別紙様式第2

別紙(2)-4

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 2009年5月7日	新医薬品等の区分 該当なし	厚生労働省処理欄
一般的名称	乾燥濃縮人アンチトロンビンⅢ		研究報告の公表状況	Information about Newly Emerging 2009 H1N1 Influenza Virus and Blood Safety http://www.fda.gov/cber/flu/h1n1bldsafety.htm	公表国 米国	
販売名（企業名）	アンスロビンP-ベーリング（CSLベーリング株式会社）					

研究報告の概要

問題点（2009 年の新興の H1N1 型インフルエンザウイルス感染と血液の安全性）

米国で 2009 年に新興の H1N1 型インフルエンザウイルス感染が発生していて、このウイルスが輸血により感染するか疑問視されている。

米国や他の国において輸血による季節性インフルエンザが伝播した症例は報告がなく、現在まで輸血による H1N1 型インフルエンザウイルスの伝播の報告はない。FDA は継続して CDC と共同作業しており、またこのインフルエンザの発生と血液の安全性及び有用性に対するインパクトを監視するため、AABB のパンデミックインフルエンザ及び血液供給に関する組織間作業委員会と密接に連絡を取っている。今のところ、臨床上必要な場合、輸血のベネフィットが血液や血液製剤による H1N1 型インフルエンザウイルス伝播の理論的な危険性を含むリスクを上回ることを忘れないのが重要である。FDA の規制（FDA regulations at 21 CFR 640.3）において、健康でない人は献血には適していないし、血液事業者はこれらの潜在的な供血者の供血を保留しなければならない。

現在、血液事業者が実施している供血者スクリーニングにより、H1N1 型インフルエンザウイルスの症状を有する患者を同定すべきである。H1N1 型インフルエンザウイルスの人での症状は、通常のヒトインフルエンザと似ていて発熱、咳や喉の痛み、体の痛み、頭痛、寒気や疲労である。H1N1 型インフルエンザウイルスに関連した下痢や嘔吐の報告もある。メキシコや米国において重症化や死亡例が報告されている。現在実施している供血者スクリーニングは、特にヒトに H1N1 型インフルエンザが発生している地域での H1N1 型インフルエンザ伝播のリスクを減少する上で重要な手段である。さらに、良い衛生状態を維持する際に血液事業者が実施している標準的な手法や感染制御の手法は、血液事業における H1N1 型インフルエンザの起こりうる拡大を最小限にするのに役立つであろう。

2006 年 10 月の FDA ガイダンス" Biologic Product Deviation Reporting for Blood and Plasma Establishments"に従い、血液事業者は、供血者のインフルエンザ様疾患の供血後報告（a post donation report）が、既に収集された製品の適切性またはその供血者の将来の供血の適格性を評価すべきかを示していないか検討すべきである。さらに H1N1 型インフルエンザが同定された症例の国及び現地当局への通常の報告に加えて、インフルンザの輸血による伝播に関する懸念を引き起こす症例がある血液事業者は、州及び現地健康部門と同様に適切に"Therapeutics and Blood Safety Branch of the CBER Office of Biostatistics and Epidemiology"に電話する。

新興の 2009 年の H1N1 型インフルエンザウイルスはエンベロープを有する大きなウイルスである。製造販売業者が実施したバリデーションテストでは、現在の血液製剤の製造工程により類似ウイルスが不活化・除去されることが示されている。

報告企業の意見	今後の対応
本剤によるインフルエンザウイルス伝播の報告はない。 鳥インフルエンザウイルスが 60℃10 時間の液状加熱で不活化される報告があるため、本剤の製造工程でインフルエンザウイルスが不活化されると考えられる。	今後とも新しい感染症に関する情報収集に努める所存である。

使用上の注意記載状況・その他参考事項等

1.27

ABJ2009204

2009 H1N1 Flu Virus

Information about Newly Emerging 2009 H1N1 Influenza Virus and Blood Safety

I. Background

The ongoing outbreak of new emerging 2009 H1N1 Influenza Virus (H1N1 flu) infections in the United States has raised questions about whether this virus can be transmitted through blood transfusion. No case of transfusion transmitted seasonal influenza has ever been reported in the United States or elsewhere, and, to date, no cases of transfusion transmitted H1N1 flu have been reported. FDA is continuing to work with the Centers for Disease Control and Prevention (CDC) and is in close contact with the AABB Interorganizational Task Force on Pandemic Influenza and the Blood Supply to monitor this outbreak and its impact on blood safety and availability.

