

医薬品 研究報告 調査報告書

識別番号・報告回数		報告日	第一報入手日 2008. 3. 25	新医薬品等の区分 該当なし	機構処理欄
一般的名称	解凍人赤血球濃厚液			公表国	
販売名(企業名)	解凍赤血球濃厚液「日赤」(日本赤十字社) 照射解凍赤血球濃厚液「日赤」(日本赤十字社) 解凍赤血球-LR「日赤」(日本赤十字社) 照射解凍赤血球-LR「日赤」(日本赤十字社)		研究報告の公表状況 AABB Weekly Report. 2008 Feb 29.	米国	
研究報告の概要	<p>○インフルエンザパンデミックと血液供給に関するAABBの組織横断作業部会がパンデミック時に献血間隔の例外的な取り扱いを認めるようFDAに要求</p> <p>インフルエンザパンデミックと血液供給に関するAABBの組織横断作業部会が、2月14日付で米国食品医薬品局に送付した文書である。</p> <p>パンデミック時には、供血者が発症したり家族を看病したりするために、基準に合致する供血者の数が少なくなり、血液の安定供給に影響するという懸念が広がっている。</p> <p>作業部会は、全血と赤血球採血の献血間隔を半分に短縮(8週間のところを4週間、16週間のところを8週間)することを提案した。これはパンデミック時の血液供給の問題を最小限にするためにFDAが取りうる手段としては最も効果的であると主張している。</p> <p>また、作業部会の前回のミーティングでは、過去6ヵ月以内に血液が使用された供血者については、感染症検査の前に供給するという方法が紹介された。これについてのFDAの意見を求めている。</p>				使用上の注意記載状況・ その他参考事項等 解凍赤血球濃厚液「日赤」 照射解凍赤血球濃厚液「日赤」 解凍赤血球-LR「日赤」 照射解凍赤血球-LR「日赤」 血液を介するウイルス、 細菌、原虫等の感染 vCJD等の伝播のリスク
	報告企業の意見 インフルエンザパンデミックと血液供給に関するAABBの組織横断作業部会はパンデミック時に献血間隔の例外的な取り扱いを認めるようFDAに求めているとの報告である。	今後の対応 日本赤十字社では家禽に高病原性トリインフルエンザの流行が認められた場合、当該飼養農場の関係者や防疫作業従事者の献血制限を行っている。新型インフルエンザが流行した場合、献血者減少につながることも予想される。今後も引き続き情報の収集に努める。			

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Advance Registration for 2008 Spring Conference Ends March 7

Only one week remains to register in advance for the 2008 [AABB Spring Conference](#). After March 7, individuals who have not signed up for the conference can still attend but must register on-site. The conference, which will be held March 28-29 in Orlando, Fla., features educational sessions in four tracks — Blood Inventory Management, Cellular Therapy, Perioperative Blood Management and Tissue Management. Registration includes entrance to educational sessions in any of the four tracks, course materials, continental breakfast and access to the exhibits.

AABB Task Force Asks FDA for Exception to Interdonation Interval During Influenza Pandemic

The AABB Interorganizational Task Force on Influenza Pandemics and the Blood Supply sent a letter to the Food and Drug Administration on Feb. 14 asking the agency to review a template to be used by blood facilities to request an exception to the interdonation interval requirements in the event of an influenza pandemic. According to the [letter](#), there is widespread concern that a pandemic would severely impact the availability of blood products by limiting the number of eligible donors. The task force stated that shortening the interdonation interval for whole blood and red blood cell collection is the most significant step the agency can take to minimize supply issues during a pandemic.

