

## CORRESPONDENCE



## Zoonotic *Chlamydia caviae* Presenting as Community-Acquired Pneumonia

**TO THE EDITOR:** *Chlamydia caviae* is a member of the family of gram-negative intracellular bacteria Chlamydiaceae. Bacteria of this family cause a broad spectrum of diseases in animals and humans and are currently subdivided into a single genus and 11 species.<sup>1</sup> Among these species, *C. psittaci* and *C. abortus* are known for their zoonotic potential, causing psittacosis and abortion, respectively, in humans.<sup>2,3</sup> In contrast, only one case of mild conjunctivitis has previously been documented in association with *C. caviae*.<sup>4</sup>

We describe three unrelated cases of infection in otherwise healthy adults in their early 30s who had respiratory failure caused by severe community-acquired pneumonia (see chest radiographs in Section S1 of the Supplementary Appendix, available with the full text of this letter at [NEJM.org](http://NEJM.org)) after exposure to ill guinea pigs (Table 1). The three cases, which appeared over a period of approximately 3 years, occurred in persons from different families, at different hospitals, and in different geographic areas. Two patients were treated with mechanical ventilation in the intensive care unit for several days.

Chlamydia DNA was detected in specimens obtained from the respiratory tract, serum, or both in all three patients, and the species was identified as *C. caviae* by means of the Dutch

national surveillance system for psittacosis, in which samples identified as positive in a polymerase-chain-reaction assay are genotyped by sequencing a part of the gene that encodes the outer membrane protein A, *ompA*<sup>5</sup> (details are provided in Sections S2 and S3 in the Supplementary Appendix). In one patient, chlamydia seroconversion was detected by means of complement fixation, which revealed an increase in the antibody titer by a factor of 4 (see Section S3 in the Supplementary Appendix for details). No other causes of community-acquired pneumonia were found (see Section S4 in the Supplementary Appendix). Although different antibiotic regimens were used to treat the patients, in accordance with local protocols (Table 1), all three patients recovered after being treated with doxycycline.

One of the guinea pigs owned by Patient 2 showed signs of respiratory illness before community-acquired pneumonia developed in the patient. *C. caviae* was isolated from a conjunctival swab. To confirm transmission between this guinea pig and its keeper, we performed a tandem repeat analysis and sequenced the *ompA* coding region in a sample of the patient's bronchoalveolar lavage fluid (GenBank accession numbers, KY777669 and KY777670), the guinea pig isolate (GenBank numbers, KY777661 and KY777662), and several samples from other *C. caviae* strains (GenBank numbers, KY777663–KY777668). The sequences of *ompA* and the single variable-number tandem-repeat (VNTR) region that were identified (from among 27 potential VNTRs) were identical in the bronchoalveolar lavage fluid from the patient and her guinea pig and different from the *C. caviae* reference strain GPIC (GenBank accession number, AE015925; details are provided in Sections S5 through S10 in the Supplementary Appendix). This finding is in line

### THIS WEEK'S LETTERS

- 992 Zoonotic *Chlamydia caviae* Presenting as Community-Acquired Pneumonia
- 994 Early, Goal-Directed Therapy for Septic Shock — A Patient-Level Meta-Analysis
- 996 Buprenorphine for the Neonatal Abstinence Syndrome

**Table 1. Patient Data and Findings.\***

Characteristics	Patient 1	Patient 2	Patient 3
<b>Before hospitalization</b>			
Appearance of symptoms	February 2013	September 2014	September 2015
Age (yr)	32	31	34
Sex	Male	Female	Female
Medical history	Unremarkable	Traumatic epidural hematoma (in 1991), post-traumatic stress disorder, and obesity	Fibromyalgia
Clinical signs	Fever, malaise, coughing, headache, myalgia	Fever, coughing, shortness of breath, myalgia	Fever, headache, drowsiness, nausea, vomiting, abdominal pain
Treatment	No response to amoxicillin–clavulanic acid plus NSAIDs, prescribed by general practitioner	No response to amoxicillin–clavulanic acid plus NSAIDs, prescribed by general practitioner	No treatment
Diagnosis	Pneumonia and severe respiratory insufficiency; hospitalization needed	Pneumonia and severe respiratory insufficiency; hospitalization needed	Pneumonia; hospitalization needed
<b>During hospitalization</b>			
Clinical situation	ICU admission, mechanical ventilation	ICU admission, mechanical ventilation	Admission to general ward
Laboratory findings			
C-reactive protein (mg/liter)	485	379	212
Reference range at local hospital	≤8	≤8	≤5
White-cell count (per mm <sup>3</sup> )	13,300	3600	NA
Reference range at local hospital	4000–10,000	4000–10,000	NA
Sodium (mmol/liter)	131	NA	NA
Reference range at local hospital	135–145	NA	NA
Alkaline phosphatase (U/liter)	NA	294	171
Reference range at local hospital	NA	33–98	0–120
Alanine aminotransferase (IU/liter)	NA	NA	43
Reference range at local hospital	NA	111	<35
γ-Glutamyltransferase (U/liter)	NA	<38	NA
Reference range at local hospital	NA	420	NA
Lactate dehydrogenase (U/liter)	NA	<247	NA
Reference range at local hospital			
Diagnostic measures	Radiography and examination of bronchoalveolar lavage fluid followed by positive PCR assay for <i>Chlamydia psittaci</i> ; further typing revealed <i>C. caviae</i>	Radiography and examination of bronchoalveolar lavage fluid followed by positive PCR assay for <i>C. psittaci</i> ; further typing revealed <i>C. caviae</i>	Radiography and sputum smear followed by positive PCR assay for <i>C. psittaci</i> ; further typing revealed <i>C. caviae</i>
Treatment	Ceftriaxone plus ciprofloxacin, followed by ceftriaxone plus doxycycline, followed by meropenem plus doxycycline	Penicillin plus ciprofloxacin, followed by doxycycline plus ciprofloxacin	Amoxicillin plus ciprofloxacin, followed by doxycycline
Additional anamnesis	2 Guinea pigs at home that had respiratory symptoms before development of patient's community-acquired pneumonia	25 Guinea pigs at home that had respiratory symptoms before development of patient's community-acquired pneumonia	Guinea pigs with conjunctivitis and rhinitis and a dyspnoeic, indolent wild rabbit at workplace (a veterinary clinic)

