including pig liver and intestines at a barbecue restaurant on August 14, 2004.[21] Blood samples from the relatives were tested for HEV markers with informed consent. Seven of the family members who ate grilled pig liver and/or intestines had IgM- and/or IgG-class anti-HEV in the blood samples taken 37 to 92 days after the barbecue party. Retrospectively, in the previous 6 months or more, dining out at that restaurant was the only occasion all the 13 relatives had eaten together.

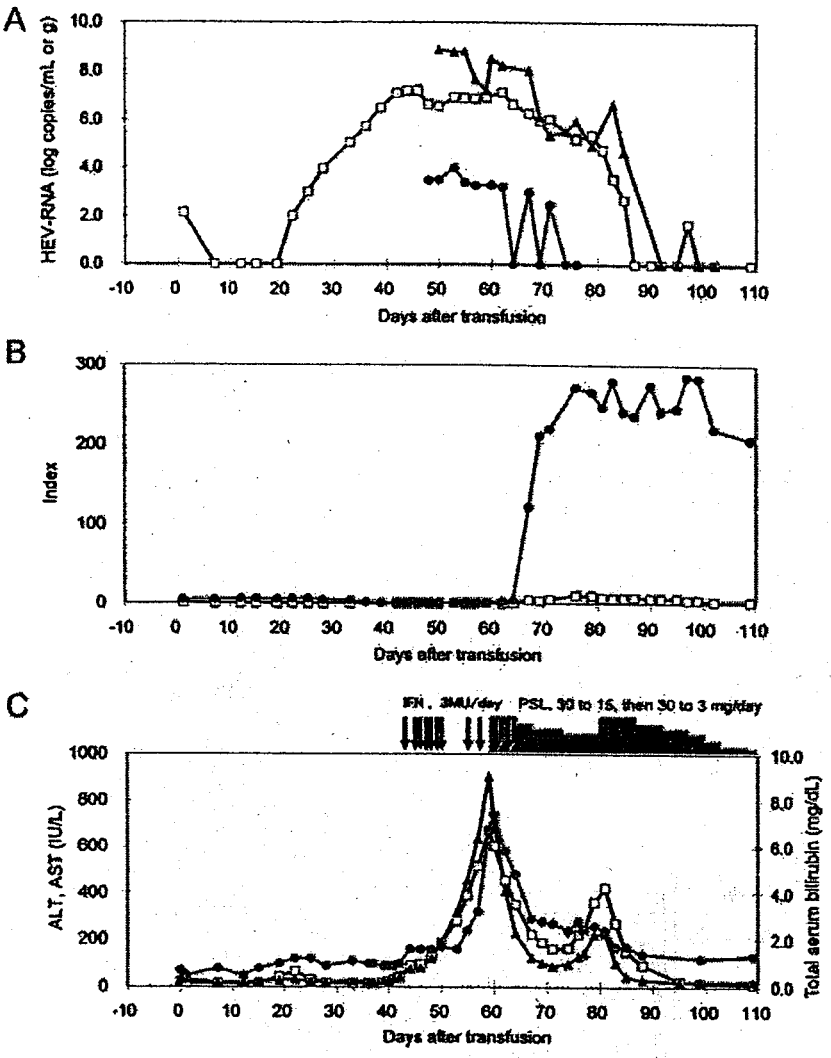


**Fig. 2. Clinical course of transfusion-transmitted hepatitis E with kinetics of (A) HEV RNA, (B) serologic, and (C) biochemical markers after transfusion. The patient had transfusion of PLT concentrates contaminated with HEV on Day 0. (A) HEV RNA load was represented as log copies per mL of serum (□) or saliva (●) or per g of feces (▲). There were no data between Day 0 and Day 44 in feces and saliva. (B) Cutoff values of anti-HEV IgM (□) and IgG (●) antibodies are 30 and 13, respectively. (C) Medications were administered with IFN-α from Day 43 through Day 62 and with PSL from Day 59 through Day 112. (□) ALT; (▲) AST; (●) total serum bilirubin.**

