Nosocomial Transmission of Human Granulocytic Anaplasmosis in China

Lijuan Zhang, MD, PhD
Yan Liu, MD
Daxin Ni, MD
Qun Li, MD
Yanlin Yu, MD
Xue-jie Yu, MD, PhD
Kanglin Wan, MD, PhD
Dexin Li, MD
Guodong Liang, MD
Xingao Jiang, MD
Huaqi Jing, MD
Jing Run, MD
Mingchun Luan, MD
Xiuping Fu, MD
Jingshan Zhang
Weizhong Yang, MD
Yu Wang, MD, PhD
J. Stephen Dumler, MD
Zijian Feng, MD
Jun Ren, MD
Jing Run, MD
Jianxi Xu, MD, PhD

Context Human granulocytic anaplasmosis (HGA) is an emerging tick-borne disease in China. A cluster of cases among health care workers and family members following exposure to a patient with fulminant disease consistent with HGA prompted investigation.

Objective To investigate the origin and transmission of apparent nosocomial cases of febrile illness in the Anhui Province.

Design, Setting, and Patients After exposure to an index patient whose fatal illness was characterized by fever and hemorrhage at a primary care hospital and regional tertiary care hospital’s isolation ward, secondary cases with febrile illness who were suspected of being exposed were tested for antibodies against *Anaplasma phagocytophilum* and by polymerase chain reaction (PCR) and DNA sequencing for *A. phagocytophilum* DNA. Potential sources of exposure were investigated.

Main Outcome Measure Cases with serological or PCR evidence of HGA were compared with uninfected contacts to define the attack rate, relative risk of illness, and potential risks for exposure during the provision of care to the index patient.

Results In a regional hospital of Anhui Province, China, between November 9 and 17, 2006, a cluster of 9 febrile patients with leukopenia, thrombocytopenia, and elevated serum aminotransferase levels were diagnosed with HGA by PCR for *A. phagocytophilum* DNA in peripheral blood and by seroconversion to *A. phagocytophilum*. No patients had tick bites. All 9 patients had contact with the index patient within 12 hours of her death from suspected fatal HGA while she experienced extensive hemorrhage and underwent endotracheal intubation. The attack rate was 32.1% vs 0% (P=.04) among contacts exposed at 50 cm or closer, 45% vs 0% (P=.001) among those exposed for more than 2 hours, 75% vs 0% (P<.001) among those reporting contact with blood secretions, and 87.5% vs 0% (P=.004) among those reporting contact with respiratory secretions from the index patient.

Conclusion We report the identification of HGA in China and likely nosocomial transmission of HGA from direct contact with blood or respiratory secretions.

JAMA. 2008;300(19):2263-2270 www.jama.com

©2008 American Medical Association. All rights reserved.
ported from countries in Europe, where the median seroprevalence rate is 6.2%, similar to that in North America. Se-
erological and molecular evidence also suggests that human infection exists in Korea, Japan, and China. Herein, we report the first cases of HGA acquired in China, as well as the usual finding of nosocomial human-to-human transmission.

**METHODS**

**Laboratory Diagnosis**

Patients suspected of HGA exposure were tested for serum IgG to *A phagocytophilum* using the IgG IFA kit (Focus Diagnostics, Cypress, California), screening at a 1:64 dilution and titrating if reactive.13 Nested polymerase chain reaction (PCR) using blood DNA (QIAamp DNA Mini Kit, QIAGEN, Hilden, Germany) was used to detect *A phagocytophilum* DNA with Anaplasma and Ehrlichia genus-common and *A phagocytophilum* species-specific rrs primers (16S rRNA gene),16 and *A phagocytophilum* species-specific groEL primers.17 An *A phagocytophilum* rrs plasmid and DNA from healthy people or distilled water were used as controls. Positive reactions were confirmed by direct sequencing. Polymerase chain reaction was conducted in 2 independent laboratories, the National Institute for Communicable Disease Control and Prevention in Beijing, and at the Anhui Province Center for Disease Prevention and Control in Hefei city. Each laboratory used its own primers, reagents, and patient blood DNA. All samples were tested concurrently with negative and no template controls (water) under the same conditions. Polymerase chain reaction samples from healthy people and negative controls consistently had negative results.