\* ICU denotes intensive care unit, NA not available, NSAIDs nonsteroidal antiinflammatory drugs, and PCR polymerase chain reaction.

with a *C. caviae* transmission event, although the molecular features described (see Sections S8 through S10 in the Supplementary Appendix) were not unique but were shared with two German *C. caviae* strains.

Altogether, the data imply that the transmission of *C. caviae* from guinea pig to human in these cases resulted in severe community-acquired pneumonia. Both veterinarians and physicians should be aware of the zoonotic potential of *C. caviae*. Although the extent to which *C. caviae* actually contributes to community-acquired pneumonia is unclear, awareness may help to clarify this issue.

Bart P. Ramakers, M.D., Ph.D.

Bernhoven  
Uden, the Netherlands

Marloes Heijne, D.V.M.

Wageningen Bioveterinary Research  
Lelystad, the Netherlands  
marloes.heijne@wur.nl

Natascha Lie, M.D.

Zuyderland Medical Center  
Heerlen, the Netherlands

Thuy-Nga Le, M.D.

Gelderse Vallei Hospital  
Ede, the Netherlands

Monique van Vliet, M.D.

Zuyderland Medical Center  
Heerlen, the Netherlands

Vivian P.J. Claessen, M.D.

Municipal Health Service South Limburg  
Geleen, the Netherlands

Paulien J.P. Tolsma, M.D.

Municipal Health Service Brabant Hart voor Brabant  
Den Bosch, the Netherlands

Mauro De Rosa, M.D.

Dutch Food and Health Authority (NVWA)  
Utrecht, the Netherlands

Hendrik I.J. Roest, D.V.M., Ph.D.

Wageningen Bioveterinary Research  
Lelystad, the Netherlands

Daisy Vanrompay, Ph.D.

Ghent University  
Ghent, Belgium

Edou R. Heddema, M.D., Ph.D.

Zuyderland Medical Center  
Sittard-Geleen, the Netherlands

Peter Schneeberger, M.D., Ph.D.

Mirjam H.A. Hermans, Ph.D.

Jeroen Bosch Hospital  
Den Bosch, the Netherlands

Drs. Ramakers and Heijne contributed equally to this letter.

Supported by a grant from the Dutch Ministry of Health, Welfare, and Sport through the National Institute for Public Health and the Environment, Bilthoven, the Netherlands (3910014586).

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

1. Sachse K, Bavoi PM, Kaltenboeck B, et al. Emendation of the family Chlamydiaceae: proposal of a single genus, Chlamydia, to include all currently recognized species. *Syst Appl Microbiol* 2015; 38:99-103.

2. Pospischil A, Thoma R, Hilbe M, Grest P, Zimmermann D, Gebbers JO. Abortion in humans caused by *Chlamydia abortus* (*Chlamydia psittaci* serovar 1). *Schweiz Arch Tierheilkd* 2002;144:463-6. (In German.)

3. Beekman DS, Vanrompay DC. Zoonotic *Chlamydia psittaci* infections from a clinical perspective. *Clin Microbiol Infect* 2009;15:11-7.

4. Lutz-Wohlgroth L, Becker A, Brugnera E, et al. Chlamydiales in guinea-pigs and their zoonotic potential. *J Vet Med A Physiol Pathol Clin Med* 2006;53:185-93.

5. Heddema ER, van Hannen EJ, Bongaerts M, et al. Typing of *Chlamydia psittaci* to monitor epidemiology of psittacosis and aid disease control in the Netherlands, 2008 to 2013. *Euro Surveill* 2015;20:21026.

DOI: 10.1056/NEJMc1702983

---

## Early, Goal-Directed Therapy for Septic Shock — A Patient-Level Meta-Analysis

**TO THE EDITOR:** In reporting the results of their meta-analysis of individual patient data from three trials, the Protocolized Resuscitation in Sepsis Meta-Analysis (PRISM) investigators (June 8 issue)<sup>1</sup> conclude that early, goal-directed therapy (EGDT) did not result in better outcomes than usual care in the resuscitation of patients with septic shock. I was hoping that the meta-analysis

would answer an important question — what is usual care? EGDT is a well-defined intervention to guide hemodynamic resuscitation according to targets for central venous pressure, mean arterial blood pressure, urinary output, and central venous oxygen saturation.

Which monitoring tools and hemodynamic targets (other than central venous pressure, mean