Report Finds Alternatives for Blood Irradiators, Other Radiation Sources to Improve National Security

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EventCalendar

March 3-6 – The Allm International Exposition & Conference [read more »](#)

March 4-5 – International Plasma Protein Congress [read more »](#)

March 5 – AABB Audioconference: Hematopoietic Cell Donation: Ensuring Safety for the Donor, Product and Recipient [CT read more »](#)

March 5-6 – Southeastern Area Blood Bankers Annual Meeting [read more »](#)

March 6-7 – President’s Council on Bioethics Meeting [read more »](#)

March 19 – AABB Audioconference: Serological to Molecular Testing: Points to Consider for Successful Conversion [read more »](#)

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New Web Resources

Updates to the Variances for Collection of Blood and Blood

Letter to the FDA on a Draft Template for a Shorter Inter-donation Interval During an Influenza Pandemic – 2/14/08

Alan Williams, PhD
Associate Director for Regulatory Affairs (HFM-300)
Food and Drug Administration
Center for Biologics Research and Review
Woodmont Office Center, Suite 400N
1401 Rockville Pike
Rockville, MD 20852

Dear Dr. Williams:

The AABB Interorganizational Task Force on Influenza Pandemics and the Blood Supply appreciates the Food and Drug Administration's (FDA) assistance in working to ensure that patients' blood needs can be met in the event of a severe influenza pandemic. As we have discussed, there is widespread concern that a severe pandemic will severely impact the availability of blood products as individuals who are sick or caring for sick loved ones will not be able to donate.

In an effort to prevent critical blood shortages, the Task Force has developed a template to request an exception for a shorter inter-donation interval for Whole Blood and Red Blood Cell donations in the event of a pandemic. Experience with donors with hemochromatosis has shown that donors can tolerate phlebotomy much more frequently than the standard eight-week requirement, so long as they have acceptable hemoglobin levels. The Task Force believes that allowance for a shorter inter-donation interval is the most significant step that FDA can take to alleviate shortages during a pandemic. We are asking FDA to acknowledge that the language proposed in the attached draft template is appropriate so that the Task Force can distribute it to blood collection facilities working to prepare for a severe pandemic.

In addition, during the last meeting of the Task Force, the concept of a "walking donor" pool – i.e., allowing blood collected from individuals who had successfully donated in the previous six months to be distributed prior to infectious disease testing, which would be completed subsequently – was introduced. The Task Force would welcome your expansion on how you see such an approach being applied. Would the donor examination or history be amended or truncated? Would testing requirements be relaxed? Please let us know your thoughts.

Thank you for your efforts to address blood supply issues relating to a possible influenza pandemic. The Task Force looks forward to your response to the above requests.

Sincerely,

Louis Katz, MD
Chair

Attachment

Cc: Elizabeth Callaghan

Request for Exception to Inter-Donation Interval in the Event of an Influenza Pandemic

Director, Division of Blood Applications (HFM-375)
 Food and Drug Administration
 Center for Biologics Research and Review
 C/O Document Control Center (HFM-99)
 Woodmont Office Center, Suite 200N
 1401 Rockville Pike
 Rockville, MD 20852-1448

n: (Blood Center/Bank Name)
 (Mailing Address)
 (License Number, if licensed, or Registration Number, if registered)

Request for Exception to Inter-Donation Interval in the Event of an Influenza Pandemic

Request: Our establishment requests an exception under 21 CFR 640.120 to allow, in the event of an influenza pandemic:

1. Single unit collection of Whole Blood and Red Blood Cells (RBCs) from donors who had donated a single unit less than eight weeks but at least four weeks previously, or a double unit of RBCs less than 16 weeks but at least eight weeks previously, provided the donor meets the other donor eligibility criteria in 21 CFR 640.3(b) and 640.3(c).
2. Double unit collection of Whole Blood and Red Blood Cells from donors who had donated less than sixteen weeks but at least eight weeks previously, provided the donor meets the other donor eligibility criteria in 21 CFR 640.3(b) and 640.3(c).

Justification: There is widespread concern in the transfusion medicine community that a pandemic could severely impact the availability of blood products in the United States since individuals who are sick or caring for sick loved ones will not be able to donate. This exception would be granted to enhance the adequacy of the blood supply in the event of an influenza pandemic in the United States that the AABB Organizational Task Force on Domestic Disasters and Acts of Terrorism, with the concurrence of FDA, declares has or will negatively impact the blood supply, either at a regional or national level.

