antibiotic tailoring in this setting is carried out. This would also inform the development of a future decision-support tool for tailoring antibiotic duration in PICU patients. We believe that such a tool will result in shorter antibiotic treatments adjusted by individual needs, improve the safety of antibiotic use, and decrease antibiotic selection pressure in this high-risk population.

Thus, with the study proposed herein we aim to describe the clinical and laboratory markers currently used to tailor antibiotic duration in pediatric patients admitted to PICUs in Canada, U.S., France, Brazil, Saudi Arabia, Japan, and Italy. ***We hypothesize that pediatric intensivists use a common set of clinical and laboratory infection markers, including core temperature, WBC, CPR, and procalcitonin, to tailor antibiotic treatment duration in children with severe bacterial infections.***

Between October 2014 and April 2015, we have administered the electronic survey to 62 (60%) Pediatric Critical Care physicians and 37 (36%) Pediatric Infectious Diseases specialists who work in hospitals in Canada. We will now administer the same survey to pediatric intensivists in the U.S., France, Brazil, Saudi Arabia, Japan, and Italy. The survey contains questions and clinical scenarios about the use of different infection markers for antibiotic tailoring in PICUs.

BACKGROUND

1. Antibiotic resistance and side effects: an important problem in PICUs

Antibiotics are frequently used in PICUs. A prevalence survey performed by Grohskopf et al in 2005 showed that 71% of patients admitted to 35 U.S. PICUs were receiving ≥1 antibiotic on the survey day, 49% of them for empiric reasons.[14] While essential for the treatment of severe bacterial infections, antibiotic use is associated with adverse events, such as toxicity and the selection of pathogenic organisms (e.g., *Clostridium difficile)*, and with an increase in economic costs, as antibiotics account for >30% of hospital pharmacy budgets.[15,16]

Antibiotic use is also associated with increasing antibiotic resistance, a major problem worldwide. The Centers for Disease Control and Prevention (CDC) estimate that antibiotic-resistant infections lead to $20 billion in excess healthcare costs, $35 billion in societal costs, and 8 million additional hospital-days/year in the U.S.[17] In Canada, Birnbaum et al calculated that the excess direct cost of resistant infections is between 9-14 million Canadian dollars/year.[18] Antibiotic resistance is driven by selection pressure, as the use of antibiotics destroys susceptible microorganisms while resistant strains thrive and expand.[19,20] Thus, hospital units where antibiotics are often used, such as PICUs, are particularly affected by the emergence and spread of antibiotic resistant bacteria.[14]

Antibiotic adverse events and resistance are important threats to patient safety. ***The best strategy to deal with these threats is to reduce unnecessary antibiotic exposure. Due to their critical condition, antibiotics must be started in PICU patients with suspected severe bacterial infections. However, we should tailor treatment duration according to patient individual needs.***[15]

2. Recommendations about optimal antibiotic duration are not evidence-based

Presently, there is a lack of evidence regarding the optimal duration of antibiotic therapy in bacterial infections, with most recommendations being based on expert opinion. One example is the Infectious Diseases Society of America guidelines for meningitis, which state that the duration of antibiotic therapy in bacterial meningitis (7-21 days) has been based more on "tradition" than on evidence-based data.[21,22] The proposed durations aim to extend coverage long enough to safely establish infection cure in most patients.

Moreover, when trying to account for individual needs, the directives given tend to be vague and based on subjective criteria. The 2012 "Surviving Sepsis Campaign" guidelines, which are used worldwide, recommend antibiotic therapy for 7 to 10 days, with longer courses being suggested in patients who have "a slow clinical response", for which a definition is not provided.[23] In addition, decisions to continue or stop antibiotics should be made "on the basis of clinical judgement and clinical information". ***The subjectivity of these criteria feeds the physicians' fear of stopping antibiotics too early with consequent bad patient outcomes.*** This also leads to the prolongation of treatment over many days and antibiotic overuse in PICUs.

3. Factors influencing antibiotic use in PICUs: how do PICU physicians make their decisions?

No study has specifically evaluated the decision process behind antibiotic use in PICUs. Custer et al. studied the cognitive process used by ICU physicians to make clinical decisions in general and reported that the process includes building a patient–related mental model using clinical and laboratory data, physical exam, pertinent medical literature, and case histories.[24] However, due to time pressure, severity of disease, and delays in receiving culture results, it is possible that ICU physicians also use other cognitive processes to make decisions about antibiotic use, such as intuition and medical specific knowledge stored in long-term memory for initial decisions, and a Bayesian approach based on the evaluation of new data for decisions regarding duration or stopping antibiotic treatment.[25-27]

Furthermore, there is currently a lack of data about which clinical and laboratory factors influence antibiotic use in adult and pediatric ICUs. Sintchenko et al. showed that the fear of medical-legal implications (90%) and a strong clinical suspicion of infection (77%) were important factors for adult intensivists.[28] However, other factors, e.g., uncertainty about causal agent, physician's experience, and infection markers (e.g., temperature, white

blood cell count - WBC), which frequently influence other specialists' antibiotic prescribing, were not evaluated.[29-34]

In the last years, some research groups have proposed the use of different algorithms to tailor antibiotic use for ICU patients. Bouadma et al. proposed an algorithm solely based on procalcitonin, a new biomarker very specific for bacterial infections.[7] Despite their positive results, a major limitation of Bouadma's study was protocol deviation. Because the algorithm did not include clinical or other laboratory variables to evaluate patient improvement, physicians refused to stop antibiotics in 79 cases (26%) because they judged that patients were still clinically unstable.[7] ***Importantly, this suggests that the antibiotic tailoring decision process for ICU patients also includes the use of clinical and laboratory infection markers.***

In addition, Micek et al. and Singh et al. proposed antibiotic discontinuation policies for patients with ventilator-associated pneumonia and community-acquired pneumonia, respectively, that included the monitoring of traditionally used clinical (fever and sputum/tracheal secretion aspect), laboratory (WBC, PaO_2/FiO_2 index, and tracheal aspirate culture results), and radiology (X-ray images) infection markers. Differently from Bouadma's study, the rates of protocol deviation in both studies were quite low, showing that the policies had been well accepted by the healthcare teams involved in the studies, probably because they were similar to decision process routinely used by ICU physicians.

