

id-fast bacilli (Figure). We grew cultures of acid-fast bacilli on trypticase soy agar after 2 to 4 days. The colonies were nonchromogenic, smooth to mucoid, and off-white to cream on Middlebrook 7H10 and trypticase soy agar.

We tested the in vitro antimicrobial susceptibility using the broth dilution method (7). The isolate susceptible to amikacin, cefoxitin, imipenem, doxycycline, and ciprofloxacin and resistant to sulfamethoxazole, clarithromycin, and tobramycin. We initiated treatment of the patient with moxifloxacin, minocycline, and amikacin 1 day after the athroscopy and the patient's fever subsided within 72 hours. We continued amikacin therapy for 1 month and administered moxifloxacin and minocycline for 6 months.

This patient is unique because she had a case of bacteremia caused by *M. wolinskyi*, and she had no history of major traumatic injury. The bacterium might have been introduced during implantation of the venous port or during minor trauma that went unnoticed. The chemotherapeutic regimen administered to our patient may have played a role in the infection. Immunosuppression by treatment with rituximab (an anti-CD20 monoclonal antibody) and a steroid during chemotherapy may have worsened the patient's B-cell function and thereby weakened her immunity. Surgical debridement followed by antimicrobial therapy for at least 6 months is the suggested treatment for *M. wolinskyi* infection, and we followed this regimen. Because of the frequency of relapse and resistance, we used combination therapy with multiple antimicrobial agents.

This case suggests that immunocompromised patients may be vulnerable to infection by rapidly growing mycobacterium such as *M. wolinskyi*. In such cases, we suggest antimicrobial drug treatment, based on in vitro susceptibility. More data on antimicrobial drug susceptibility should be collected for treatment of this type of infection.

#### Acknowledgment

We thank Ning-Sheng Lai for guidance and comments during the course of treatment.

**Yu-Chuan Chen, Ruwen Jou,  
Wei-Lun Huang,  
Shao-Tsung Huang,  
Keng-Chang Liu,  
Chorng-Jang Lay,  
Shu-Mei Chang, Chih-En Tseng,  
Chun-Liang Lai,  
and Yu-Chieh Su**

Author affiliations: Buddhist Tzu Chi Dalin General Hospital, Chiayi, Taiwan (Y.-C. Chen, K.-C. Liu, C.-J. Lay, S.-M. Chang, C.-E. Tseng, C.-L. Lai, Y.-C. Su); Centers for Disease Control Department of Health, Taipei, Taiwan (R. Jou, W.-L. Huang); Chest Hospital Health Executive Yuan, Tainan, Taiwan (S.-T. Huang); and Tzu Chi University School of Medicine, Hualien, Taiwan (K.-C. Liu, C.-J. Lay, S.-M. Chang, C.-E. Tseng, C.-L. Lai, Y.-C. Su)

DOI: 10.3201/eid1411.080003

#### References

1. Brown BA, Springer B, Steingrube VA, Wilson RW, Pfyffer GE, Garcia MJ, et al. *Mycobacterium wolinskyi* sp. nov. and *Mycobacterium goodii* sp. nov., two new rapidly growing species related to *Mycobacterium smegmatis* and associated with human wound infections: a cooperative study from the International Working Group on Mycobacterial Taxonomy. *Int J Syst Bacteriol.* 1999;49:1493–511.
2. Brown-Elliott BA, Wallace RJ Jr. Clinical and taxonomic status of pathogenic nonpigmented or late-pigmenting rapidly growing mycobacteria. *Clin Microbiol Rev.* 2002;15:716–46. DOI: 10.1128/CMR.15.4.716-746.2002
3. Wallace RJ Jr, Nash DR, Tsukamura M, Blacklock ZM, Silcox VA. Human disease due to *Mycobacterium smegmatis*. *J Infect Dis.* 1988;158:52–9.
4. Adekambi T, Drancourt M. Dissection of phylogenetic relationships among 19 rapidly growing *Mycobacterium* species by 16S rRNA, *hsp65*, *sodA*, *recA* and *rpoB* gene sequencing. *Int J Syst Evol Microbiol.* 2004;54:2095–105. DOI: 10.1099/ijs.0.63094-0
5. Holberg-Petersen M, Steinbakk M, Figen-schau KJ, Eng J, Melby KK. Identification of clinical isolates of *Mycobacterium* spp. by sequence analysis of the 16S ribosomal RNA gene. *Experience from a clinical laboratory.* *APMIS.* 1999;107:231–9.
6. Harmsen D, Dostal S, Roth A, Niemann S, Rothgänger J, Sammeth M, et al. RIDOM: comprehensive and public sequence database for identification of *Mycobacterium* species. *BMC Infect Dis.* 2003;3:26. DOI: 10.1186/1471-2334-3-26
7. Woods GL, Brown-Elliott BA, Desmond EP, et al. 2003. Susceptibility testing of mycobacteria, nocardia and other actinomycetes. Approved Standard M24-A, vol. 23, no. 18. Wayne (PA): National Committee for Clinical Laboratory Standards; 2003.