To exclude other infections, serological, antigen detection, and PCR diagnostic tests were conducted. These included tests on blood from the first 3 to 5 days after onset for reverse transcription (RT)-PCR of PCR for nucleic acids of Lassa fever virus, Ebola virus, Marburg virus, Hantaan virus, Junin virus, yellow fever virus, Crimean-Congo hemorrhagic fever virus, coxsackievirus, respiratory syncytial virus, adenovirus, *Mycoplasma pneumoniae*, *Chlamydia* species, *Ehrlichia* species, *Rickettsia* species, and *Orientia tsutsugamushi*.

Tests were also conducted on oropharyngeal swabs from the first 3 to 5 days after onset for influenza A virus antigens, and by PCR for influenza A viruses, influenza B virus, and influenza virus subtype H5 nucleic acids. Tests for acute-phase serum were conducted to detect IgM and IgG to severe acute respiratory syndrome virus, as well as to detect IgM or IgM plus IgG antibodies by capture enzyme-linked immunosorbent assay against Bunyaviridae, Filoviridae, Lassa fever virus, Ebola virus, Marburg virus, Hantaan virus, Junin virus, yellow fever virus, and Crimean-Congo hemorrhagic fever virus.

**Epidemiological Investigation**

All contacts of the index patient, including patients with similar clinical presentations and healthy persons, were interviewed before laboratory diagnostic results were obtained. A possible case of HGA was defined as a patient with a clinically compatible illness (fever, headache, chills) and laboratory findings including thrombocytopenia and leukopenia but who lacked serological or molecular tests for *A phagocyto-

philum*. A confirmed case was defined as a patient with a clinically compatible illness (as above) and in keeping with the US Centers for Disease Control and Prevention (CDC) criteria (http://www.cdc.gov/ncphi/diss/nndss/casedef/ehrlichiosis_2008.htm) by either seroconversion, a 4-fold increase in *A phagocytophilum* IgG antibody titer in acute and convalescent sera, or a positive PCR result for both *A phagocytophilum* rrs and groEL confirmed by direct sequence analysis.15

**Contact Questionnaire**

All contacts of the index patient were asked to complete a questionnaire about their health status and profession; experience with tick bites; exposure to the index patient—where, when, and how they had contact; exposure to wild animals; extent of outdoor activity; exposure to the index patient’s blood and respiratory secretions or to grossly bloody oropharyngeal secretions; presence of skin lesions during exposure; whether skin surfaces were washed after exposure; whether they were exposed to the patient’s stool or urine; and the timing of these events. Health care workers were asked about their use of masks and gloves.

**Ethical and Human Subjects Review**

The study was approved by the ethics committee of China CDC, according to the medical research regulations of Ministry of Health, China. Oral informed consent was obtained from all study participants.

**Statistical Analysis**

All statistical calculations were performed using Epi Info 6.04d (http://www.cdc.gov/epiinfo). To identify specific exposure risk factors, retrospective cohort comparisons were evaluated by calculating attack rates, relative risk, and 95% confidence intervals and by Fisher exact test; significance was defined as a 2-tailed P < .05.

**RESULTS**

**Index Case**

A 50-year-old woman with a 1-day abrupt onset of sudden fever (39.2°C), headache, myalgia, arthralgia, dizziness, and malaise presented to the village clinic on October 31, 2006, and was treated with ribavirin, cephalothin, dexamethasone, and amidopyrine for 4 days. At 9 PM on November 3, she was admitted to the local hospital because of gum bleeding, facial edema, nausea, vomiting, and oliguria, a temperature of 39.7°C, blood pressure of 85/60 mm Hg, and pulse rate of 96/min; a rash was noted over her trunk. Laboratory testing showed leukopenia (white blood cell count, 3300/µL), thrombocytopenia (platelet count, 18 × 10³/µL), elevated serum aspartate aminotransferase...
shown in the onset of illness. A timeline of events is “wild animal carcasses” 3 days before band had hunted and brought home 9 days before onset, and her husband: she had killed several mice in her ten by a tick 12 days before onset of fe-