### Clinical course of the patient

It was confirmed that the PLT concentrate (approx. 200 mL) contaminated with HEV was transfused to a 64-year-old Japanese male patient with non-Hodgkin's lymphoma on September 9, 2004, as shown Day 0 in Fig. 2. The patient had been treated with autologous peripheral blood stem cell transplantation accompanied with heavy chemotherapy since July 30, 2004. In the first 3 weeks after the transfusion, liver function tests sustained to be normal. On Day 22, the ALT level increased transiently at 67 IU per L, and HEV was detected in serum. While the ALT level returned to normal, the viral load in serum showed an exponential increase. Levels of aspartase aminotransferase (AST) and ALT took an upward turn on Day 41. There was no evidence for acute infection of hepatitis A virus, HBV, HCV, cytomegalovirus, or Epstein-Barr virus. He was diagnosed as acute hepatitis E. On Day 45, he was referred to the liver unit of Teine Keijinkai Hospital to treat presumed developing acute hepatitis E. Despite antiviral therapy with interferon (IFN) from Day 45, 2′,5′-oligoisoadenylate synthetase in serum never showed apparent increase and no obvious decrement of viral load had obtained (Fig. 2A). Levels of AST and ALT indicated creeping increase to reach highest levels of 903 and 673 IU per L on Day 59, respectively (Fig. 2C). The treatment was switched from IFN to predonisolone (PSL) in expectation of its anti-inflammatory effect. From Day 59 after induction of PSL treatment, AST and ALT showed rapid decrease and improvement of prothrombin time was observed (data not shown). Dosage of PSL was tapered gradually and discontinued on Day 113. Soon after anti-HEV IgG emerged on Day 67, HEV load in the serum sample had declined rapidly, although anti-HEV IgM in the serum sample remained negative (Figs. 2A and 2B). The levels in aminotransferases were normalized after Day 95 (Fig. 2C). The HEV strain JST-KitAsa04C detected in the patient was genotype 4 and its entire sequence analysis showed only a 1-nucleotide difference of 7255 nucleotides, suggesting the two isolates were identical (Fig. 1).

### Serial quantitative changes of HEV load in serum, saliva, and feces of the patient

HEV RNA and anti-HEV were measured for every serum sample before and after the transfusion. In addition, HEV loads were also assessed prospectively for feces and saliva after his transference to the liver unit on Day 45. Any marker for HEV was not detected in serum sampled 37 days before the transfusion. A small amount of HEV RNA was transiently detected in his serum on Day 1, the next day of the transfusion. After the reappearance on Day 22, HEV RNA showed exponential increment with doubling every 29 hours and reached the peak level of 7.2 log copies per mL on Day 44. Beyond its plateau phase lasting 3 weeks, viral load revealed gradual decline over 2 weeks and thereafter decreased promptly. HEV viremia had been finally sustained for 63 days. HEV RNA remained detectable up to Day 97 in serum, Day 71 in saliva, and Day 85 in feces. Peak levels of HEV RNA were found on Day 53 in saliva at 4.0 log copies per mL and on Day 50 in feces at 8.9 log copies per g, respectively. HEV RNA was no longer detectable after Day 99 (Fig. 2A).

## DISCUSSION

In Japan, a nonendemic country for hepatitis E, HEV infection is occurring more frequently than previously recognized. The prevalence of anti-HEV IgG in healthy Japanese persons ranged from 1.9 to 14.1 percent, depending on the geographic area,[20] and the prevalence of HEV RNA among Japanese blood donors with ALT level of at least 201 IU per L was 2.8 percent.[21] The risks of transfusion transmission of HEV might be low; however, five molecularly confirmed cases of transfusion-transmitted HEV infection have been reported in nonendemic countries so far.[12-16] In none of them, HEV infection routes of the causative donors are known. In this report, we have described the first case that the infection route of donor is clarified as zoonotic food-borne. The conclusion is based mainly on two observations.

First, by the epidemiologic study, the donor was determined to be infected in a minioutbreak of HEV infection in the context of food-borne transmission. Six of the 13 relatives who dined out together were positive for the presence of HEV RNA and/or IgM anti-HEV in their serum samples obtained 37 to 92 days after dining at the restaurant (Appendix 1). As for 4 relatives who were positive for the presence of IgM anti-HEV, HEV viremia might have transiently occurred without any symptom and had subsided by the time when blood samples were taken. Since IgM anti-HEV are regarded as the markers of acute HEV infection besides HEV RNA,[10] these facts strongly suggest that family members had recently become infected with HEV probably at the same time and remained asymptomatic. The party at the barbecue restaurant was the only opportunity all the 13 members had eaten together in the estimated period of HEV infection, 2 to 10 weeks.[22,23] Although it was difficult to identify the source of infection because no meat was left, they ingested various kinds of pig meats including liver and intestines, according to the replies to the questionnaire from the family members.[24] From this retrospective research, it is strongly suspected that the family members shared the motive of infection with HEV by ingestion of pig liver and intestines. In Japan, HEV has been isolated from farmed pigs,[9,25] wild deer,[8,26,27] and wild boar[10,11,26,27] as well as humans and recent studies also indicated that HEV is moderately resistant to heat inactivation.[28,29] Some reports suggest that a number of hepatitis E cases in Japan may be via a zoonotic food-borne route.[8-11,25-27,30]