There is substantial evidence that donors can tolerate a more frequent inter-donation frequency, as evidenced by the FDA guidance, *Guidance for Industry: Variance for Blood Collection from Individuals with Hereditary Hemochromatosis*, August 2001.

Sincerely,

Responsible Person

医薬品 研究報告 調査報告書

識別番号・報告回数		報告日	第一報入手日 2008. 2. 18	新医薬品等の区分 該当なし	機構処理欄
一般的名称	新鮮凍結人血漿	研究報告の公表状況	Robinson JL, Lee BE, Patel J, Bastien N, Grimsrud K, Seal RF, King R, Marshall F, Li Y. Emerg Infect Dis. 2007 Dec;13(12):1865-70.	公表国	
販売名(企業名)	新鮮凍結血漿「日赤」(日本赤十字社) 新鮮凍結血漿-LR「日赤」(日本赤十字社)			カナダ	
研究報告の概要	○幼児におけるブタインフルエンザ(H3N2)感染および市中伝播の可能性:カナダ ブタ起源と思われるインフルエンザ(H3N2)ウイルス(A/Canada/1158/2006)が、カナダの共同農場に居住する、7ヶ月齢の入院患児より分離された。当該患児は無事に回復した。A/Canada/1158/2006の赤血球凝集抑制反応を利用した血清学的検査を当該農場の農民90名のうち54名に実施した。初発患者およびその家族7名中4名、家族以外の農民46名中4名に血清陽性が示された;この前年に呼吸器疾患による入院歴を持つ者はいなかった。当該ブタインフルエンザ株の血清エビデンスは、当該農場のブタ10頭(12週齢~6ヶ月齢)中1頭に認められた。カナダではブタインフルエンザウイルスのヒトへの感染は、過少に評価されており、ウイルス株は農場に順応または再集合が可能であり、その結果、効率的なヒト-ヒト伝播にいたることから、パンデミックインフルエンザ対策の一環として、養豚業従事者の定期的な調査を検討すべきである。				使用上の注意記載状況・ その他参考事項等
					新鮮凍結血漿「日赤」 新鮮凍結血漿-LR「日赤」 血液を介するウイルス、 細菌、原虫等の感染 vCJD等の伝播のリスク
報告企業の意見			今後の対応		
ブタ起源と思われるインフルエンザH3N2ウイルスが、カナダの共同農場に居住する7ヶ月齢の入院患児より分離され、患児の家族7名中4名、家族以外の農民46名中4名と、当該農場のブタ10頭中1頭に血清陽性が認められたとの報告である。			新型インフルエンザが流行した場合、献血者減少につながることも予想される。今後も引き続き情報の収集に努める。		

Swine Influenza (H3N2) Infection in a Child and Possible Community Transmission, Canada

Joan L. Robinson,*† Bonita E. Lee,* Jagdish Patel,‡ Nathalie Bastien,§ Karen Grimsrud,¶ Robert F. Seal,† Robin King,‡ Frank Marshall,# and Yan Li†§

An influenza A virus (H3N2) of probable swine origin, designated A/Canada/1158/2006, was isolated from a 7-month-old hospitalized child who lived on a communal farm in Canada. The child recovered uneventfully. A serosurvey that used a hemagglutination-inhibition assay for A/Canada/1158/2006 was conducted on 54 of the 90 members of the farm. Seropositivity was demonstrated in the index patient, 4 of 7 household members, and 4 of 46 nonhousehold members; none had a history of hospital admission for respiratory illness in the preceding year. Serologic evidence for this strain of swine influenza was also found in 1 of 10 pigs (12 weeks–6 months of age) on the farm. Human infection with swine influenza virus is underrecognized in Canada, and because viral strains could adapt or reassort into a form that results in efficient human-to-human transmission, routine surveillance of swine workers should be considered as part of pandemic influenza preparedness.