RATIONALE

Antibiotic adverse events and resistance cause an important burden to PICU patients. Tailoring of antibiotic use according to patient needs is already performed in PICUs. ***However, we currently do not know which clinical and/or laboratory infection markers pediatric intensivists and Pediatric Infectious diseases specialists use to tailor antibiotic treatment in Canada, U.S., France, Brazil, Saudi Arabia, Japan, and Italy.*** Answering this crucial question would improve our understanding about how antibiotic tailoring in this setting is performed. It would also greatly inform the development of a future decision-support tool to tailor antibiotic therapy in pediatric patients with severe bacterial infections.

RESEARCH QUESTIONS

The proposed cross-sectional study aims to answer the following questions:

1. What are the antibiotic tailoring determinants currently used in PICUs?
2. Are there differences in the way pediatric intensivists use antibiotics in different countries?

HYPOTHESIS AND OBJECTIVES

Primary hypothesis: pediatric intensivists and pediatric Infectious Diseases specialists in Canada, U.S., France, Brazil, Saudi Arabia, Japan, and Italy use a core set of clinical and laboratory infection markers to tailor antibiotic treatment duration in children with severe bacterial infections.

Primary aim: to describe the clinical and laboratorial markers currently used to tailor antibiotic duration in pediatric patients admitted to PICUs in Canada, U.S., France, Brazil, Saudi Arabia, Japan, and Italy.

Secondary hypothesis*:* the importance of infection markers in the decision making process about antibiotic use in critically ill children differs between countries.

Secondary aim: to compare the results obtained for Canada, U.S., France, Brazil, Saudi Arabia, and Italy.

METHODS

1. Study design and sampling frame:

We performed the phase I of this cross-sectional study between October 2014 and April 2015, when the survey was sent to 103 Canadian pediatric intensivists and 105 pediatric infectious diseases specialists. We will perform the phase II of this project between May and September 2016, when we will send the same survey to pediatric intensivists in the U.S., France, Brazil, and Saudi Arabia. The sampling frame for the second phase includes 250 pediatric intensivists in the U.S., 265 pediatric intensivists in France, 280 pediatric intensivists in Brazil, and 50 pediatric intensivists in Saudi Arabia (total 595 eligible participants). We will obtain the contact information of potential participants using the membership lists of the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI – U.S.), Groupe Francophone de Réanimation et Urgences Pédiatriques (GFRUP – France), and the Saudi Arabia Critical Care Society (Saudi Arabia), by contacting the directors of 14 PICUs in Brazil, by using already existent contact information lists for pediatric intensivists in Japan and Italy.

2. Survey development:

We developed the proposed survey using a multi-step methodological approach.[35] Initially, we performed a literature review about determinants of antibiotic tailoring in severe bacterial infections. Using the results of our literature review, we conducted focus group sessions with pediatric critical care, Infectious Diseases specialists, and epidemiologists to identify the domains and concepts that should be addressed in the survey. Domains included demographics, clinical and laboratory determinants, and use of procalcitonin for bacterial infection diagnosis and antibiotic tailoring.

Once all possible items for inclusion were identified, we turned them into questions and/or incorporated them to different clinical scenarios developed by pediatric intensivists (item generation process). We then performed an “item reduction” process using the same previously described focus group to remove redundant items, while maintaining all important concepts. Finally, we formatted and translated the survey into French, Portuguese, Japanese, and Italian. Co-investigators (JP, SL, FD, PF, JP, AK, SK, FC), whose native languages are French, Portuguese, Japanese, and Italian ensured the appropriateness of the translation.

3. Survey testing:

Ten physicians (5 pediatric intensivists and 5 pediatric Infectious Diseases specialists) piloted the original survey and provided feedback regarding its clarity, relevance, completeness, face validity, content validity, redundancy, and time for completion. We revised the questionnaire based on the provided feedback. To test intra-rater reliability, we invited 2 pediatric intensivists and 2 pediatric Infectious Diseases specialists to complete the survey on 2 occasions 2 weeks apart. We modified the questionnaire based on the results of the reliability test (see “Statistical analysis”). The final version of the survey is presented in Appendix A.

4. Survey administration:

We will administer the survey in 2 parts using a Web-based software (www.limesurvey.org/en/). The initial contact with eligible responders will be made through an invitation email containing the link to the electronic survey. In case of nonresponse, we will send 2 electronic reminders (emails) 2 weeks apart. Remaining non-respondents will receive 1 mailed letter including an invitation letter, a paper version of the survey, and a stamped return envelope, 2 weeks after the last electronic reminder.

5. Research Ethics Board (REB) and ethical conduct:

The survey has been approved and endorsed by the Canadian Critical Care Trials Group (CCCTG), PALISI, GFRUP, and the Association of Medical Microbiology and Infectious Disease Canada (AAMMI Canada). We have obtained the permission to contact members via mailing lists from all executives. A statement describing the purpose of the study is included on the cover page of the questionnaire. Respondents will be informed that participation in this study is voluntary, that their answers will remain anonymous, and that all data obtained will be exclusively used for scientific purposes. We will also include that informed consent is implied by the completion and submission of the survey. This project has already been approved by the Scientific Committee and REB of the McGill University Health Center.

