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## PRESS RELEASE

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Media contact: Dr Anka Stegmeier-Petroianu

[pressofficer@ersnet.org](mailto:pressofficer@ersnet.org)

### **Pneumonia: a heated response may be better in the long term**

**High fever and chills in patients presenting with pneumonia may be a good sign according to a recent Swiss study. The findings to be published ahead of print in the *European Respiratory Journal*, the official scientific publication of the *European Respiratory Society*, suggest a better long-term prognosis for those patients suffering from pneumonia who exhibit more pronounced proinflammatory responses reflected by chills, high body temperature and high peak levels of the inflammatory blood marker C-reactive protein (CRP). In addition, a new serum biomarker, adrenomedullin, may be useful in identifying high-risk patients.**

Pneumonia that is contracted outside the hospital setting, so-called community-acquired pneumonia (CAP), continues to be a leading cause of death worldwide especially in elderly patients, or those with preexisting lung disease or other comorbidities.

While the short-term mortality (within 30 days of being diagnosed with pneumonia) is well documented in the literature, less is known about the long-term prognosis of these patients. Previous data suggest that patients who survive an initial episode of community-acquired pneumonia are at increased risk of mortality and recurrent infections in the months subsequent to hospital discharge, especially in patients over 40 years of age.

The study included 877 patients with community-acquired pneumonia who had been hospitalised, and who were then followed-up for a total of 18 months. Almost all patients had comorbidities, such as chronic obstructive pulmonary disease (COPD), coronary heart disease, diabetes or renal disease. Their

initial risk had been assessed by using the pneumonia severity index (PSI), a clinical prediction tool that is employed to calculate the probability of morbidity and mortality among patients with community-acquired pneumonia. The PSI is largely age-driven and incorporates important comorbidities which may explain its long-term prognostic performance.

Professor Beat Mueller of the Kantonsspital Aarau, Switzerland and his colleagues found that initial risk assessment with PSI had been accurate to predict long-term mortality. In the study, overall mortality (all-cause mortality) was 17.3% (95%CI 14.8-19.8) with a 12.8% (95%CI 10.9%-15.0%) mortality incidence rate per year.

However, the authors point out that PSI may not be optimal for assessing long-term prognosis because it includes severity criteria of the infection – such as body temperature– which may be associated with short-term mortality, but not adverse long-term prognosis, as the present study has shown.

“An interesting finding of this study is that the extent of inflammatory host response mirrored by a history of chills, high initial body temperature, and high peak levels of CRP were protective for long-term survival. This was also true when adjusted for potential confounders such as age and comorbidities.”

“This finding is somewhat counterintuitive as most studies have shown that a strong inflammatory response is associated with adverse short-term outcomes. It is tempting to hypothesise that survival of a clinically and biochemically pronounced CAP may mirror a more robust host defence and a better general condition with resulting lower complications at long-term in this population.”

In contrast, high levels of another serum biomarker, the vasoactive peptide pro-adrenomedullin (proADM) seem to predict severity and indicate a high mortality risk in patients with community-acquired pneumonia.

Adrenomedullin (ADM) is a very promising prognostic biomarker in patients with infections, and also in patients with cardiovascular disease for prediction of short term adverse events and mortality. It is a very potent vasodilating agent with additional immune modulating and metabolic properties.

However, measurement of ADM is challenging, since it is rapidly cleared from the circulation. For this reason the authors did not measure ADM directly, but instead used a new sandwich immuno-assay that has recently been developed, which measures the more stable mid regional fragment of pro-adrenomedullin (proADM), explains Dr Philipp Schütz of the Harvard School of Public Health & Beth Israel Deaconess Medical Center (BIDMC), Department of Emergency Medicine in Boston, USA.

In the study, male sex, pre-existing chronic obstructive pulmonary disease, cancer and the highest quartile of peak proADM levels (>1.97nmol/l) were independently associated with mortality. Conversely, history of chills, highest temperature quartile (>38.7°C) and highest quartile of peak CRP levels (>265mg/dl) were associated independently with a lower mortality risk.

Different clinical studies have shown that proADM levels measured on admission accurately predicted short term mortality risk in patients – similar to well established and complex clinical risk scores – such as the Pneumonia Severity Index. Importantly, previous studies investigated only short term mortality

risks associated with increased proADM; within this long term follow up cohort, proADM was still very accurate for mortality prediction in the long-term, which is a new and newsworthy finding.

It remains unclear whether the association of high proADM level and lower long-term survival reflects a more severe initial infection, or whether it is due to a worse general condition of the patient associated with impaired immune function leading to a more rapidly spreading respiratory infection (or both), the authors write.

Despite clinical recovery after suffering from pneumonia, many patients leave the hospital with ongoing inflammation, and this residual inflammation may be associated with an increased risk of death in the follow-up. A closer follow-up in patients at highest risk may translate into better outcomes, the physicians conclude.

Contact: (For journalists' personal use only, not for publication)

Prof. Beat Mueller, Department of Internal Medicine, Kantonsspital Aarau, Aarau, Switzerland

Email: [Happy.mueller@unibas.ch](mailto:Happy.mueller@unibas.ch)

Or

Dr. Philipp Schuetz, Harvard School of Public Health, Boston, USA

Email: [pschuetz@HSPH.harvard.edu](mailto:pschuetz@HSPH.harvard.edu)

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