Address for correspondence: Yu-Chieh Su, Division of Hematology-Oncology, Department of Internal Medicine, Buddhist Tzu Chi Dalin General Hospital, 2 Min Sheng Rd, Dalin Town, Chiayi, Taiwan, Republic of China; email: hepatoma@ms3.hinet.net

## Incubation Period for Human Cases of Avian Influenza A (H5N1) Infection, China

**To the Editor:** Since 1997, more than 400 human cases of highly pathogenic influenza A virus (H5N1) infection have been reported worldwide, including 30 from mainland China. Ascertainment of the incubation period for influenza virus (H5N1) is important to define exposure periods for surveillance of patients with suspected influenza virus (H5N1) infection. Limited data on the incubation period suggest that illness onset occurs  $\leq 7$  days after the last exposure to sick or dead poultry (1–4). For clusters in which limited human-to-human virus transmission likely occurred, the incubation period appeared to be 3–5 days (5–7) but was estimated to be 8–9 days in 1 cluster (5). In China,

exposure to sick or dead poultry in rural areas and visiting a live poultry market in urban areas were identified as sources of influenza A virus (H5N1) exposures (8), but the incubation period after such exposures has not been well described.

We conducted a retrospective descriptive study of 24 of 30 influenza virus (H5N1) cases in China to estimate and compare incubation periods for different exposure settings, including case-patients exposed only to sick or dead poultry versus those exposed only to a wet poultry market, where small animals and poultry may be purchased live or slaughtered (see [www.searo.who.int/en/Section23/Section1001/Section1110\\_11528.htm](http://www.searo.who.int/en/Section23/Section1001/Section1110_11528.htm)). Exposures may be direct (e.g., touching poultry) or indirect (e.g., no physical contact, but in close proximity to poultry, poultry products, or poultry feces). We excluded 6 cases, including 2 with unavailable epidemiologic data, 1 without an identified exposure source, 2 in a cluster with limited person-to-person transmission (6), and 1 in which the patient was exposed to both a wet poultry market and to sick or dead poultry. Epidemiologic data were collected through patients and family interviews and a review of case-patients' medical records.

The incubation period was defined as the time from exposure to symptom onset. The maximum time from first exposure to illness onset was limited to 14 days for biological

plausibility. For case-patients with exposures on multiple days, we calculated each case-patient's median incubation period and then calculated the overall median and range of the distribution of these median incubation periods. Similarly, the minimum and maximum incubation periods for case-patients with exposures on multiple days was estimated by using the last or first known exposure day, respectively. The overall incubation period among these case-patients was estimated by determining the median of the distribution of case-patients' median incubation periods. Incubation periods were compared by using the Wilcoxon rank-sum test. All statistical tests were 2-sided with a significance level of  $\alpha = 0.05$ .

Of the 24 case-patients, 16 (67%) had exposure to sick or dead poultry only (median age = 25 years [range 6–44]; 25% male; 100% lived in rural areas). Eight (33%) had visited a wet poultry market only (median age = 30 years [range 16–41]; 63% male; 88% [7/8] lived in urban areas) (Table). For case-patients with  $\geq 2$  exposure days ( $n = 18$ ), and for case-patients with a single exposure day ( $n = 6$ ), the overall median incubation period was longer for those who had visited a wet poultry market than for those who were exposed to sick or dead poultry, but the difference was not significant. When data for single and multiple exposure days were combined, the overall median incubation period for case-patients

exposed to a wet poultry market ( $n = 8$ ) was significantly longer than for case-patients ( $n = 16$ ) exposed to sick or dead poultry (7 days [range 3.5–9] vs. 4.3 days [range 2–9];  $p = 0.045$ ).