At this time, it is important to remember that, when clinically indicated, the benefits of a transfusion far outweigh the risks, including any theoretical risk of H1N1 flu transmission through blood or blood products.

II. Blood Safety Provisions

Donor Deferral

Under FDA regulations, individuals who are not in good health are not suitable to donate blood and blood establishments must defer these potential donors. (See FDA regulations at 21 CFR 640.3.) Blood donor screening procedures currently in place at blood establishments should identify persons with symptoms of H1N1 flu infection. The symptoms of H1N1 flu in people are similar to the symptoms of regular human influenza and include fever, cough, sore throat, body aches, headache, chills and fatigue. Some people have reported diarrhea and vomiting associated with H1N1 flu. Severe illness and deaths have been reported among infected individuals in Mexico and in the U.S.

The donor screening procedures in place today are important measures in reducing the theoretical risk of transfusion transmitted H1N1 flu, particularly in areas where human cases are occurring. In addition, the continued standard practice of blood establishments in maintaining good hygiene and infection control practices will help to minimize possible spread of H1N1 flu in blood establishments. Staff member hand washing between contacts with different donors is especially important.

Additional information on illness with H1N1 flu and general control strategies can be obtained at the Centers for Disease Control and Prevention (CDC) website at http://www.cdc.gov/swineflu/index.htm.

Potential Component Quarantine and Retrieval

Consistent with FDA's October 2006 Guidance on Biologic Product Deviation Reporting for Blood and Plasma Establishments (see http://www.fda.gov/cber/gdlns/devbld.htm) Medical Directors of blood establishments should consider whether a post donation report of a flu-like illness in a donor indicates that the previously collected products are unsuitable and that the donor's suitability for future donations should be assessed (e.g. deferral until well.) In addition to routine reporting of identified cases of H1N1 flu to state and local health departments, medical directors with any case

raising concerns regarding potential transfusion transmission of influenza, may contact us at the Therapeutics and Blood Safety Branch of the CBER Office of Biostatistics and Epidemiology at 301-827-3974, as well as the CDC via state and local health departments, as appropriate.

Safety of Plasma Derivatives

The newly emerging 2009 H1N1 Influenza Virus is a large lipid-enveloped virus. Validation studies performed by the product manufacturers have shown that viruses with similar characteristics to this agent are effectively inactivated and/or removed by the manufacturing processes in place for these products.

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Updated: April 30, 2009

別紙様式第2-1
番号5

医薬品
医薬部外品　　研究報告　調査報告書
化粧品

識別番号・報告回数			報告日	第一報入手日 2009年4月22日	新医薬品等の区分 該当なし	厚生労働省処理欄

一般的名称	①ポリエチレングリコール処理抗破傷風人免疫グロブリン ②乾燥抗破傷風人免疫グロブリン	研究報告の公表状況	CDC／MMWR 2009; 58(DISPATCH): 1-3	公表国 アメリカ
販売名 (企業名)	①テタノブリンーIH（ベネシス） ②テタノブリン（ベネシス）			

研究報告の概要

米カリフォルニア南部におけるブタインフルエンザA（H1N1）ウイルス感染症例2例および感染源特定などのため現在実施中の調査に関する報告である。

2009年4月17日，米CDCは，カリフォルニア南部の隣接する地区に居住する小児2例の熱性呼吸器疾患はブタインフルエンザA（H1N1）ウイルス感染が原因であると特定した。2例からのウイルスはアマンダジンとリマンダジンに抵抗性があり，米国およびその他の国でのブタインフルエンザ又はヒトインフルエンザウイルスにおいてこれまでに報告されていない固有の遺伝子断片の組み合わせが含まれていた。両症例ともブタに接触していなかった。感染源は不明である。感染源を同定するために、他にブタインフルエンザウイルスで感染している人がいないか調査を現在進めている。

