THE AMERICAN JOURNAL of MEDICINE®

The Reply

We thank Cunha et al for their interesting response and for proposing additional risk factors for early rule out of *Legionella* pneumonia on the basis of their experience. In the original derivation study, we evaluated different previously published predictors for *Legionella*, including C-reactive protein, creatinine kinase, hemoglobinuria, white blood count, and thrombocytopenia, among others.[1] We used multivariate regression analysis and selected a parsimonious set of 6 predictors that showed a high discriminatory value in the initial cohort[1] and in the recently published multinational validation cohort with an area under the curve of 0.91.[2] Therefore, the proposed score seems robust and gives clinicians an estimate of the probability that a patient presenting with pneumonia has *Legionella* disease.

In accordance with the predictors proposed by Cunha et al, fever and high C-reactive protein were independent predictors in the original study,[1] whereas hematuria showed a positive correlation only in univariate analysis. Of note, slight thrombocytopenia was found to be positively correlated in the original study but lost significance in multivariate analysis in the validation study,[2] while being used as a "laboratory eliminator" by Cunha et al. We cannot comment on erythrocyte sedimentation rate, ferritin and serum phosphate levels, or clinical features such as sore throat and myalgias because these were not analyzed. Elevated liver enzymes were correlated positively in univariate analysis in the original study. One might hypothesize that ferritin would act in the same way, but we do not have such data. **Table** shows a comparison of all variables.

Whether the proposed score could be further improved by the inclusion of additional predictors as proposed by Cunha et al is an interesting hypothesis and should be evaluated in future prospective studies, ideally using the same scoring methodology as described earlier. Also, instead of erythrocyte sedimentation rate, procalcitonin may be an interesting predictor in *Legionella* as proposed in the previous studies.[3] In the meantime, we believe that our score may help to optimize initial empiric therapy strategies in patients presenting with pneumonia. Of note, a recent application ("Biomarker") that is available free of charge in the iTunes store allows clinicians to easily enter the 6 predictors and calculates the probability of *Legionella* on the basis of our score.

Funding: None.

Conflict of Interest: BM and PS received support from BRAHMS to attend meetings and fulfill speaking engagements. BM has served as a consultant and received research support.

Authorship: All authors had access to the data and played a role in writing this manuscript.

Table Comparison of Variables Between the Mentioned Studies

Predictors and Eliminators Proposed by Cunha et al	Original Study[1]/Database	Validation Study[2]/Database
Predictors		
Core temperature >102°F/38.9°C	Yes (part of score, cutoff >102.9°F/39.4°C)	Yes (part of score)
ESR >90 mm/h or CRP >180 mg/L	CRP: yes (part of score; cutoff >187 mg/L); no data available for ESR	CRP: yes (part of score); no data available for ESR
Serum ferritin >2× normal	No data available	No data available
Serum phosphate less than normal	No data available	No data available
Creatinine phosphokinase >2× normal	No data available	No data available
Microscopic hematuria	Yes (univariate OR, 2.95; 95% CI, 1.64-5.32, but lost significance in multivariate analysis)	No data available
Eliminators		
Sore throat	No data available	No data available
Severe myalgias	No data available	No data available
Leukopenia	Yes, but not analyzed	Yes, but not analyzed
Thrombocytopenia	Yes (part of score); but as predictor!	Yes (part of score)
Infiltrate in chest radiograph	Yes (inclusion criterion)	Yes (inclusion criterion)

CI = confidence interval; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; OR = odds ratio.

Sebastian Haubitz, MD[a]
Chistoph Andreas Fux, MD[b,c]
Beat Mueller, MD[b]
Philipp Schuetz, MD, MPH[b]
[a]*University Clinic of Infectious Diseases*
University Hospital Bern
Bern, Switzerland
[b]*Medical University Clinic*
Kantonsspital Aarau
Aarau, Switzerland
[c]*Clinic for Infectious Diseases*
Kantonsspital Aarau
Aarau, Switzerland

http://dx.doi.org/10.1016/j.amjmed.2015.03.004

References

1. Fiumefreddo R, Zaborsky R, Haeuptle J, et al. Clinical predictors for Legionella in patients presenting with community-acquired pneumonia to the emergency department. *BMC Pulm Med*. 2009;9:4.
2. Haubitz S, Hitz F, Graedel L, et al. Ruling out Legionella in community-acquired pneumonia. *Am J Med*. 2014;127:1010.e11-1010.e19.
3. Haeuptle J, Zaborsky R, Fiumefreddo R, et al. Prognostic value of procalcitonin in Legionella pneumonia. *Eur J Clin Microbiol Infect Dis*. 2009;28:55-60.