Reviewer's report

Title: Outbreak of Pneumonia in the Setting of Fatal Pneumococcal Meningitis among US Army Trainees: Potential Role of Chlamydia pneumoniae Infection

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Reviewer: Daniel Feikin

Reviewer's report:

Is the question posed by the authors well defined? Yes.

2. Are the methods appropriate and well described? Mostly. Suggest another control group among another company of trainees.

3. Are the data sound? Yes, but laboratory evidence for pneumococcal pneumonia is not strong.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition? Yes.

5. Are the discussion and conclusions well balanced and adequately supported by the data? No. see comments about lack of evidence for pneumococcal pneumonia.

6. Are limitations of the work clearly stated? Need more discussion of limitations related to calling this a pneumococcal pneumonia outbreak.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes. But more review of respiratory outbreaks in military is warranted.

8. Do the title and abstract accurately convey what has been found? Yes.

9. Is the writing acceptable? Yes, well written.

This is an investigation of an outbreak of meningitis and pneumonia among military trainees. The survey done at the end of the outbreak was well-done and did ample and thorough testing. I see two main limitations of the paper as is. The evidence for pneumococcal pneumonia seems weak considering that limited diagnostic testing was done at the time that the cases were occurring – it is hard to diagnose pneumonia outbreaks retrospectively. As such much of the discussion related to pneumococcal pneumonia outbreaks, which is informative, might not be relevant for this outbreak. To stick closer to the data, the authors might consider more discussion about Chlamydia pneumoniae in these settings, and bacterial meningitis, particularly pneumococcus, and respiratory outbreaks in general in military settings. The link between the Chlamydia and pneumococcus in pneumonia can still be mentioned, but in a more speculative way and not as the centerpiece for the paper, given the dearth of supporting data. Second, a comparison group among companies at the base without respiratory illness outbreaks might have supplemented the two control groups used, which differed
in their exposures from the trainees. This should be discussed as a possible limitation.

Intro. Page 4, Line 5. Discretionary. Restructure sentence. As is, it seems that pneumo outbreaks in military recruits are common. They still are rare just not so rare as in general population.

Methods.

Page 4. Setting. Minor essential. Sentence starting “During the same period…” Needs more detail on timing of the meningitis cases and respiratory cases.

Page 5. Setting. Minor essential. Unclear relationship between IET and AIT. Do they live together? Are they in the same company? Are AIT only in some companies. Is the 554th battalion exclusive to Alpha and Hotel companies. This perhaps would be clarified by a table or a figure.

Page 6. Minor essential. n paragraph on FRI surveillance, the sampling strategy is not clear. It says a portion of trainees are sampled, but does not describe how this portion is selected. Is it random? Distributed across all battalions, and if so why were alpha and hotel companies not sampled in February.

Page 7. Minor essential. Under cross-sectional survey. It is not clear if the alpha company new recruits were tested immediately upon their arrival. Had they been the barracks some time before being sampled? Where did they come from – another military institution with equally close living quarters?

Page 8. Minor essential. The sampling strategy seems to be a mix of those with current illness and those ill in the last month but without recent/current illness. What is the distribution of these two groups. In the Results section it would be interesting to see if their results differed. It is possible that whatever was circulating among trainees at the time of the survey was different from what was causing pneumonia earlier in the month.


Discretionary. Who were the two recruits who died? Did they have underlying conditions? More on their clinical history would be indicated – did they have pneumonia for instance.

Page. 9. Major. It would be helpful to know more about the radiologic pneumonia. What percentage was lobar versus diffuse infiltrates? Particularly as the authors are trying to make a case for pneumococcal pneumonia, it would strengthen it if there was a typical radiologic pattern.

Page 9. Minor essential. Was urine antigen testing done for S. pneumoniae among pneumonia cases?

Page 9. Minor essential. It mentions Chlamydia was found. What about other pathogens tested for in pneumonia patients? Particularly influenza.

Page 9. Minor essential. Only blood culture results for alpha and hotel companies was given. What about blood cultures for other companies with pneumonia cases at same time. Any pneumococcus among them?

Page 9. Minor essential. Only 1 of 21 pneumonia cases were hospitalized. This
seems mild. Can the authors give any other indications of severity of illness. Were they out of work for some time?