The Web-based software (Lime survey) used to administer the survey will allow us to identify the eligible participants who did not complete the survey on line. These latter will receive a paper version of the survey that will contain no identifier. Once data collection is completed and data are cleaned, all nominal data will be removed and respondents will be identified using a unique identifier. All data will be maintained in password-protected files and kept confidential in locked research offices at the Montreal Children's Hospital for a minimum of 10 years. Only Dr. Fontela and Mrs. Shauna O'Donnell will have access to the data.

6. Data management:

Mrs. Shauna O'Donnell is responsible for survey programming, database development, and data management. The database will be kept in a secure facility according to Health Canada best practices.

7. Statistical analysis:

7.1 ***Sample size calculation***:

Our sampling frame includes 103 pediatric intensivists and 105 pediatric Infectious Diseases specialists in Canada, 250 pediatric intensivists in the U.S., 265 pediatric intensivists in France, 280 pediatric intensivists in Brazil, 50 pediatric intensivists in Saudi Arabia, 100 pediatric intensivists in Japan, and 50 pediatric intensivists in Italy (total 1,198 eligible participants). Based on similar studies and on the results we obtained in Canada, we expect a response rate of 65%.[36,37] Therefore, our estimated sample size is 779 participants (710 pediatric intensivists and 69 pediatric Infectious Diseases specialists). This sample size will allow estimation of 95% confidence intervals (95%CIs) of 46% and 54%, and of 38% and 62% around a response item to which 50% of pediatric intensivists and 50% of pediatric Infectious Diseases specialists chose, respectively.[5]

7.2 ***Statistical analysis according to specific aims***:

For the assessment of inter-rater reliability, we used weighted Kappa coefficient.[38] We will summarize survey responses using descriptive statistics including means with 95%CIs or medians with interquartile ranges (IQRs) for continuous data and proportions for categorical data. We will collapse categories, when appropriate, to summarize responses in a meaningful manner. Potential open-ended answers will be coded and then classified in different categories. When not possible, we will perform content analysis and summarize text responses. McNemar's test will be used to compare categorical responses obtained by the same individuals but in different scenarios. Paired t-test will be used to compare continuous responses obtained by the same individuals but in different scenarios and also to compare the chosen duration of antibiotic treatment for the baseline clinical scenario and the modified clinical scenarios (i.e., when different infection markers were added). In addition, we will perform multivariable logistic regression models to evaluate associations between respondent's characteristics and practice setting and the following dependent variables: determinants for antibiotic tailoring and use of procalcitonin. Finally, we will also use multivariable logistic regression to compare the answers obtained in different countries. $P < 0.05$ will be considered statistically significant. We will analyze the data using R 3.1.2.

BUDGET

A detailed budget is attached to this protocol (Appendix B).

RESEARCH TEAM

Dr. Patricia Fontela is a pediatric intensivist who holds a Ph.D. in Epidemiology and is an expert in infectious disease epidemiology in critical care units. She will lead the research team and oversee study logistics, data collection, analysis, and interpretation, writing of manuscript, and knowledge transfer. ***Dr. Jacques Lacroix*** is a pediatric intensivist with research expertise in PICU infectious diseases epidemiology, and has vast experience in developing/conducting multinational PICU surveys. He will assist in study logistics, data interpretation, knowledge translation, and survey distribution in France. ***Dr. Caroline Quach*** is a Pediatric Infectious Diseases specialist with expertise in infection control and antibiotic stewardship in PICUs. She will assist in the interpretation of results and knowledge translation. ***Dr. Douglas Willson*** is a pediatric intensivist with research expertise in acute lung injury and ventilation associated pneumonia who has experience in multicenter PICU studies. He will assist in survey development and evaluation, interpretation of results, and knowledge translation. ***Dr. Steven Reynolds*** is an adult intensivist and infectious diseases specialist who is an expert in the use of procalcitonin in adult ICU patients. ***Dr. Elaine Gilfoyle*** is a pediatric intensivist who holds a MSc in Medical Education. She will assist in survey evaluation, interpretation of results, and knowledge translation. ***Dr. James Dayre McNally*** is a pediatric intensivist who holds a Ph.D. in Biochemistry. He will assist in survey evaluation and interpretation of results. ***Mrs. Milagros Gonzales*** holds a M.Sc. in Epidemiology and will be responsible for survey programming, database development and data management. ***Dr. Jefferson Piva*** is a pediatric intensivist who holds a PhD in Pediatrics. He will oversee study logistics and data collection in Brazil. ***Dr. Yasser Kazzaz*** is a pediatric intensivist and a member of the Saudi Critical Care Society. He will oversee study logistics and data collection in Saudi Arabia. ***Dr. Stéphane Leteurtre*** is a pediatric intensivist and

a member of the GFRUP. He will oversee study logistics and data collection in France. ***Dr. François Dubos*** is a pediatric infectious diseases specialist and a member of the GFRUP. He will help Dr. Leteurtre to oversee study logistics and data collection in France. ***Dr. Atsushi Kawaguchi*** is a pediatric intensivist and a member of the Japanese Society of Critical Care. He will oversee study logistics and data collection in Japan. ***Dr. Shuji Kuwabara*** is a pediatric intensivist and a member of the Japanese Society of Critical Care. He will help Dr. Kawaguchi to oversee study logistics and data collection in Japan. ***Dr. Fabrizio Chiusolo*** is a pediatric intensivist and a member of the Societá Italiana di Anestesia, Analgesia e Terapia Intensiva Pediatrica. He will oversee study logistics and data collection in Italy.