Her condition progressively deteriorated, so she was transferred to a regional hospital at 11 AM, November 4. By 7 PM, the patient became obtunded, cyanotic, and purpuric and was bleeding from her nose and mouth. This extensive mouth and nose bleeding re-
quired frequent aspiration and con-
taminated the working area surfaces, health care workers, and family mem-
bers who were with her. Family mem-
bers assisted with patient care by wip-
ing blood from the patient’s mouth and nose, rinsing and reusing the same tow-
els. By 7:38 PM the patient developed rapidly progressive dyspnea and wors-
ening oxygen saturation and required endotracheal intubation. The patient re-
ained hypoxic and hypotensive with multiorgan failure and copious bleed-
ing from the nose and mouth. Despite all efforts, the patient died at 6:45 AM, November 5, 2006. The final diagno-
sis was hemorrhagic fever with renal syndrome, even though no IgG anti-
bodies to Hantaan virus were de-
tected. A postmortem examination was not performed, and no blood or tissue samples remained for retrospective laboratory testing.

Retrospective questioning of the pa-
tient’s family revealed that she was bitten by a tick 12 days before onset of fe-
ver: she had killed several mice in her home 9 days before onset, and her hus-
band had hunted and brought home “wild animal carcasses” 3 days before onset of illness. A timeline of events is shown in the FIGURE.

Nosocomial Cases of HGA

Between November 9 and 17, 2006, 9 patients were identified at the regional hospital with fever higher than 38.0°C (9 of 9 patients), myalgia (5 of 9), diarrhea (7 of 9), leukopenia (white blood cell count, 1200-3700/µL in 9 of 9), thrombocytopenia (platelets, 39-115 × 10^6/µL in all 9), and elevated serum aspartate aminotransferase and alanine aminotransferase (7 of 9) (TABLE 1). All patients had contact with the index patient, including 5 family members, 2 physicians, and 2 nurses who had accompanied or treated her between November 4 and 5 (Figure).

The initial secondary case experienced fever on November 9, 4 days after death of the index case, followed on November 11 by another patient, on November 12 by 3 patients, and on No-

November 14 by 3 more patients. The last patient reported illness on November 17, 12 days after the death of the in-
dex patient. The patients were be-
tween 25 and 67 years (mean, 36.2 years), and 6 were men. All were pre-
viously healthy. The average incuba-
tion period was 7.8 days (range, 4-12 days). All had fever of at least 38.5°C for 1 to 6 days (mean, 4 days). Diar-

rhea was characterized as 1 to 3 loose stools per day persisting for 1 to 2 days. All patients had relative bradycardia. One patient developed acute respira-
tory distress syndrome as a complica-
tion of Aspergillus pneumonia and tu-
erculosis during his hospitalization. The other 8 patients were mildly af-
fected, recovered, and were dis-
charged in good health.

Contact Investigation

The index patient had contact with 63 persons after onset of illness: 21 family members and 42 health care workers. Of the 42 health care workers, 18 were from the local hospital, including 2 from the village clinic, and 24 were from the re-
gional hospital. Of the 21 family mem-
bers, 4 had contact with the index pa-
tient in only the local hospital, 13 only in the regional hospital, and 4 in both. The 9 secondary cases occurred among the 39 health care workers and rela-
tives with patient exposure at the re-
gional hospital, representing an attack rate of 23%. All 9 cared for the index case in the final 12 hours of her life while she was in the critical care unit and during the endotracheal intubation pro-
dure. No one whose only contact with the index patient was before these 12 hours was infected.