この報告は、この2症例と現在進行中の調査を簡潔に述べる。

ヒトにおけるインフルエンザAの新しいサブタイプではないが、ブタ・インフルエンザA(H1N1)の新しい株は、ヒト・インフルエンザA(H1N1)ウイルスとかなり相異する。かなりの人口が感染し、季節性インフルエンザワクチンH1N1株で予防できないかもしれない。

2症例ともブタに接触していないことは、この新しいインフルエンザウイルスのヒトーヒト感染が起こった可能性を大きくしている。

臨床医は、発熱性の呼吸疾患にかかっている以下に該当する患者の鑑別診断として、季節的なインフルエンザウイルス感染と同様に動物インフルエンザについても考慮すべきである。1）サンディエゴ郡およびインペリアル郡に居住する、2）これらの郡に旅行するかまたはこれらの疾患発症の7日前にこれらの郡から来た発症者と接触があった、3）ブタに最近接触した。

患者がブタインフルエンザに感染していることを推測する臨床医は、呼吸器検体を採取し、州の公共衛生研究所での検査を容易にするために国又は地方の衛生当局に連絡すべきである。

報告企業の意見	今後の対応
米カルフォルニア南部の小児2例の熱性呼吸器疾患はブタインフルエンザA（H1N1）ウイルスによるものであり、当該ウイルスにはブタ及びヒトインフルエンザウイルスでこれまで報告されていない固有の遺伝子断片の組み合わせが含まれていたとするCDCからの報告である。 インフルエンザA(H1N1)はオルソミクソウイルス科に属し、ビリオンは球形で、直径80～120nmの脂質エンベロープを有するRNAウイルスである。万一、インフルエンザA(H1N1)が原料血漿に混入したとしてもBVDをモデルウイルスとしたウイルスバリデーション試験成績から、本剤の製造工程にて十分に不活化・除去されると考えている。	本報告は本剤の安全性に影響を与えないと考えるので、特段の措置はとらない。

使用上の注意記載状況・その他参考事項等

代表としてテタノブリンーIHの記載を示す。

2. 重要な基本的注意

(1) 本剤の原材料となる血液については、HBs抗原、抗HCV抗体、抗HIV-1抗体、抗HIV-2抗体陰性で、かつALT(GPT)値でスクリーニングを実施している。更に、プールした試験血漿については、HIV-1、HBV及びHCVについて核酸増幅検査（NAT）を実施し、適合した血漿を本剤の製造に使用しているが、当該NATの検出限界以下のウイルスが混入している可能性が常に存在する。本剤は、以上の検査に適合した高力価の破傷風抗毒素を含有する血漿を原料として、Cohnの低温エタノール分画で得た画分からポリエチレングリコール4000処理、DEAEセファデックス処理等により抗破傷風人免疫グロブリンを濃縮・精製した製剤であり、ウイルス不活化・除去を目的として、製造工程において60℃、10時間の液状加熱処理及びろ過膜処理（ナノフィルトレーション）を施しているが、投与に際しては、次の点に十分注意すること。

MMWR

Dispatch

April 21, 2009 / 58 (Dispatch);1-3

Swine Influenza A (H1N1) Infection in Two Children --- Southern California, March--April 2009

On April 17, 2009, CDC determined that two cases of febrile respiratory illness occurring in children who resided in adjacent counties in southern California were caused by infection with a swine influenza A (H1N1) virus. The viruses from the two cases are closely related genetically, resistant to amantadine and rimantadine, and contain a unique combination of gene segments that previously has not been reported among swine or human influenza viruses in the United States or elsewhere. Neither child had contact with pigs; the source of the infection is unknown. Investigations to identify the source of infection and to determine whether additional persons have been ill from infection with similar swine influenza viruses are ongoing. This report briefly describes the two cases and the investigations currently under way. Although this is not a new subtype of influenza A in humans, concern exists that this new strain of swine influenza A (H1N1) is substantially different from human influenza A (H1N1) viruses, that a large proportion of the population might be susceptible to infection, and that the seasonal influenza vaccine H1N1 strain might not provide protection. The lack of known exposure to pigs in the two cases increases the possibility that human-to-human transmission of this new influenza virus has occurred. Clinicians should consider animal as well as seasonal influenza virus infections in their differential diagnosis of patients who have febrile respiratory illness and who 1) live in San Diego and Imperial counties or 2) traveled to these counties or were in contact with ill persons from these counties in the 7 days preceding their illness onset, or 3) had recent exposure to pigs. Clinicians who suspect swine influenza virus infections in a patient should obtain a respiratory specimen and contact their state or local health department to facilitate testing at a state public health laboratory.