Influenza A is endemic in a broad range of species, with avian and swine strains having the greatest potential for transmission to humans. Pandemics of influenza A occur when a major change occurs in the proteins of circulating strains of the virus. During the pandemics of the past century, this antigenic shift resulted from reassortment of human and avian strains or adaptation of avian viruses to facilitate person-to-person transmission (1). Avian influenza preferentially binds to sialic acid–galactose receptors with an

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α -2,3 linkage that is abundant on duck intestinal epithelium; human influenza preferentially binds to sialic acid–galactose receptors with an α -2,6 linkage that is abundant on human respiratory epithelium. The respiratory epithelium of swine contains both types of receptors and can potentially be simultaneously infected with avian and human influenza (2). Human infection with avian influenza subtype H5N1 is of great concern, with 194 deaths of 321 cases reported worldwide through August 16, 2007 (3). Swine infected with avian subtype H5N1 have been identified in Vietnam (4), raising the possibility that swine could act as the “mixing vessel” that allows avian influenza (H5N1) to reassort with a human influenza strain, resulting in a virus with high pathogenicity and a high potential for person-to-person spread.

Another theoretical mechanism for the origin of an influenza pandemic would be the adaptation of a swine strain that results in efficient person-to-person transmission, although cross-protection by antibodies to recently circulating human strains may prevent this from occurring with swine influenza virus (SIV) H1 and H3 strains. Infection of humans with SIV was first recognized in 1974 with an H1N1 strain (5); the solitary outbreak occurred in military recruits at Fort Dix, New Jersey, USA, in 1976 (6). Human infection with SIV subtype H3N2 was first described in Europe in 1993 (7). The first reported case of probable infection of a person in North America with a non-H1N1 subtype of SIV occurred in Ontario, Canada, in 2005 with an H3N2 strain detected in the respiratory tract of an adult with no serologic evidence of infection (8). We describe a case of SIV (H3N2) infection in a Canadian infant, confirmed by viral isolation and serologic testing.

Case Report

A 7-month-old boy was admitted to the hospital on September 10, 2006, with a 3-day history of fever, rhinitis, and cough. He had had no previous contact with ill persons. The child was born at term and was hospitalized for 21 days at 5 weeks of age when he received ventilation for 6 days for pneumonia due to respiratory syncytial virus. He lived on a communal farm (90 occupants) with horses, cows, swine, sheep, dogs, cats, turkeys, geese, ducks, and chickens but had no direct contact with the animals. The swine were contained in barns and did not mix with the other animals. His household contacts did not work directly with animals, but his father occasionally spent time in the barns, and his uncle, who lived next door, worked in the swine barns.

On admission, the child was afebrile with a heart rate of 120 beats/min, respiratory rate 56/min, and oxygen saturation of 85% on room air. Diffuse wheeze was noted. Chest radiograph results were unremarkable. Direct fluorescent antibody testing on a nasopharyngeal aspirate was positive for influenza A, and the virus was isolated in rhesus monkey cell culture. The isolate was sent to the National Microbiology Laboratory for influenza subtyping as a requirement of the Canadian influenza surveillance program, where it was subsequently designated A/Canada/1158/2006. The child stayed in the hospital for 2 days and then made an uneventful recovery at home. A cough and rhinitis developed in his 19-month-old brother on the day the index patient was admitted to the hospital, but the brother was not assessed by a physician.

Methods

Antigenic Analysis

For the antigenic characterization of A/Canada/1158/2006, hemagglutination-inhibition (HI) assay was performed by using 4 hemagglutination units of virus, 0.7% v/v guinea pig erythrocytes, and postinfection fowl serum specimens for the currently circulating human strains (A/New Caledonia/20/99 [H1N1], A/Wisconsin/67/2005 [H3N2]), past circulating human strains (A/Panama/2007/99 and A/Nanchang/933/95), and swine serum for A/Swine/Texas/4199-2/98 (H3N2) treated with receptor-destroying enzyme (9).