Serological and Molecular Diagnosis

Anaplasma phagocytophilum IgG sero-

conversions were detected for all 9 pa-

tients, and a 4-fold IgG titer increase 

was observed in 7 of 9 patients (Table 1). Nested PCR using genus-

common rrs and species-specific rrs and groEL primers identified A phagocyto-

philum DNA in the blood samples from all 9 patients when they were in the acute phase, whereas all healthy and template controls had negative test results. The identity of amplicons from each of the 9 patients was confirmed by sequencing; all rrs sequences (206 base pairs) were identical and all groEL se-

quences (446 nt) were identical (Gen-

Bank accession numbers: rrs EF211110-17 and EF473210; groEL EF47320108 and EF473209). Although the rrs sequences were identical to most other human-derived strains globally, sequences from groEL were identical to some US strains (Wiscon-
sin and New York) but differed from A phagocytophilum in China (93.6%; EU008083), Germany (99.4%; AY281850), and California (99.7%; U96727). These data support the premise that a single clone was responsible for all of the 9 secondary cases. Al-

though peripheral blood smears were 

examined for all 9 patients at the time of illness, no convincing evidence of A phagocytophilum morulae was ob-

served. All RT-PCR, PCR, antigen de-
tection, and IgM antibody detection tests for microbial and viral etiologies were negative.

Risk Factors

The exposure data implicate transmis-

sion at the regional hospital, permit-
ting focus on risk factors in 39 indi-

viduals, including 24 health care workers and 15 family members (TABLE 2). Two family members who
Figure. Timeline of Critical Events for the Index Patient and Direct Contact Intervals of Family Members and Health Care Workers With the Index Patient and Exposure of Patients With Nosocomial Human Granulytic Anaplasmosis

Top, epidemic curve showing progression of outbreak and key events during the index patient’s illness. Bottom, each bar indicates the period of potential exposure while family members were in the hospital and while health care workers were assigned to care for the index patient. Duration of exposure in minutes is shown in parentheses and may not have occurred continuously during the exposure period. Capital letters designate the corresponding secondary cases in the top and bottom panels.
had contact with the index case after her death were not included.
None of the 9 secondary cases reported tick bites, exposure to wild animals, or participation in hunting activity in the preceding 2 months, and only 1 reported recent outdoor activity. For all 9 secondary cases, culture serological, antigen detection, and nucleic acid detection studies for other infectious etiologies were negative.

Of 24 regional hospital health care workers who had contact with the index patient, 18 were on duty during the final 12 hours, and 4 of the 18 who were involved in the endotracheal intubation were infected. Of these 4, 3 were involved in endotracheal intubation and care during times of hemorrhage. Sixteen of 24 health care workers (67%) from the regional hospital wore masks and 9 of 24 (38%) wore gloves.

Of 24 regional hospital health care workers who had contact with the index patient, 18 were on duty during the final 12 hours, and 4 of the 18 who were involved in the endotracheal intubation were infected. Of these 4, 3 were involved in endotracheal intubation and care during times of hemorrhage. Sixteen of 24 health care workers (67%) from the regional hospital wore masks and 9 of 24 (38%) wore gloves.

Of 17 family members who reported contact with the index patient at the regional hospital, 13 were present during endotracheal intubation, 5 of whom were infected. Of these 5 individuals, 3 reported blood contamination of skin and possible mucocutaneous exposures, suggesting direct contact with blood or respiratory secretions as the mechanism of transmission.

Among the 28 individuals who reported close contact (≤50 cm) with the index patient during the final 12 hours of her life, 9 were infected. In contrast, none of the 11 individuals who reported a physical distance of more than 50 cm from the index patient during the same time was infected. The index patient was exposed to 20 contacts for more than 2 hours, and 9 were infected, whereas none of 19 contacts exposed fewer than 2 hours was infected. All 9 infected patients reported contact with blood ($P = .002$) and 7 had contact with respiratory secretions (relative risk, 7.0; 95% confidence interval, 1.7-29.1; Table 2). Those persons with skin exposure to blood ($P < .001$) or respiratory secretions ($P = .004$), or those with preexisting skin lesions or injuries followed by exposure to blood (relative risk, 3.6; 95% confidence interval, 1.1-7.6; $P = .02$) were significantly more likely to be infected (Table 3). Neither exposure to stool nor exposure to