STUDY LIMITATIONS

As with any survey-based study, selection bias and a low response rate are potential limitations. Thus, we built a strategy to send multiple electronic and mailed reminders to eligible responders to maximize response rate. In addition, another limitation of this study is that we will ascertain stated practice and not actual practice. Therefore, we plan to perform a qualitative methods study about antibiotic tailoring practices to complement and extend the results of the proposed survey.

KNOWLEDGE TRANSLATION

As first step, our results will inform the development the decision-support tool during a meeting when we will gather experts in pediatric and adult critical care, infectious diseases, infection control and antibiotic stewardship, epidemiology, biostatistics, PICU nurses, pharmacists, public health officers, and research coordinators. Subsequently, we will evaluate the tool in a RCT. We will disseminate the key-scientific findings of this study through conference presentations and publications in peer-reviewed journals, and also present them to the CCCTG, PALISI, Canadian Critical Care Society, GRFUP, Canadian Pediatric Society, AMMI Canada, and Pediatric Infectious Diseases Society.

TIMELINE

Please refer to Table 1 for a detailed timeline of the proposed study.

SUMMARY

Antibiotic overuse is a major problem in PICUs. To decrease unnecessary antibiotic exposure, it is imperative to better understand how PICU physicians tailor antibiotic treatment for children with severe bacterial infections, as well as how they define bacterial infection cure. The proposed study is a crucial step to develop a decision-support tool that can realistically help to reduce antibiotic overuse, antibiotic-related adverse events and resistance, consequently improving the health outcomes of critically ill pediatric patients and the cost-effectiveness of the health system.

REFERENCES

1. Ding H, Yang Y, Chen Y, Wang Y, Fan S, Shen X. Antimicrobial usage in paediatric intensive care units in China. Acta Pædiatrica 2008;97:100-4.
2. Ansar W, Ghosh S. C-reactive protein and the biology of disease. Immunol Res 2013:1-12.
3. Boxer LA. Chapter 122: leukocytosis. In: Behrman RE, Kliegman RM, Jenson HB, eds. Nelson texbook of Pediatrics. Philadelphia: saunders; 2004:723-25.
4. Levy ERM, Swami SM, Dubois SGM, Wendt RB, Banerjee RMDP. Rates and appropriateness of antimicrobial prescribing at an academic children's hospital, 2007–2010. Infect Control Hosp Epidemiol 2012;33:346-53.
5. Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. Stat Med 1998;17:857-72.
6. Schimit X, Vincent JL. The time course of blood C-reactive protein concentrations in relation to the response to initial antimicrobial therapy in patients with sepsis. Infection 2008;36:213-19.
7. Bouadma L, Luyt C-E, Tubach F, et al. Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial. Lancet 2010;375:463-74.
8. Heyland DK, Johnson AP, Reynolds SC, Muscedere J. Procalcitonin for reduced antibiotic exposure in the critical care setting: a systematic review and an economic evaluation. Crit Care Med 2011;39:1792-9.
9. Hochreiter M, Kohler T, Schweiger AM, et al. Procalcitonin to guide duration of antibiotic therapy in intensive care patients: a randomized prospective controlled trial. Crit Care 2009;13:R83.
10. Nobre V, Harbarth S, Graf JD, Rohner P, Pugin J. Use of procalcitonin to shorten antibiotic treatment duration in septic patients: A randomized trial. American Journal of Respiratory and Critical Care Medicine 2008;177:498-505.
11. Schroeder S, Hochreiter M, Koehler T, et al. Procalcitonin (PCT)-guided algorithm reduces length of antibiotic treatment in surgical intensive care patients with severe sepsis: results of a prospective randomized study. Langenbecks Arch Surg 2009;394:221-6.
12. Stolz D, Smyrnios N, Eggimann P, et al. Procalcitonin for reduced antibiotic exposure in ventilator-associated pneumonia: a randomised study. Eur Respir J 2009;34:1364-75.
13. Esposito S, Tagliabue C, Picciolli I, et al. Procalcitonin measurements for guiding antibiotic treatment in pediatric pneumonia. Respiratory Medicine 2011;105:1939-45.
14. Fischer JE, Ramser M, Fanconi S. Use of antibiotics in pediatric intensive care and potential savings. Intensive Care Med 2000;26:959-66.
15. Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clin Infect Dis 2007;44:159-77.
16. John JF, Fishman NO. Programmatic role of the infectious diseases physician in controlling antimicrobial costs in the hospital. Clin Infect Dis 1997;24:471-85.
17. Briassoulis G, Natsi L, Tsorva A, Hatzis T. Prior antimicrobial therapy in the hospital and other predisposing factors influencing the usage of antibiotics in a pediatric critical care unit. Ann Clin Microbiol Antimicrob 2004;3:4.

18. Birnbaum D, Canadian Committee on Antibiotic Resistance. Antimicrobial resistance: a deadly burden no country can afford to ignore. Can Commun Dis Rep 2003;29:157-64.

19. Audry-Degardin E, Dubos F, Leteurtre S, Beaucaire G, Leclerc F. Évaluation de la prescription antibiotique dans un service de réanimation pédiatrique. Arch Pediatr 2007;14:157-63.

20. Olofsson SK, Cars O. Optimizing drug exposure to minimize selection of antibiotic resistance. Clin Infect Dis 2007;45:S129-S36.

21. Ehl S, Gering B, Bartmann P, Högel J, Pohlandt F. C-reactive protein is a useful marker for guiding duration of antibiotic therapy in suspected neonatal bacterial infection. Pediatrics 1997;99:216-21.

22. Bomela H, Ballot DE, Cory B, Cooper P. Use of C-reactive protein to guide duration of empiric antibiotic therapy in suspected early neonatal sepsis. Pediatr Infect Dis J 2000;19:531-5.