Molecular Characterization

All 8 RNA segments of A/Canada/1158/2006 were amplified by reverse transcriptase-PCR (RT-PCR) and sequenced. A universal primer set for the full-length amplification of all influenza A viruses was used for the RT-PCR (10). Viral RNA was extracted from 100 μ L of tissue culture fluid with the RNeasy Mini Kit (QIAGEN, Mississauga, Ontario, Canada). Viral RNA was amplified in a OneStep RT-PCR reaction (QIAGEN) following the

manufacturer's recommendations. Briefly, 5 μ L RNA was added to the RT-PCR mixture containing 2 μ L QIAGEN OneStep RT-PCR enzyme mix, 10 μ L 5 \times QIAGEN OneStep RT-PCR buffer, 400 μ mol/L dNTP, 0.6 μ mol/L of each primer, and 10 μ L Q-solution in a final volume of 50 μ L. The conditions used for the Gene Amp 97700 (Applied Biosystems, Streetsville, Ontario, Canada) thermocycler were as follows: 50°C for 30 min for reverse transcription, 95°C for 15 min for the activation of the HotStart DNA polymerase; then 35 cycles of 94°C for 20 s, 58°C for 30 s, 72°C for 4 min, followed by an extension of 10 min at 72°C. The PCR products were purified by using QIAquick PCR purification kit (QIAGEN) and sequenced on an ABI 377 Sequencer, using a fluorescent dye-terminator kit (Applied Biosystems). The DNA sequences were assembled and analyzed with SEQMAN, EDITSEQ, and MEGALIGN programs in Lasergene (DNASTAR, Madison, WI, USA). Phylogenetic trees were generated by the neighbor-joining method using the MEGA program (11).

Serologic Testing

Once it became evident that A/Canada/1158/2006 was closely related to swine influenza viruses, HI was performed on serum specimens collected from the index patient, the symptomatic sibling, and both parents 29 days after the hospitalization. To further investigate the spread of SIV to humans, approval was then granted by the Health Research Ethics Board of the University of Alberta to obtain information and serum specimens from other members of the communal farm. The study team visited the farm 3 months after the hospitalization of the index patient and explained the study to the occupants. Serum specimens were then collected from the other 4 siblings of the index patient and 46 other occupants who lived in a total of 17 households. Participants provided the following data: age, exposure to swine (none, <1 hour/week, or \geq 1 hour/week), and history of influenza-like illnesses (ILI; defined as cough and fever) in the preceding year. Serum samples were tested by using an HI assay against the currently circulating human strains A/New Caledonia/20/99 (H1N1), A/Wisconsin/67/2005 (H3N2), and the isolate from the index patient, A/Canada/1158/2006. HI titers were defined as the reciprocal of the highest dilution of serum that completely inhibited hemagglutination of a 0.7% solution of guinea pig erythrocytes. Specimens were considered seropositive for influenza virus at a titer of \geq 32.

Swine Investigation

The purpose of these investigations was to determine the extent of recent swine influenza in swine on the farm and to look for evidence of infection with the SIV strain isolated from the index child. The history of influenza or unexpected respiratory illness in the swine on the farm was

obtained. Nasal swabs were obtained from grower pigs (4 to 16 weeks of age) and processed by RT-PCR for influenza A matrix gene. Serologic testing for influenza, using an ELISA for H1N1 and H3N2 strains and HI for A/Canada/1158/06, was performed on samples from grower-finisher pigs (12 weeks to 6 months of age). Five grower pigs that were doing poorly were killed and pulmonary autopsies were performed. All swine used in these investigations were on the farm at the time the index child was ill.

Results

Antigenic and Molecular Characterization of A/Canada/1158/06

Initial HI testing showed that the isolate was not inhibited by antiserum against recent (A/Wisconsin/77/2005 and A/New Caledonia/20/99) and past (A/Panama/2007/99 and A/Nanchang/933/95) human influenza A strains but was inhibited by antiserum against A/swine/Texas/4199-2/98 (H3N2) virus with HI titer of 128. These findings indicate that the A/Canada/1158/06 virus was antigenically related to SIV (Table 1). The results also indicate that the assay is specific because no cross-reactivity was observed between the human reference strain antiserum and the swine influenza viruses (Table 1). Nucleotide sequences of the full-length coding regions of all 8 RNA segments of the isolate further determined that it was most closely related to A/swine/Ontario/33853/2005 (H3N2) virus, which shares the same human/classic swine/avian triple reassortant genotype as the H3N2 subtype viruses that emerged in swine in the United States in 1998 (8). Sequence analysis showed that nucleic acid homology between A/Canada/1158/2006 and A/swine/Ontario/33853/2005 ranges from 98.4% (HA) to 100% (M1), and that amino acid (aa) identities range from 97.9% (HA) to 100% (NP, NS2, M1). A deletion of 4 aa at position 156-159 was observed in the HA1 region of the A/Canada/1158/2006 HA protein. Amino acid substitutions were found in the HA (HA1 domain: G7, K142, S162; HA2 domain: T77, Q139, M149, E150, N160), neurami-