Our findings are subject to limitations. Proxies for deceased case-patients may not have known all of the case-patient's exposures. Surviving case-patients may not have recalled or identified all exposures that occurred, including environmental exposures. It was impossible to ascertain when infection occurred for case-patients with multiple days of exposures. Our limited data did not permit the use of other methods such as survival analysis to better define incubation periods. We did not quantify exposure duration and could not determine whether repeated exposures (dose-response) or a threshold of exposure to influenza A virus (H5N1) exists to initiate infection of the respiratory tract. Laboratory testing was not performed to confirm that the exposure sources contained influenza virus (H5N1) or to quantify exposures.

Despite exposures of many persons in China to sick or dead poultry or to wet poultry markets, human influenza A (H5N1) disease remains very rare. Our findings suggest that the incubation period may be longer after exposure to a wet poultry market than after exposure to sick or dead poultry, and, therefore, a longer incubation period than the 7 days that is used widely (4,9) could be considered for

Table. Estimated incubation period of 24 human cases of infection with avian influenza A virus (H5N1), China\*

Exposure data	Case-patients with exposure to sick/dead poultry only	Case-patients with exposure to wet poultry market only	p value	All case-patients
No. case-patients with exposures on multiple days	12	6		18
Overall median incubation period, d (range)	4.5 (2–9.5)	6.3 (3.5–7)	0.276	5 (2–9.5)
Median of minimum incubation period, d (range)	1 (0–5)	0 (0–2)	0.315	0.5 (0–5)
Median of maximum incubation period, d (range)	7.5 (4–14)	11.5 (7–14)	0.108	8.5 (4–14)
No. case-patients with single known exposure	4	2		6
Overall median incubation period, d (range)	3.5 (2–6)	8.5 (8–9)	0.064	5 (2–9)
All case-patients	16	8		24
Overall median incubation period, d (range)	4.3 (2–9)	7 (3.5–9)	<b>0.045</b>	5 (2–9.5)
Overall median of minimum incubation period, d (range)	1.5 (0–6)	1 (0–9)	0.752	1.5 (0–9)
Overall median of maximum incubation period, d (range)	6 (2–14)	9 (7–14)	<b>0.031</b>	7.5 (2–14)

\***Boldface** represents significant results (Wilcoxon rank-sum test).

surveillance purposes. However, because of the small number of influenza virus (H5N1) case-patients, our study was too underpowered to draw any firm conclusions; results should be interpreted cautiously. In a study of cases in Vietnam, 5 case-patients did not have any identified exposure  $\leq 7$  days of illness onset (10). In China, the exposure period for surveillance of suspected cases now includes exposure to a wet poultry market  $\leq 14$  days before illness onset. Although data on person-to-person virus transmission are limited, close contacts of patients infected with influenza virus (H5N1) in China are monitored daily for 10 days after the last known exposure. Further studies are needed to quantify the incubation period after exposure to sick or dead infected poultry, a wet poultry market, or to an influenza A virus (H5N1) case-patient and to investigate the basis for any differences.

#### Acknowledgments

We thank the Centers for Disease Control and Prevention of the Hunan, Anhui, Sichuan, Fujian, Guangdong, Hubei, Liaoning, Shanghai, Jiangxi, Guangxi, Zhejiang, Xinjiang, and Jiangsu Provinces and the local governments that assisted us in coordinating our field investigations, in data collection, and in logistical support. We also thank Ratana Somrngthong and Sapon Iamisirithaworn, for review of the manuscript.

**Yang Huai, Nijuan Xiang,  
Lei Zhou, Luzhao Feng,  
Zhibin Peng,  
Robert S. Chapman,  
Timothy M. Uyeki,  
and Hongjie Yu**

Author affiliations: Chinese Center for Disease Control and Prevention, Beijing, People's Republic of China (Y. Huai, N. Xiang, L. Zhou, L. Feng, Z. Peng, H. Yu); Chulalongkorn University, Bangkok, Thailand (Y. Huai, R.S. Chapman); and Centers for Disease Control and Prevention, Atlanta, Georgia, USA (T.M. Uyeki)