23. Hengst J. The role of C-reactive protein in the evaluation and management of infants with suspected sepsis. Adv Neonatal Care 2003;3:3-13.

24. Custer JW, White E, Fackler JC, et al. A qualitative study of expert and team cognition on complex patients in the pediatric intensive care unit. Pediatr Crit Care Med 2012;13:278-84

25. Charlin B, Lubarsky S, Millette B, et al. Clinical reasoning processes: unravelling complexity through graphical representation. Med Educ 2012;46:454-63.

26. Claessens Y-E, Wannepain S, Gestin S, et al. How emergency physicians use biomarkers: insights from a qualitative assessment of script concordance tests. Emerg Med J 2013 April 4 [Epub ahead of print].

27. Rashotte J, Carnevale FA. Medical and nursing clinical decision making: a comparative epistemological analysis. Nurs Philos 2004;5:160-74.

28. Sintchenko V, Iredell JR, Gilbert GL, Coiera E. What do physicians think about evidence-based antibiotic use in critical care? A survey of Australian intensivists and infectious disease practitioners. Intern Med J 2001;31:462-9.

29. Butler CC, Rollnick S, Pill R, Maggs-Rapport F, Stott N. Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throats. BMJ 1998;317:637-42.

30. Kumar S, Little P, Britten N. Why do general practitioners prescribe antibiotics for sore throat? Grounded theory interview study. BMJ 2003;326:138.

31. Macfarlane J, Lewis SA, Macfarlane R, Holmes W. Contemporary use of antibiotics in 1089 adults presenting with acute lower respiratory tract illness in general practice in the U.K.: implications for developing management guidelines. Resp Med 1997;91:427-34.

32. Weiss M, Fitzpatrick R, Scott D, Goldacre M. Pressures on the general practitioner and decisions to prescribe. Family Practice 1996;13:432-8.

33. Lode H, Torres A, Cockle A. What drives our choices? Evidence, guidelines or habit? Int J Antimicrob Agents 2007;29, Supplement 1:S17-S22.

34. Timmermans DRM, Sprij AJ, De Bel CE. The discrepancy between daily practice and the policy of a decision-analytic model: the management of fever of unknown origin. Med Decis Making 1996;16:357-66.

35. Burns KEA, Duffett M, Kho ME, et al. A guide for the design and conduct of self-administered surveys of clinicians. CMAJ 2008;179:245-52.

36. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ 2010;340:c2096.

37. Centers for Disease Control and Prevention (CDC). World health day: media fact sheet. Antimicrobial resistance: no action today, no cure tomorrow. 2011. (Accessed September 15, 2013, at http://www.cdc.gov/media/releases/2011/f0407_antimicrobialresistance.pdf.)

38. Szklo M, Niet FJ. Chapter 8: quality assurance and improvement. In: Epidemiology beyond the basics. Sudbury: Jones and Bartlett Publishers; 2006:297-350.

TABLE 1 – Proposed timeline

Research project milestones	**2014-2015**	**2016**				**2017**					
	Jan-Dec	Jan-March	April-June	July-Sept	Oct-Dec	Jan-Feb	March-April	May-June	July-Aug	Sept-Oct	Nov-Dec
First phase											
Science and REB approval in France, Brazil, and Saudi Arabia											
Survey administration											
Data analysis											
Data interpretation											
Manuscript preparation											
Manuscript submission											

APPENDIX A – Final version of survey

Determinants of antibiotic tailoring in Pediatric Intensive Care Units (PICUs): a survey

Investigators:
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Institution:
The Montreal Children's Hospital, McGill University, Montreal, Canada.

Funding source:
Department of Pediatrics and The Montreal Children's Hospital Research Institute, McGill University

Purpose of this survey:
This survey focuses on the use of antibiotics for children with suspected/proven severe bacterial infections admitted to a PICU. The aims of this survey are:

1. To describe the clinical and laboratory infection markers currently used by pediatric intensivists and pediatric Infectious Diseases specialists to tailor antibiotic treatment duration in pediatric patients admitted to PICUs

All your answers will remain anonymous and will be used exclusively for the aims presented above. All data will be maintained in password-protected files and kept confidential in locked research offices at the Montreal Children's Hospital for a minimum of 10 years.

Your participation is voluntary and you may decline to participate or withdraw from the study at any time without penalty. If you choose to complete the survey, this will be interpreted as indicating that you have consented to participate. Completion of a separate consent form is not required.

This survey should take 15-20 minutes to complete.

If you have any question or concerns about this survey, please contact (name of the investigator responsible for the survey in each country) at X (XXX) XXX-XXXX, extension XXXX, or (email)

Thank very much for taking the time to complete this survey! Your participation is much appreciated and will help us to understand how antibiotics are tailored in PICUs to ultimately improve the care of critically ill children.

PART 1 – DEMOGRAPHICS (PICU AND PARTICIPANT)

1. Please indicate the country where your PICU is located:
   ( ) Canada ( ) U.S. ( ) Brazil ( ) France ( ) Saudi Arabia

2. Hospital:
   _____

3. What is your gender?
   ( ) male ( ) female

4. What is (are) your specialty (ies)? Please check all that apply
   ( ) Pediatric critical care specialist ( ) Pediatric infectious diseases
   ( ) General pediatrics ( ) Medical microbiology
   ( ) Cardiology ( ) Cardiac surgery
   ( ) Anesthesia ( ) Other surgical specialty
   ( ) Other: _____

5. How many years of clinical experience do you have working in (please include fellowship years):
   ( ) Pediatric intensive care: _____ years

6. Are you the PICU director? (if yes, this person is invited to answer questions 7 to 14; if not, skip to next section)
   ( ) Yes ( ) No