nadase (NA) protein (P45, K74, N150, M349, L354), NS1 (M112), PB1 (K211, D738), PB2 (K368, S661, T722), and PA (V44, R99, I42) proteins. Phylogenetic analysis showed that all of the genes of A/Canada/1158/06 clustered with Canadian swine isolates from 2005 (9) (data not shown). Nucleic acid identity between the HA and NA genes of A/Canada/1158/06 and the current vaccine strain A/Wisconsin/67/05 was 90.9% and 94.6%, and the aa identities were 90.2% and 94.5%, respectively.

Serologic Testing

Seropositivity (HI titer ≥ 32) to A/Canada/1158/2006 was demonstrated in the index patient, the symptomatic sibling, 1 asymptomatic sibling, and both parents (Table 2, household A). Three other siblings were seronegative. Four children from 2 other households were also seropositive (Table 2, households B and C); the father from household B, 1 other child from household B, and the mother from household C were seronegative. The father from household C worked in the swine barn but was unavailable for testing. History of ILI within the preceding 12 months in seropositive participants was reported only for the index patient and for a 3-year-old girl from household C who was not hospitalized or tested for influenza virus during her illness. Seronegative results were obtained from another 20 adults (14 women and 6 men) and 19 children (8 girls and 11 boys) from 14 different households. For these households, swine exposure was reported as none for 9 adults and 7 children, <1 hour/week for 11 adults and 8 children, and ≥ 1 hour/week for 4 children including 3 teenagers who worked in the swine barns. When serum samples from the 54 participants in the study were tested for HA-specific antibodies to the current human influenza A virus H3N2 and H1N1 subtypes, one of the patients who was seropositive for SIV at a titer of 32 had an identical titer for A/Wisconsin/67/2005 (H3N2) (Table 2), and one of the adults who was seronegative for SIV had a titer of 32 for A/New Caledonia/20/99 (H1N1) (data not shown). All other persons tested were seronegative for the 2 human strains of influenza.

Table 1. Hemagglutination-inhibition reaction of A/Canada/1158/2006 isolates with reference antiserum against currently circulating human and swine viruses

Antigen	Antiserum (titers)				
	A/New Caledonia/ 20/99 (human H1N1)	A/Wisconsin/ 67/2005 (human H3N2)	A/Panama/ 2007/99 (human H3N2)	A/Nanchang/ 933/95 (human H3N2)	A/Swine/Texas/ 4199-2/98 (swine H3N2)
Control					
A/New Caledonia/20/99 (human H1N1)	320	<4	<4	<4	<4
A/Wisconsin/67/2005 (human H3N2)	<4	320	64	8	8
A/Ontario/RV1273/2005 (swine H3N2)	<4	<4	<4	<4	256
Patient					
A/Canada/1158/2006	<4	<4	<4	<4	128

RESEARCH

Table 2. Clinical features and hemagglutination-inhibition reaction of positive antiserum from 9 members of 3 different households of a communal farm with recently circulating swine influenza (H3N2) virus A/Canada/1158/2006*

Household	Age, y	Sex	A/Wisconsin/ 67/2005 titer	A/New Caledonia/ 20/99 titer	A/Canada/ 1158/2006 titer	Swine exposure	Clinical features
A (index patient)	0.6	M	<4	<4	256	None	Hospitalization with ILI and isolation of swine influenza
A†	1	M	<4	<4	256	None	None (URI coincident with ILI in index case)
A	35	F	<4	<4	32	None	None
A	38	M	8	<4	32	<1 h/wk	None
A	8	M	<4	<4	64	<1 h/week	None
B	7	M	32	<4	32	<1 h/wk	None
C	8	M	4	<4	64	≥1 h/week	None
C	5	M	<4	<4	128	<1 h/week	None
C	3	F	<4	<4	128	None	ILI 1 mo before index case

*URI, upper respiratory illness; ILI, influenza-like illness.