Second, a single transmission route of HEV in this minioutbreak is corroborated by molecularly confirmed facts. From full-length sequence analysis, HEV RNAs detected in the donor and recipient were identical and closely related to that in his father. Among the strains of genotype 4 indigenous to Hokkaido, Japan, these three strains were segregated into a distinct cluster with a bootstrap value of 99 percent in a phylogenetic tree based on the entire or nearly entire sequences of HEV genome. Moreover, when comparing 412-nucleotide sequences (nucleotides 5985-6396 of HRC-HE14C) of ORF2 region, where many sequences of Japanese swine HEV are retrievable in DDBJ/EMBL/GenBank nucleotide sequence databases, high similarity (409/412 nucleotides, 99.3%) was observed between the HEV sequences derived from the causative donor and his father and strain swJL145 (AB105902),[9] which was detected in pig liver sold at a drug store in Hokkaido, Japan.

To date, in acute hepatitis E including transfusion transmission cases, dynamic relationships between infection markers for HEV and disease progression throughout the course from HEV transmission to convalescence of disease have not been demonstrated. This is the first case of acute hepatitis E, in which HEV kinetics in serum as well as in feces and saliva were described by using quantitative RT-PCR for HEV RNA from transfusion up to the end of viremia accompanied by disease progression, and the emergence and increase of anti-HEVs. In the current case, HEV viremia had lasted for 9 weeks or more and viral load reached its peak 15 days before the peak of aminotransferase level and died out promptly right after the appearance of anti-HEV IgG on Day 67. The results led us to understand the chronologic relationship between preceding viremia and after emergence and increase of anti-HEV.

Besides serum, the kinetics of HEV load in feces and saliva were concomitantly observed for the first time in hepatitis E in humans. After the transmission, HEV RNA remained detectable until Day 71 in saliva and Day 85 in feces. Among sera, saliva, and feces, every time point at peak viral loads resembled each other, 50 to 60 days after transmission. These facts may indicate that viral loads in

saliva and feces would also reflect viremia state. In addition, the results for saliva suggest that besides fecal-oral route, oral-oral transmission manner can be another route of human-to-human infection of HEV.

Soon after the transference to liver unit in the hospital, IFN-α therapy was started against HEV infection, indicating the exponential increase of viral load in sera. The levels in 2′,5′-oligoadenylate synthetase, however, induced by IFN and regarded as a predictive marker for favorable IFN efficacy,[31] did not show sufficient increase in serum (data not shown), and HEV load monitored concomitantly indicated no actual decrement during treatment. Thereafter, single-nucleotide polymorphisms in markers predicting the therapeutic efficacy of IFN, such as mannose-binding lectin,[32] MxA,[33] LMP7,[34] and osteopontin,[35] were examined, and all of them did not show the phenotype associated with favorable efficacy of IFN (data not shown).

Throughout his clinical course, no distinct positive result for IgM anti-HEV was observed. It is possible that the concentration of IgM anti-HEV was too low to be detected by the method we used. In fact, some of his samples showed equivocal reaction. Furthermore, underlying disease and the preceding treatment including autologous peripheral blood stem cell transplantation and large dosage chemotherapy might have led the patient to an immunocompromised state that responds inadequately for HEV infection. In fact, both serum levels in IgG and IgM had been indicated consistently less than lower limitation of normal ranges in the entire course (data not shown).

We should note that the present case was not revealed if the two practices had not been introduced, which are not widespread outside Japan. They are ALT screening and donor blood sample repository system. As a safety measure, the Japanese Red Cross Blood Center introduced ALT testing for a surrogate marker for non-A, non-B hepatitis virus infection. Because ALT testing contributes little for HCV infection after HCV antibody testing started, ALT screening has been discontinued in the United States and some other countries. Although the cutoff value may need to be reevaluated, the current case suggests that ALT testing may contribute to excluding blood with the presence of HEV. On the other hand, the Japanese Red Cross has established storing repository samples of all donations since 1996. Blood samples are collected from each donation and stored for 10 years at –30°C to investigate for lookback study such as the suspected cases of transfusion-transmitted infection and alloantibodies for TRALI. This system plays a very important role in the hemovigilance system in Japan.[36,37]