7. Maximum PICU number of beds:
   Acute cases: _____ beds Intermediate care / step down: _____ beds

8. Number of patients admitted to your PICU over a one-year period during the last year (please include patients transferred from other units within your hospital and form other institutions):
   ( ) Less than 500 patients/year ( ) 1000 to 1499 patients/year
   ( ) 500 to 749 patients/year ( ) 1500 to 1999 patients/year
   ( ) 750 to 999 patients/year ( ) 2000 or more patients/year

9. PICU academic profile:
   ( ) Teaching (PICU affiliated to a university) ( ) Community (PICU not affiliated to a university)

10. Patient population treated in your PICU (check all items that apply):
    ( ) Medical ( ) General surgery
    ( ) Cardiac surgery ( ) Neurosurgery
    ( ) Trauma center ( ) Infants, children, and adolescents
    ( ) Neonates

11. Treatment modalities offered in your PICU and/or in your hospital (check all items that apply):
    ( ) High frequency oscillatory ventilation (HFOV) ( ) Continuous renal replacement therapy (CRRT)
    ( ) Extracorporeal life support (ECLS) ( ) Bone marrow transplantation
    ( ) Solid organ transplantation

12. Is there a Pediatric Critical Care fellowship program in your PICU?
    ( ) Yes ( ) No

13. What was the average PRISM III or PIM 2 score in your PICU last year?
    ( ) PRISM III score: _____ ( ) PIM 2: _____ ( ) Not available

14. Who makes the decision regarding choice, duration, and cessation of antibiotics in your PICU?
    ( ) PICU staff only ( ) Pediatric infectious diseases (ID) specialist only

PART 2 – QUESTIONS ABOUT DETERMINANTS OF ANTIBIOTIC USE

( ) PICU team (fellow and staff) ( ) Combined decision between PICU team and ID team

1. In your opinion, what should be the **minimal**, **the ideal**, and **the maximal duration of antibiotic treatment** for the following **community-acquired non-complicated bacterial infections:**

Infection	Minimal duration (in days)	Ideal duration (in days)	Maximal duration (in days)
Pneumonia			
Meningitis			
Intra-abdominal			
Sepsis			

COMMENTS

2. Clinical scenarios

INSTRUCTIONS
We have provided scenarios to illustrate common clinical situations. These vignettes were designed to reflect decision-making and may not contain all of the information that you might consider important. We ask that you complete the survey even though you may feel that you would need additional information. Remember that the scenarios represent common clinical situations.

Clinical scenario 1 – Suspected bacterial pneumonia

Three days ago, a previously healthy 8 year-old boy was admitted to your PICU with **suspected bacterial pneumonia**. At admission, he presented fever (core temperature 39°C), HR 120 beats/min, RR 45 breaths/min, BP 110/50 mmHg, oxygen saturation 80% on room air and 90% on a non-rebreathing mask, severe subcostal and intercostal retractions, and tracheal tugging. On auscultation, there were bilateral crackles. He also presented good peripheral and central pulses, capillary refill 2 seconds, urine output 1 ml/kg/h, and Glasgow coma score (GCS) 15. Blood work showed leukocytosis (total leukocyte count was 14 X 10^9 cells/L) and the results of a capillary blood gas showed pH 7.28, PCO_2 45 mmHg, HCO_3 20 mEq/L. Chest X-rays (CXR) showed bilateral infiltrates and patchy areas, with no areas of collapse and a normal cardiac silhouette. The patient was started on appropriate empiric antibiotic therapy based on hospital guidelines. Within his first hour in the PICU, his level of consciousness deteriorated and he was intubated and started on mechanical ventilation (synchronized intermittent mandatory ventilation – SIMV-, tidal volume 6 ml/kg, PIP 25 cmH_2O, PEEP 6 cmH_2O, RR 18 breaths/min, FiO_2 0.5 - oxygen saturation 93% -, and pressure support 6 cmH_2O). Blood and endotracheal secretions cultures were collected.

Over the last 3 days, the patient's respiratory status improved significantly and he is now on minimal mechanical ventilation setting. Moreover, his temperature pattern improved (maximum core temperature 38.3°C on day 2), he remained hemodynamically stable and did not present other organ dysfunctions. Culture results were negative, **but they were collected after starting antibiotic treatment**.

During morning rounds on day 3 of PICU admission, you are asked about the expected duration of antibiotic treatment Based on the scenario above, **what would be the total duration of antibiotic treatment that you would recommend for this patient**?
_____ days

How likely would you **stop** the antibiotics for this patient on day 3?
( ) Never ( ) Rarely ( ) Sometimes ( ) Often ( ) Always
What is the total duration of antibiotic treatment that you would recommend for this patient if, **on day 3 of PICU admission**, the previous scenario was **modified** as follows (encircle one response per line):

	Antibiotic treatment duration (in days)
Clinical findings on day 3	
Patient still had a fever	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient had developed 2 or more organs dysfunction	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient is still requiring to be fully ventilated	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Endotracheal tube (ETT) secretions were thick and yellow/green	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient still requiring $FiO_2 \geq 0.5$ to have an oxygen saturation of 92%	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient developed signs and symptoms of severe sepsis	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Laboratory results on day 3	
Persistent leukocytosis (14 X 10^9 cells/L)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Persistently elevated C-reactive protein (CRP), similar to the level at the time of admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Persistently elevated erythrocyte sedimentation rate (ESR), similar to the level at the time of admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Persistently elevated procalcitonin level (PCT), similar to the level at the time of admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Normal WBC count	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Lower C-reactive protein (CRP) levels compared to admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Lower erythrocyte sedimentation rate (ESR) compared to admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Lower procalcitonin level (PCT) compared to admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive ETT culture for *S. pneumoniae*	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive ETT culture for *S. aureus*	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive ETT culture for *P. aeruginosa*	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Identification of respiratory syncytial virus in nasopharyngeal or ETT secretions	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Imaging results on day 3	
Persistence of abnormalities on chest X-ray (CXR)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Presence of pleural effusion on CXR or US that was found to be an empyema	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Thorax computed tomography (CT) showing consolidation	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Other	
PRISM III score at admission > 10 (high risk or mortality)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Presence of immunodeficiency	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient is 15 years instead of 8 years old	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient is 3 months instead of 8 years old	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient has cystic fibrosis	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
This was a ventilator-associated pneumonia (VAP)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