<table>
<thead>
<tr>
<th>Clinical findings</th>
<th>Infected Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical findings&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2</td>
</tr>
<tr>
<td>Days hospitalized</td>
<td>19</td>
</tr>
<tr>
<td>Temperature ≥38.5°C</td>
<td>Yes</td>
</tr>
<tr>
<td>Malaise</td>
<td>Yes</td>
</tr>
<tr>
<td>Chills</td>
<td>Yes</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Yes</td>
</tr>
<tr>
<td>Myalgia</td>
<td>Yes</td>
</tr>
<tr>
<td>Coryza/pharyngitis</td>
<td>No</td>
</tr>
<tr>
<td>Headache</td>
<td>Yes</td>
</tr>
<tr>
<td>Nausea</td>
<td>No</td>
</tr>
<tr>
<td>Edema</td>
<td>No</td>
</tr>
<tr>
<td>Gum bleeding</td>
<td>No</td>
</tr>
<tr>
<td>Dysuria</td>
<td>No</td>
</tr>
<tr>
<td>Laboratory values</td>
<td>2600</td>
</tr>
<tr>
<td>Lowest blood count, range of normal</td>
<td>150-350 × 10&lt;sup&gt;3&lt;/sup&gt;/µL&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Anaplasma phagocytophilum IgG titers</td>
<td>252</td>
</tr>
<tr>
<td>ALT, men &lt;40; women &lt;31</td>
<td>84</td>
</tr>
<tr>
<td>ALT, men &lt;40; women &lt;31</td>
<td>84</td>
</tr>
<tr>
<td>ALT, men &lt;40; women &lt;31</td>
<td>84</td>
</tr>
</tbody>
</table>

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ND, not done; PCR, polymerase chain reaction.
*Clinical findings that were documented during the course of each patient’s hospitalization.*
urine from the index case resulted in increased risk (0.6 and 1.1, respectively).

**COMMENT**

Nine cases of *A phagocytophilum* infection were confirmed at the regional hospital in the Anhui Province of China in a 9-day period. All presented with HGA as described in North America and Europe, and fulfilled the US CDC laboratory criteria for the diagnosis of HGA. The most remarkable aspect of these cases was that transmission was very unlikely to be tick-borne, but was closely associated with blood or respiratory secretion exposure from an index patient who died of a fulminant febrile illness with hemorrhage. Although the index patient can only be categorized as a possible case, clinical and historical support for the diagnosis of HGA is strong. She had a tick bite within the known incubation period and had a clinical presentation compatible with severe HGA. Moreover, the epidemiological investigation of exposed individuals with HGA implicates her as the index case. Unfortunately, no tissue or serum sample is available to confirm retrospectively her diagnosis.

Human granulocytic anaplasmosis and human monocytic ehrlichiosis were initially identified with presentations now recognized as relatively uncommon for their natural histories. Infection can be severe, with intensive care unit admission required in 7% of patients and fatalities occurring in up to 1%, yet most infections are sporadic and probably self-limited. Based on the mild to moderate severity observed in 8 of the 9 secondarily infected patients, Chinese HGA conforms to the spectrum of clinical severity observed in North America. The fatal outcome in the index case is clinically similar to that observed for other HGA fatalities, including exsanguination with sepsis syndrome possibly relating to cytokine overproduction, opportunistic infections, and increased HGA severity in the setting of preexisting medical conditions such as diabetes mellitus.

*A phagocytophilum* transmission in China and Asia is predicated on the presence of this zoonotic agent in vector ticks and vertebrate hosts. Although studies in Asia are limited, at least 8 have examined *A phagocytophilum* infection of ticks, including 2284 *Ixodes persulcatus* ticks, of which 4.4% carried *A phagocytophilum* DNA, a prevalence similar to that in European and North American *Ixodes* species ticks. Likewise, 9% and 24% of *Apodemus* species field mice in northern China and Korea, respectively, and 64% of *Crosidura lasiura* shrews in Korea are infected. Although no proven cases of HGA have been previously identified in China, at least 1 study describes *A phagocytophilum* DNA in the blood of 4 Chinese patients with tick bites, and seroepidemiological investigations demonstrate that 2% to 9% of febrile patients in Korea and between 0.5% and 6% of healthy Chinese residents have *A phagocytophilum* antibodies.