In the present case of transfusion-transmitted acute hepatitis E, the infection route in the blood donor was, for the first time, clarified to be zoonotic food-borne manner. In addition, the entire course including incubation period and disease progression in acute HEV infection was followed by serologic and virologic markers, and the patient was treated by monitoring them. To our knowledge, this is the first report for acute HEV infection in humans, in which various infection markers were prospectively monitored simultaneously with disease progression, excepting experimental hepatitis E in a volunteer.[38]

Our data suggest that hepatitis E is likely caused by consumption of contaminated pig meat, and there is a risk of transfusion transmission of HEV in Japan. The most effective preventive measure to reduce the risk of blood-borne transmission is to screen the blood supply for HEV or to implement pathogen inactivation. The epidemiology and the transfusion-related risks for HEV infection have not been fully understood in industrialized countries including Japan. We are undertaking epidemiologic studies of HEV infection in Japanese blood donors and a feasibility study of NAT screening for HEV in Hokkaido, Japan.

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## APPENDIX 1

**HEV infection markers in the 13 family members who participated in the dinner on August 14, 2004**

| Number* | Age (years) | Sex | Days after Aug 14, 2004 | ALT (IU/L) | HEV markers | | |
|---|---|---|---|---|---|---|---|
| | | | | | RNA ($10^6$/mL) | IgM† (index) | IgG‡ (index) |
| 1 | 39 | Male | 23 | 27 | +(3.1) | –(3.4) | –(2.0) |
| | | | 37 | 236 | +(4.8) | +(60.4) | +(14.2) |
| | | | 49 | 70 | +(2.1) | +(269.5) | +(154.7) |
| | | | 53 | 44 | – | +(257.8) | +(150.5) |
| | | | 77 | 20 | – | +(174.6) | +(163.0) |
| 2 | 69 | Male | 41 | 1511 | +(2.6) | +(187.2) | +(271.4) |
| 3 | 43 | Male | 92 | 34 | – | +(174.7) | +(297.7) |
| 4 | 68 | Male | 79 | 15 | – | +(51.7) | +(283.3) |
| 5 | 37 | Female | 79 | 13 | – | +(110.9) | +(90.3) |
| 6 | 15 | Male | 90 | 17 | – | +(63.3) | +(250.6) |
| 7 | 58 | Female | 79 | 25 | – | –(4.0) | +(25.9) |
| 8 | 67 | Female | 79 | 15 | – | –(1.4) | –(12.9) |
| 9 | 38 | Female | 89 | 12 | – | –(6.1) | –(1.1) |
| 10 | 15 | Male | 77 | 19 | – | –(0.3) | –(0.5) |
| 11 | 14 | Male | 77 | 19 | – | –(7.5) | –(0.3) |
| 12 | 46 | Male | 90 | 15 | – | –(2.2) | –(0.4) |
| 13 | 6 | Female | 90 | 15 | – | –(26.6) | –(1.1) |

Data shown were originally reported by Kato et al.[24] without describing quantitative test results of antibodies and viral RNA and follow-up data of the causative donor.
* Number 1 is the causative donor; Number 2 is the donor's father and died of hepatitis E; others are their relatives.
† Positive ≥30 index.
‡ Positive ≥13 index.

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**研究報告の概要**

＜目的＞
中国の4つの都市における血液ドナー中のHEV陽性率を評価し、HEV感染を排除するためのALT測定の価値を評価すること。
＜方法＞
ルーチンのスクリーニング検査（HCV抗体、HIV 1/2抗体、HBsAg、梅毒およびALT）で陰性と判定されたドナー検体とALT値が高いだけの検体を、中国の4つの都市（北京、ウルムチ、昆明、広州）の4つの血液センターから2005年に収集し、-40℃で冷凍した。全部で6,665の血液ドナーの検体について、2007年にHEV IgG抗体、HEV IgM抗体、HEV Agの測定を行った。
＜結果＞
検査を実施した6,665の血液ドナーのうち、HEV IgG抗体、HEV IgM抗体、HEV Agの各々の陽性率は、24.23%(1,615/6,665)、1.08%(72/6,665)、0.03%（2/6,665）であった。ALTのみが高かった487のドナーのHEV IgG抗体、HEV IgM抗体、HEV Agの陽性率（30.80%、2.05%、0.21%）はすべて、ルーチンスクリーニングで陰性であった6,178のドナーの陽性率（23.71%、1.00%、0.02%）よりも高かった（P<0.05）。2名のHEV Ag陽性ドナーのうち、1名はルーチンのスクリーニングで陰性で、HEV Ag ELISA S/COの平均値が3.4、HEV IgG抗体が陰性、HEV IgM抗体が陰性であった。他方の1名はALTのみが高く、HEV Ag ELISA S/COの平均値が18.0、HEV IgG抗体が陽性でS/COの平均値が10.8、HEV IgM抗体が陰性であった。
＜結論＞
HEVは中国における風土病である。中国におけるルーチンのスクリーニングで陰性と判定された血液ドナーの中で、1%がHEV IgM抗体陽性またはHEV Ag陽性であり、HEVに感染性がある可能性がある。ALTスクリーニングは、中国ではHEV感染血液の排除に一定の役割を有している可能性がある。