COMMENTS

Clinical scenario 2 – Suspected bacterial meningitis

Three days ago, a previously healthy 8 year-old boy was admitted to your PICU after having presented a short generalized tonic-clonic seizure and suspected bacterial meningitis. At admission, he presented fever (core temperature 39°C), HR 120 beats/min, RR 15 breaths/min, BP 110/50 mmHg, oxygen saturation 95% on room air and no respiratory distress. He also presented good peripheral and central pulses, capillary refill 2 seconds, urine output 1 ml/kg/h. He had positive meningeal signs and his Glasgow coma score (GCS) was 13. Blood work showed leukocytosis (total leukocyte count was 14 X 10^9 cells/L) and the results of a capillary blood gas were pH 7.30, PCO_2 45 mmHg, HCO_3 25 mEq/L. Cerebrospinal fluid (CSF) analysis showed 10 cells/mm^3 (40% neutrophils, 30% lymphocytes, 20% monocytes). Patient was started on appropriate empiric antibiotic therapy based on hospital guidelines. Within his first hour in the PICU, his level of consciousness deteriorated (Glasgow 10) and he was intubated and started on mechanical ventilation (synchronized intermittent mandatory ventilation – SIMV-, tidal volume 6 ml/kg, PIP 20 cmH_2O, PEEP 5 cmH_2O, RR 18 breaths/min, FiO_2 0.3 - oxygen saturation 97% -, and pressure support 6 cmH_2O). Blood, CSF, urine, and endotracheal cultures were collected.

Over the last 3 days, the patient's neurological status improved significantly and no more seizures were observed (clinically and on EEG). His current GCS is 15. He was successfully extubated on day 2. Moreover, his temperature pattern improved (maximum core temperature 38.3°C on day 2), he remained hemodynamically stable, and did not present other organ dysfunctions. Culture results were negative, **but they were collected after starting antibiotic treatment**.

During morning rounds on day 3 of PICU admission, you are asked about the expected duration of antibiotic treatment Based on the scenario above, **what would be the total duration of antibiotic treatment that you would recommend for this patient**?
_____ days

How likely would you **stop** the antibiotics for this patient on day 3?
( ) Never ( ) Rarely ( ) Sometimes ( ) Often ( ) Always

What is the total duration of antibiotic treatment that you would recommend for this patient if, **on day 3 of PICU admission**, the previous scenario was **modified** as follows (encircle one response per line):

	Antibiotic treatment duration (in days)
Clinical findings on day 3	
Patient still had a fever	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient developed 2 or more organ dysfunctions	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Glasgow coma score (GCS) is still 10	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient is still having seizures	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Cerebrospinal fluid (CSF) aspect at lumbar puncture was purulent	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient developed signs and symptoms of severe sepsis	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Laboratory results on day 3	
Persistent leukocytosis (14 X 10^9 cells/L)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Persistently elevated C-reactive protein (CRP), similar to the level at the time of admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Persistently elevated erythrocyte sedimentation rate (ESR), similar to the level at the time of admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Persistently elevated procalcitonin level (PCT), similar to the level at the time of admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Normal WBC count	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Lower C-reactive protein (CRP) levels compared to admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Lower erythrocyte sedimentation rate (ESR) compared to admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Lower procalcitonin level (PCT) compared to admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

CSF with 100 cells/mm^3 (100% neutrophils)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
CSF with 100 cells/mm^3 (90% lymphocytes)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive CSF culture for *S. pneumoniae*	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive CSF culture for aerobic Gram-negative bacilli	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive CSF culture for *N. meningitidis*	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive CSF culture or PCR for enterovirus	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Imaging results on day 3	
Presence of subdural fluid collection on head computed tomography (CT)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Other	
PRISM III score >10 (high risk or mortality)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Presence of immunodeficiency	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient is 15 years instead of 8 years old	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient is 3 months instead of 8 years old	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
This was a hospital-acquired CNS infection	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

COMMENTS

Clinical scenario 3 – Suspected bacterial intra-abdominal infection

Three days ago, a previously healthy 8 year-old boy was admitted to your PICU for monitoring after having been diagnosed with peritonitis. At admission, he presented with nausea and vomiting, fever (core temperature 39°C), HR 150 beats/min, RR 50 breaths/min, BP 85/50 mmHg, oxygen saturation 88% on room air and moderate respiratory distress. He was severely dehydrated, with faint peripheral and central pulses, capillary refill 4 seconds, urine output 0.2 ml/kg/h. His GCS was 15. Blood work showed leukocytosis (total leukocyte count was 14 X 10^9 cells/L) and the results of a capillary blood gas showed pH 7.25, PCO_2 25 mmHg, HCO_3 12 mEq/L. Abdominal exam showed important distension and diffuse tenderness, as well as absence of bowel sounds. A nasogastric tube was inserted to help decompress the abdomen. Abdominal CT showed distended bowel loops, small amount of free fluid, and no signs of abscess or ischemia. The patient received 60 cc/kg of normal saline with improvement of dehydration signs and was started on appropriate empiric antibiotic therapy based on hospital guidelines. Blood and urine cultures were collected.