†Symptomatic sibling.

Swine Investigation

Influenza (H3N2) was last documented in the swine herd in September 2005. The herd received breeding animals from a Manitoba herd, where swine influenza of an unknown subtype had recently been documented. Nasal swabs collected from 25 grower pigs ≈3 weeks after the index child was ill were negative for SIV. Serum specimens obtained from 10 grower-finisher pigs were all negative by ELISA for swine influenza (H1N1), but 4 were positive for swine influenza (H3N2) strains, with 1 of these 4 strains being seropositive for A/Canada/1158/2006 by HI assay (HI titer 32). Results of the lung autopsies all showed evidence of subacute bronchointerstitial pneumonia, varying from mild to moderate. Lesions typical for swine influenza were not noted, but an initial insult due to SIV could not be excluded.

Discussion

We describe an infant with virologic and serologic evidence of infection with SIV (H3N2) and an ILI. Serologic evidence of infection with the same strain was found in 4 of 7 household members and in 3 of 46 nonhousehold contacts, with only 1 of the seropositive patients having a history of an ILI within the preceding year, which demonstrated unrecognized human infection with SIV. This relatively high seroprevalence is in contrast to a recent outbreak of avian influenza (H7N3) in which seropositivity was not documented in 91 persons exposed to infected poultry, including 2 poultry workers from whom the virus was isolated (12). The difference in the apparent incidence of infection may be explained in part by the fact that culling of infected poultry occurred immediately; in our study, infection of swine was not recognized and long-term human exposure may have occurred.

Infection of swine with human influenza viruses has been recognized for decades (2); in a recent US study, 22.8% of pigs were seropositive for human influenza viruses, although some may have had vaccine-induced im-

munity (13). Swine influenza (H3N2) emerged in 1998 in the United States, where subtype H1N1 viruses had predominated for 60 years (2). The isolate from this current study is closely related to triple reassorting genotype viruses that spread rapidly throughout the US swine population and have HA, NA, and RNA polymerase (PB1) genes of human influenza virus lineage; nucleoprotein, matrix, and nonstructural genes of classic swine influenza (H1N1) lineage; and RNA polymerase (PA and PB2) genes of North American avian virus lineage (8). However, triple reassortant SIV was not documented in swine in Canada until 2005 (8), which makes it unlikely that human cases occurred before that year and that seroreversion had occurred in any of the persons in the current serosurvey.

A previous study showed cross-reactivity in HI assay between the vaccine strain A/Panama/2007/99 reference antiserum and the triple reassortant A/swine/Minnesota/593/99, which is not unexpected since the HA gene of the triple reassortant viruses is a descendant of human viruses that circulated in 1995 (14,15). However, no cross-reactivity was observed between the reference human strain antiserum and the isolate from this study, which suggests that the seroconversion observed was indeed due to infection with swine influenza (H3N2) and not to cross-reactive antibody to human influenza (H3N2) infection. The low rate of seropositivity to recently circulating strains of human influenza in the study is likely explained by the fact that the farm is a relatively closed community. The child who was seropositive for both human and swine influenza viruses was likely exposed to both viruses. The HA protein of A/Canada/1158/2006 diverges significantly from the one of A/Wisconsin/67/2005, and antiserum against A/Wisconsin/67/2005 does not inhibit A/Canada/1158/2006 in HI assay.

Swine influenza (H3N2) has recently reassorted with H1N1 strains to produce H1N2 subtypes and has spread to turkeys in the United States (16) and Canada (8). A 4-aa deletion was found in the HA protein of A/Canada/1158/2006 when compared with similar swine influenza (H3N2)