Page 10. Major. 35% of FRI surveillance was positive for influenza. What about Chlamydia?

Page 11. Minor essential. It would be useful to know more about post-intervention surveillance. How long did it continue? What sort of case definitions were in place? Was surveillance enhanced? How quickly did the intervention take place? It is marked that no more cases occurred as soon as the intervention began.

Discussion
Page 13. Minor essential. First sentence. It says the pneumonia occurred “after” the meningitis cases. But this does not appear to be so in the epicurve (figure 1). Pneumonia started before meningitis. Please clarify.

Page 13. Major. The evidence for why this was an outbreak of pneumococcal pneumonia does not seem strong.

1. It suggests that because pneumo is the most common bacterial cause of pneumonia in the US, this supports this being a pneumo outbreak. This might be the case in the elderly and children, but pneumo is unlikely to be the case among young adults. Viral and atypical bacteria would likely be more common causes of pneumonia. Please clarify this statement.

2. the pneumo carriage rate of 15% does not seem particularly high among military trainees, which the authors suggest. The proper comparison group seems like it should have been another groups of trainees in a company with a lower attack rate, who living in similar close quarters. The lower carriage rate in the staff and incoming troops might be due to different, less crowded living conditions. Can the others give pneumo carriage rates in other known outbreaks of pneumococcus in military in the literature?

3. The serotype distribution of carried strains seems to be quite broad. The authors suggest that it was a type 7F and 3 outbreak, but there were several other serotypes isolated in almost the same proportion. There does not seem to be enough evidence to call this an outbreak by these two serotypes, especially type 3, which was not found in clinical isolates.

4. Apart from the two meningitis cases, there is lack of evidence for a pneumococcal pneumonia outbreak. There were no isolates from blood; there was no urine antigen testing reported; there was not mention of radiologic patterns consist with pneumococcus; the severity of illness seems mild for pneumococcal pneumonia; there was not a clear serotype predominance in carriage among the affected companies.

As such, it seems the primary implication that this was an outbreak of pneumococcal pneumonia needs to be moderated in terms of these possible limitations.

Page 14. Major. As there was documentation of pneumococcal meningitis, it seems more background on meningitis, particularly due to S. pneumoniae, in military settings is warranted, instead of the lengthy discussion about
pneumococcal pneumonia, which is not documented.

Page 14. Major. First paragraph. More background on Chlamydia pneumoniae seems warranted. How long would it be expected to be positive in the nasopharynx during infection? Would it still be present 1-3 weeks after acute infection? Would it be eradicated from the nasopharynx with antibiotics? Have there been other military outbreaks of Chlamydia?

Page 14. Minor essential. First paragraph. Given the weak evidence for a pneumococcal pneumonia outbreak, the discussion on the interaction between Chlamydia and pneumococcus is speculative.

Page 14. Major. The higher rates of Chlamydia pneumonia in trainees compared with staff and new recruits could also be due to their different living conditions. Another trainee groups without pneumonia would have been useful. This should be mentioned.

Page 14. Minor essential. It is surprising that influenza is not mentioned as a possible cause of the respiratory illness. 35% of FRI patients tested at the same time were positive for flu. Was there other evidence that flu was circulating in this area at the time? The authors should address why they think this was not influenza and give evidence, as at this time of year with concurrent evidence for circulation of flu in FRI cases on the base, it seems this would be the leading etiology of an outbreak of respiratory illness that would need to be ruled out.

Page 15. Minor. Antibiotics in outbreaks are not just to await immunity to develop, but they decrease carriage and reduced transmission.

Page 16. Minor essential. Top. Again, the suggestion of pneumococcal conjugate vaccines and protein vaccines for military recruits seems to be speculative given that there is not clear evidence that this was pneumococcal pneumonia. Might restructure discussion more about Chlamydia pneumoniae and outbreaks in military recruits, and significantly reduce speculative discussion about future pneumococcal vaccines in this population.

Figure 1. Minor essential. It is unclear if the date given is onset date or date of diagnosis. Is the increase in cases at the time the camp was set up an indication of increased diagnosis at that time, or was the really the date of onset for those cases. Also it would be good to show (or tell in legend) how long surveillance when on before and after the outbreak dates shown and if any cases were found.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
None