DOI: 10.3201/eid1411.080509

#### References

1. Areechokchai D, Jiraphongsa C, Laosiritaworn Y, Hanshaoworakul W, O'Reilly M; Centers for Disease Control and Prevention. Investigation of avian influenza (H5N1) outbreak in humans—Thailand, 2004. *MMWR Morb Mortal Wkly Rep.* 2006;55(Suppl 1):3–6.
2. Tran TH, Nguyen TL, Nguyen TD, Luong TS, Pham PM, Nguyen VC, et al. Avian influenza A (H5N1) in 10 patients in Vietnam. *N Engl J Med.* 2004;350:1179–88. DOI: 10.1056/NEJMoa040419
3. Oner AF, Bay A, Arslan S, Akdeniz H, Sahin HA, Cesur Y, et al. Avian influenza A (H5N1) infection in eastern Turkey in 2006. *N Engl J Med.* 2006;355:2179–85. DOI: 10.1056/NEJMoa060601
4. Writing Committee of the Second World Health Organization. Consultation on clinical aspects of human infection with avian influenza A (H5N1). Update on avian influenza A (H5N1) virus infection in humans. *N Engl J Med.* 2008;358:261–73. DOI: 10.1056/NEJMra0707279
5. Ungehusak K, Auewarakul P, Dowell SF, Kitphati R, Auwanit W, Puthavathana P, et al. Probable person-to-person transmission of avian influenza A (H5N1). *N Engl J Med.* 2005;352:333–40.
6. Wang H, Feng ZJ, Shu YL, Yu HJ, Zhou L, Zu RQ, et al. Probable limited person-to-person transmission of highly pathogenic avian influenza A (H5N1) virus in China. *Lancet.* 2008;371:1427–34. DOI: 10.1016/S0140-6736(08)60493-6
7. Kandun IN, Wibisono H, Sedyaningsih ER, Yusharmen, Hadisoedarsuno W, Purba W, et al. Three Indonesian clusters of H5N1 virus infection in 2005. *N Engl J Med.* 2006;355:2186–94. DOI: 10.1056/NEJMoa060930
8. Yu HJ, Feng ZJ, Zhang XF, Xiang NJ, Huai Y, Zhou L, et al. Human influenza A (H5N1) cases, urban areas of People's Republic of China, 2005–2006. *Emerg Infect Dis.* 2007;13:1061–4.
9. World Health Organization. WHO case definitions for human infections with influenza A(H5N1) virus [cited 2008 July 20]. Available from [http://www.who.int/csr/disease/avian\\_influenza/guidelines/case\\_definition2006\\_08\\_29/en/index.html](http://www.who.int/csr/disease/avian_influenza/guidelines/case_definition2006_08_29/en/index.html)
10. Dinh PN, Long HT, Tien NT, Hien NT, Mai le TQ, Phong le H, et al. Risk factors for human infection with avian influenza A H5N1, Vietnam, 2004. *Emerg Infect Dis* [serial on the Internet]. 2006 Dec [cited 2008 July 20]. Available from <http://www.cdc.gov/ncidod/EID/vol12no12/06-0829.htm>

Address for correspondence: Hongjie Yu, Office for Disease Control and Emergency Response, China CDC, 27 Nanwei Rd, Beijing 100050, People's Republic of China; email: yuhj@chinaacdc.cn

## *Mycobacterium haemophilum* Infection after Alemtuzumab Treatment

**To the Editor:** The immunosuppressive agent alemtuzumab is a DNA-derived, humanized monoclonal antibody directed against the panlymphocyte, cell-surface antigen CD52 (1). The drug is approved for the treatment of refractory B-cell chronic lymphocytic leukemia (2) and also has been used after stem cell (3) and organ transplantations (4). Alemtuzumab causes profound and prolonged lymphocyte depletion, which results in a variety of complications involving infections (5). However, mycobacteria have rarely been reported to cause infection after alemtuzumab treatment. We describe infections with *Mycobacterium haemophilum*, a fastidious nontuberculous mycobacterium, in 2 patients who experienced cutaneous lesions while they received alemtuzumab.

#### Patient 1

A 65-year-old man with refractory chronic lymphocytic leukemia had been receiving treatment with alemtuzumab for 3 months. During a 5-week period beginning 15 weeks after the alemtuzumab therapy started, 20–30 tender nodular-ulcerative lesions developed on the patient's extremities. Most of the lesions were distributed along a saphenous vein site (Figure). Immediately before receiv-