Over the last 3 days, there was return of bowel function and abdominal tenderness and distension disappeared. Moreover, the patient's temperature pattern improved (maximum core temperature 38.3°C on day 2), he remained hemodynamically stable and did not present other organ dysfunctions. Culture results were negative, **but they were collected after starting antibiotic treatment**.

During morning rounds on day 3 of PICU admission, you are asked about the expected duration of antibiotic treatment Based on the scenario above, **what would be the total duration of antibiotic treatment that you would recommend for this patient**?
_____ days

How likely would you **stop** the antibiotics for this patient on day 3?
( ) Never ( ) Rarely ( ) Sometimes ( ) Often ( ) Always

What is the total duration of antibiotic treatment that you would recommend for this patient if, **on day 3 of PICU admission**, the previous scenario was **modified** as follows (encircle one response per line):

	Antibiotic treatment duration (in days)
Clinical findings on day 3	
Patient still had a fever	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient developed 2 or more organs dysfunction	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient still present signs of peritoneal irritation and	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

ileus	
Patient developed signs and symptoms of severe sepsis	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Laboratory results on day 3	
Persistent leukocytosis (14 X 10^9 cells/L)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Persistently elevated C-reactive protein (CRP), similar to the level at the time of admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Persistently elevated erythrocyte sedimentation rate (ESR), similar to the level at the time of admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Persistently elevated procalcitonin level (PCT), similar to the level at the time of admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Normal WBC count	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Lower C-reactive protein (CRP) levels compared to admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Lower erythrocyte sedimentation rate (ESR) compared to admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Lower procalcitonin level (PCT) compared to admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive blood culture for Gram-negative bacilli	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive blood culture for anaerobes	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive blood culture for Gram-positive cocci	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive blood PCR for enterovirus	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Imaging results on day 3	
Presence of intra-abdominal abscess on computed tomography (CT)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Presence of an important amount of free fluid in the abdominal cavity	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Other	
Patient had an intra-abdominal abscess on CT that was adequately drained	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
PRISM score >10 (high risk or mortality)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Presence of immunodeficiency	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient is 15 years instead of 8 years old	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient is 3 months instead of 8 years old	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
This was a hospital-acquired intra-abdominal infection	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

COMMENTS

Clinical scenario 4 – Suspected bacterial septic shock

Three days ago, a previously healthy 8 year-old boy was admitted to your PICU for septic shock. At admission, he presented fever (core temperature 39.5°C), HR 150 beats/min, RR 50 breaths/min, BP 85/30 mmHg, oxygen saturation 80% on room air and 88% on a non-rebreathing mask, and moderate-severe subcostal retractions. He presented faint peripheral and central pulses, pink extremities, capillary refill 1 second, and urine output 0.2 ml/kg/h. His Glasgow coma score (GCS) was 13. Blood work showed leukocytosis (total leukocyte count was 14 X 10^9 cells/L) and the results of a capillary blood gas were pH 7.25, PCO_2 25 mmHg, HCO_3 12 mEq/L. He received 60 cc/kg of normal saline and subsequent BP measure was 100/40 mmHg. Dopamine infusion 8 mcg/kg/min was initiated. He was started on appropriate empiric antibiotic therapy based on hospital guidelines. Blood and urine cultures were collected.

Over the last 3 days, there was improvement of his hemodynamic status (BP 110/55 mmHg, good peripheral and central pulses, capillary refill 1-2 second) and urine output (2-3 ml/kg/h). Dopamine infusion, which had reached a maximum dose of 8 mcg/kg/min, was weaned and stopped. Moreover, the patient's temperature

pattern improved (maximum core temperature 38.3°C on day 2) and he did not present other organ dysfunctions. Culture results were negative, **but they were collected after starting antibiotic treatment**.
During morning rounds on day 3 of PICU admission, you are asked about the expected duration of antibiotic treatment Based on the scenario above, **what would be the total duration of antibiotic treatment that you would recommend for this patient**?
_____ days

How likely would you **stop** the antibiotics for this patient on day 3?
( ) Never ( ) Rarely ( ) Sometimes ( ) Often ( ) Always

What is the total duration of antibiotic treatment that you would recommend for this patient if, **on day 3 of PICU admission**, the previous scenario was **modified** as follows (encircle one response per line):

	Antibiotic treatment duration (in days)
Clinical findings on day 3	
Patient still had a fever	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient developed 2 or more organs dysfunction	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Need for inotropes or vasoactive drugs	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Laboratory results on day 3	
Persistent leukocytosis (14 X 10^9 cells/L)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Persistently elevated C-reactive protein (CRP), similar to the level at the time of admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Persistently elevated erythrocyte sedimentation rate (ESR), similar to the level at the time of admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Persistently elevated procalcitonin level (PCT), similar to the level at the time of admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Normal WBC count	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Lower C-reactive protein (CRP) levels compared to admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Lower erythrocyte sedimentation rate (ESR) compared to admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Lower procalcitonin level (PCT) compared to admission	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive blood culture for *S. pneumoniae*	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive blood culture for aerobic Gram-negative bacilli	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive blood culture for *N. meningitidis*	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Positive blood PCR for enterovirus	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Other	
PRISM III score >10 (high risk or mortality)	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Presence of immunodeficiency	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient is 15 years old instead of 8 years old	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Patient is 3 months old instead of 8 years old	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
No bacterial source of sepsis was found	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
This was a hospital-acquired sepsis	3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

COMMENTS