Rare examples of nontick transmission of HGA exist in the literature and include direct exposure to deer blood, transfusion, and transplacental transmission. Similarly, under the proper circumstances other rickettsial infections are transmissible via aerosol, direct contact with mucous

---

### Table 2. Risk Factors for Acquisition of Human Granulocytic Anaplasmosis Among 39 Contacts Exposed to Index Patient While at the Regional Hospital

<table>
<thead>
<tr>
<th>Exposure to Index Patient</th>
<th>Attack Rate With Exposure Factor</th>
<th>Attack Rate Without Exposure Factor</th>
<th>Relative Risk (95% Confidence Interval)</th>
<th><em>P</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤50 cm to nose and mouth</td>
<td>9/28 (32.1)</td>
<td>0/11 (0)</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>&gt;2 h</td>
<td>9/20 (45.0)</td>
<td>0/19 (0)</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>During or after intubation</td>
<td>9/30 (30.0)</td>
<td>0/9 (0)</td>
<td>.09</td>
<td></td>
</tr>
<tr>
<td>During massive hemorrhage period</td>
<td>4/9 (44.4)</td>
<td>5/30 (16.7)</td>
<td>2.7 (0.9-7.9)</td>
<td>.17</td>
</tr>
<tr>
<td>Any direct blood contact</td>
<td>9/22 (40.9)</td>
<td>0/17 (0)</td>
<td>.002</td>
<td></td>
</tr>
<tr>
<td>Direct respiratory or tracheal secretion contact</td>
<td>7/13 (53.8)</td>
<td>2/26 (7.7)</td>
<td>7.0 (1.7-29.1)</td>
<td>.003</td>
</tr>
</tbody>
</table>

*Infinite or not able to be calculated. b Fisher exact test (2-tailed).*

### Table 3. Risk Factors for Human Granulocytic Anaplasmosis Associated With Direct Exposure to Index Patient’s Blood and Respiratory Secretions

<table>
<thead>
<tr>
<th>Exposure Factor</th>
<th>Attack Rate With Exposure Factor</th>
<th>Attack Rate Without Exposure Factor</th>
<th>Relative Risk (95% Confidence Interval)</th>
<th><em>P</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any direct blood contact during hemorrhage</td>
<td>9/12 (75.0)</td>
<td>0/10 (0)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Open wounds or abrasions</td>
<td>4/4 (100.0)</td>
<td>5/18 (27.8)</td>
<td>3.6 (1.1-7.6)</td>
<td>.02</td>
</tr>
<tr>
<td>Not washed timely</td>
<td>4/8 (50.0)</td>
<td>5/14 (35.7)</td>
<td>1.4 (0.5-3.8)</td>
<td>.66</td>
</tr>
<tr>
<td>Direct respiratory or tracheal secretion contact</td>
<td>7/8 (87.5)</td>
<td>0/5 (0)</td>
<td>.004</td>
<td></td>
</tr>
<tr>
<td>Open wounds or abrasions</td>
<td>4/4 (100.0)</td>
<td>3/9 (33.3)</td>
<td>3.0 (1.2-7.6)</td>
<td>.07</td>
</tr>
<tr>
<td>Not washed timely</td>
<td>3/6 (50.0)</td>
<td>4/7 (57.1)</td>
<td>0.9 (0.3-2.4)</td>
<td>&gt;.99</td>
</tr>
</tbody>
</table>

*Infinite or not able to be calculated. b Fisher exact test (2-tailed).*
membranes or conjunctivae, or mechanical fomite transmission.33-38 Direct exposure to small blood volumes probably carries a low risk because experimental and natural infections of white-tailed deer result in only low-level bacteremia.39 However, it is possible that this low risk may be offset by large volumes of animal blood and tissues, such as those to which butchers are exposed.