Case Reports

Patient A. On April 13, 2009, CDC was notified of a case of respiratory illness in a boy aged 10 years who lives in San Diego County, California. The patient had onset of fever, cough, and vomiting on March 30, 2009. He was taken to an outpatient clinic, and a nasopharyngeal swab was collected for testing as part of a clinical study. The boy received symptomatic treatment, and all his symptoms resolved uneventfully within approximately 1 week. The child had not received influenza vaccine during this influenza season. Initial testing at the clinic using an investigational diagnostic device identified an influenza A virus, but the test was negative for human influenza subtypes H1N1, H3N2, and H5N1. The San Diego County Health Department was notified, and per protocol, the specimen was sent for further confirmatory testing to reference laboratories, where the sample was verified to be an unsubtypable influenza A strain. On April 14, 2009, CDC received clinical specimens and determined that the virus was swine influenza A (H1N1). The boy and his family reported that the child had had no exposure to pigs. Investigation of potential animal exposures among the boy's contacts is continuing. The patient's mother had respiratory symptoms without fever in the first few days of April 2009, and a brother aged 8 years had a respiratory illness 2 weeks before illness onset in the patient and had a second illness with cough, fever, and rhinorrhea on April 11, 2009. However, no respiratory specimens were collected from either the mother or brother during their acute illnesses. Public health officials are conducting case and contact investigations to determine whether illness has occurred among other relatives and contacts in California, and during the family's travel to Texas on April 3, 2009.

Patient B. CDC received an influenza specimen on April 17, 2009, that had been forwarded as an unsubtypable influenza A virus from the Naval Health Research Center in San Diego, California. CDC identified this specimen as a swine influenza A (H1N1) virus on April 17, 2009, and notified the California Department of Public Health. The source of the specimen, patient B, is a girl aged 9 years who resides in Imperial County, California, adjacent to San Diego County. On March 28, 2009, she had onset of cough and fever (104.3°F [40.2°C]). She was taken to an outpatient facility that was participating in an influenza surveillance project, treated with amoxicillin/clavulanate

potassium and an antihistamine, and has since recovered uneventfully. The child had not received influenza vaccine during this influenza season. The patient and her parents reported no exposure to pigs, although the girl did attend an agricultural fair where pigs were exhibited approximately 4 weeks before illness onset. She reported that she did not see pigs at the fair and went only to the amusement section of the fair. The Imperial County Public Health Department and the California Department of Public Health are now conducting an investigation to determine possible sources of infection and to identify any additional human cases. The patient's brother aged 13 years had influenza-like symptoms on April 1, 2009, and a male cousin aged 13 years living in the home had influenza-like symptoms on March 25, 2009, 3 days before onset of the patient's symptoms. The brother and cousin were not tested for influenza at the time of their illnesses.

Epidemiologic and Laboratory Investigations

As of April 21, 2009, no epidemiologic link between patients A and B had been identified, and no additional cases of infection with the identified strain of swine influenza A (H1N1) had been identified. Surveillance data from Imperial and San Diego counties, and from California overall, showed declining influenza activity at the time of the two patients' illnesses. Case and contact investigations by the county and state departments of health in California and Texas are ongoing. Enhanced surveillance for possible additional cases is being implemented in the area.

Preliminary genetic characterization of the influenza viruses has identified them as swine influenza A (H1N1) viruses. The viruses are similar to each other, and the majority of their genes, including the hemagglutinin (HA) gene, are similar to those of swine influenza viruses that have circulated among U.S. pigs since approximately 1999; however, two genes coding for the neuraminidase (NA) and matrix (M) proteins are similar to corresponding genes of swine influenza viruses of the Eurasian lineage (*1*). This particular genetic combination of swine influenza virus segments has not been recognized previously among swine or human isolates in the United States, or elsewhere based on analyses of influenza genomic sequences available on GenBank.* Viruses with this combination of genes are not known to be circulating among swine in the United States; however, no formal national surveillance system exists to determine what viruses are prevalent in the U.S. swine population. Recent collaboration between the U.S. Department of Agriculture and CDC has led to development of a pilot swine influenza virus surveillance program to better understand the epidemiology and ecology of swine influenza virus infections in swine and humans.

The viruses in these two patients demonstrate antiviral resistance to amantadine and rimantadine, and testing to determine susceptibility to the neuraminidase inhibitor drugs oseltamivir and zanamivir is under way. Because these viruses carry a unique combination of genes, no information currently is available regarding the efficiency of transmission in swine or in humans. Investigations to understand transmission of this virus are ongoing.

Reported by: *M Ginsberg, MD, J Hopkins, MPH, A Maroufi, MPH, G Dunne, DVM, DR Sunega, J Giessick, P McVay, MD, San Diego County Health and Human Svcs; K Lopez, MD, P Kriner, MPH, K Lopez, S Munday, ML, Imperial County Public Health Dept; K Harriman, PhD, B Sun, DVM, G Chavez, MD, D Hatch, MD, R Schechter, MD, D Vugia, MD, J Louie, MD, California Dept of Public Health. W Chung, MD, Dallas County Health and Human Svcs; N Pascoe, S Penfield, MD, J Zoretic, MD, V Fonseca, MD, Texas Dept of State Health Svcs. P Blair, PhD, D Faix, PhD, Naval Health Research Center; J Tueller, MD, Navy Medical Center, San Diego, California. T Gomez, DVM, Animal and Plant Health Inspection Svc, US Dept of Agriculture. F Averhoff, MD, F Alavrado-Ramy, MD, S Waterman, MD, J Neatherlin, MPH, Div of Global Migration and Quarantine; L Finelli, DrPH, S Jain, MD, L Brammer, MPH, J Bresee, MD, C Bridges, MD, S Doshi, MD, R Donis, PhD, R Garten, PhD, J Katz, PhD, S Klimov, PhD, D Jernigan, MD, S Lindstrom, PhD, B Shu, MD, T Uyeki, MD, X Xu, MD, N Cox, PhD, Influenza Div, National Center for Infectious and Respiratory Diseases, CDC.*

Editorial Note:

In the past, CDC has received reports of approximately one human swine influenza virus infection every 1--2 years in the United States (*2,3*). However, during December 2005--January 2009, 12 cases of human infection with swine influenza were reported; five of these 12 cases occurred in patients who had direct exposure to pigs, six in patients reported being near pigs, and the exposure in one case was unknown (*1,4,5*). In the United States, novel influenza A virus infections in humans, including swine influenza infections, have been nationally notifiable conditions since 2007. The recent increased reporting might be, in part, a result of increased influenza testing capabilities in public health laboratories, but genetic changes in swine influenza viruses and other factors also might be a factor (*1,4,5*). Although the vast majority of human infections with animal influenza viruses do not result in human-to-human

transmission (*2,3*), each case should be fully investigated to be certain that such viruses are not spreading among humans and to limit further exposure of humans to infected animals, if infected animals are identified. Such investigations should include close collaboration between state and local public health officials with animal health officials.

The lack of known exposure to pigs in the two cases described in this report increases the possibility that human-to-human transmission of this new influenza virus has occurred. Clinicians should consider animal as well as seasonal influenza virus infections in the differential diagnosis of patients with febrile respiratory illness who live in San Diego and Imperial counties or have traveled to these areas or been in contact with ill persons from these areas in the 7 days before their illness onset. In addition, clinicians should consider animal influenza infections among persons with febrile respiratory illness who have been near pigs, such as attending fairs or other places where pigs might be displayed. Clinicians who suspect swine influenza virus infections in humans should obtain a nasopharyngeal swab from the patient, place the swab in a viral transport medium, and contact their state or local health department to facilitate transport and timely diagnosis at a state public health laboratory. CDC requests that state public health laboratories send all influenza A specimens that cannot be subtyped to the CDC, Influenza Division, Virus Surveillance and Diagnostics Branch Laboratory.

Interim guidance on infection control, treatment, and chemoprophylaxis for swine influenza is available at http://www.cdc.gov/flu/swine/recommendations.htm. Additional information about swine influenza is available at http://www.cdc.gov/flu/swine/index.htm.

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* Available at http://www.ncbi.nlm.nih.gov/Genbank.