Another factor related to transmissibility is the blood burden of *A phagocytophilum*, which appears to increase with immunosuppression resulting in absolute infected neutrophil counts as high as 2.7 to 5.9 × 10^9/L.40,41 It is unclear to what degree the sustained dexamethasone treatment of the index case contributed to transmission. The final consideration is the likelihood of health care worker and family member exposure to sufficient volumes of infectious body fluids to account for transmission. It is not unusual for occupational blood exposure to occur among those caring for patients with hemorrhage or during procedures such as intubation or surgery, for which the relative risk is 3 to 4 times higher than for other medical specialties.42 In western societies, most family members are excluded from these events and health care workers are increasingly protected by training and barriers such as gloves, gowns, and masks.43 However, retrospective questioning of our cases clearly indicated that both family members and health care workers not only participated in these events but were unlikely to use gloves and so reported that body surfaces were contaminated by potentially infectious fluids. Moreover, many participants did not acknowledge use of postexposure precautions, such as hand and skin washing.

Although it is likely that routine blood and body fluid precautions will protect against such future events, strict adherence to protective protocols is mandatory even if communicability is deemed unlikely. The lessons of this study remain relevant to the daily hospital and health care unit operations to prevent any additional nosocomial outbreaks of HGA. Moreover, as China advances into its future, it must also now become prepared to deal with the increasing threat that tick-borne rickettsial pathogens have been already brought to the United States and Europe.

**Author Contributions:** Dr Xu had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses. Drs Zhang, Liu, Ni, Li, Y. Yu, and X. Yu contributed equally to this work.

**Study concept and design:** L. Zhang, Liu, Ni, Li, Y. Yu, Wang, Jing, Rui, Yang, Wang, Dumler, Feng, Ren, Xu. **Acquisition of data:** Liu, Ni, D. Li, Y. Yu, Yang, Wu, Q. Li, Liang, Jiang, Jing, Rui, Luan, Fu, J. Zhang. **Analysis and interpretation of data:** L. Zhang, Liu, Ni, Li, Y. Yu, Wang, Liang, Jiang, Juel, Fu, J. Zhang, Dumler, Xu. **Drafting of the manuscript:** L. Zhang, Liu, Ni, Li, Y. Yu, Wang, Liang, Jiang, Jing, Rui, Luan, Fu, J. Zhang, Dumler, Xu. **Critical revision of the manuscript for important intellectual content:** X. Yu, Q. Li, Rui, Yang, Wang, Dumler, Feng, Ren, Xu. **Statistical analysis:** L. Zhang, Ni, Li, Q. Li, Y. Yu, Yang, Wang, Liang, Jiang, Jing, Rui, Luan, Fu, Zhang. **Obtained funding:** Rui, Wang, Xu. **Administrative, technical, or material support:** Liu, Ni, D. Li, Y. Yu, X. Yu, Wu, D. Li, Liang, Jiang, Jing, Rui, Yang, Feng, Ren, Xu.

**Study supervision:** Wang, Dumler, Feng, Xu.

**Financial Disclosures:** Dr Dumler reports that he holds a patent for a method for in vitro propagation of *A phagocytophilum* for which royalty fees are paid. Otherwise no other authors report disclosures of financial or potential conflicts of interest.

**Funding/Support:** This work was supported by grants 2005CB522904 and 200802016 (Dr Xu) from the Ministry of Science and Technology and by emerging research support from National Institute of Communicable Disease Control and Prevention, China CDC, Beijing, China.

**Role of the Sponsor:** The sponsors provided funding, but had no role in determining study design, data collection, or interpretation.

**REFERENCES**


Nothing is more estimable than a physician who, having studied nature from his youth, knows the properties of the human body, the diseases which assail it, the means which will benefit it, exercises his art with caution, and pays equal attention to the rich and the poor.
—Voltaire (1694-1778)