**使用上の注意記載状況・その他参考事項等**

代表として静注用ヘブスブリン－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抗HBs抗体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HBs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。

| 報告企業の意見 | 今後の対応 |
|---|---|
| 中国における血液ドナーの約1%は、抗HEV IgM陽性又はHEV抗原陽性であり、HEV感染の可能性があるとの報告である。<br>静注用ヘブスブリン-IHについては、万一、原料血漿にHEVが混入したとしても、EMCおよびCPV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、本剤の製造工程において十分に不活化・除去されると考えている。<br>ヘブスブリンについては、EMCおよびCPV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では本剤の製造工程において十分なLRVが得られないため、製造工程における不活化・除去が十分であるとは説明困難である。そのため、ヘブスブリン用の原料血漿については、弊社にてHEVについてのミニプールNATを試行的に導入した。 | 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。 |

easy to use, FDA approved test to confirm repeat reactives or to resolve discrepant results is lacking.
Aims: To develop a supplemental test for confirming the presence of antibodies to *T. cruzi* in repeatedly reactive blood or plasma units identified by a screening assay.
Methods: The immunoblot assay is based on four different recombinant antigens (rAgs) FP3, FP6, FP10, and TcF, for the detection of antibodies to *T. cruzi*. Each rAg was constructed with multiple antigenic domains of *T. cruzi* including repetitive sequences and non-repetitive sequences. The rAgs are fitted as discrete lines onto the strip. Antibody responses were visually assessed against two internal calibrators (low and high) also applied to the immunostrip as discrete lines. The immunoblot assay sensitivity was evaluated with 688 RIPA confirmed chagasic specimens. The specificity was evaluated with 821 unscreened specimens from random U.S. blood donors and 531 specimens of 30 different unrelated medical conditions, including leishmaniasis, malaria, and autoimmune diseases, or potentially interfering substances. The interpretation of results was as follows: (a) no bands or a single test band = NEGATIVE; (b) two or more test bands with a least on band having intensity of 1+ or higher = POSITIVE; and (c) multiple faint test bands (±) = INDETERMINATE. All samples were initially tested in the PRISM Chagas screening assay; and reactive samples were also tested in two different ELISA and in a radio-immunoprecipitation assay (RIPA).
Results: All 688 chagasic samples showed two to four rAg test bands and were interpreted as positive in the immunoblot assay; sensitivity of 100% (688/688). Among 821 unscreened specimens of random donors, 819 showed none or a single test band, and one gave two faint test bands. One specimen was repeatedly reactive in PRISM Chagas assay, two reference ELISAs, and confirmed in RIPA as positive; while another specimen was non-reactive in these reference tests. Of the 531 specimens with disease states or potentially interfering substances, 525 tested negative, two confirmed positive, 1 false-positive, and three indeterminate.
Conclusions: The sensitivity of the immunoblot assay in the geographically-diverse group of chagasic specimens was 100% (688/688). The resolved specificity of random donor specimens was also 99.88% (819/820). The recombinant antigen based immunoblot assay, in multiple lots and run by multiple technicians, has demonstrated great potential as a supplemental test to confirm the presence of antibodies to *T. cruzi* in blood specimens. Design verification and validation of this assay are ongoing.

P-615

## HEPATITIS B VIRUS DETECTION AMONG VOLUNTARY BLOOD DONORS IN THE MUNICIPALITY OF STRUMICA

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In spite of the progress in the development of diagnostic, therapeutic and prophylactic methods, virus hepatitis still present a serious global health problem. The possibility of transmission of these infections through transfusion of blood and blood derivates implies obligatory control of the donated blood.
Aim: To show the prevalence of Hepatitis B (HBsAg) in volunteer blood donors for the period from 2001 till 2006.
Materials: The presence of virus markers was analyzed in the serum of 9166 blood donors who donated blood at the Department of transfuziology, General Hospital-Strumica, in the period from 2001 till 2006.
Methods: The samples were tested for the presence of viral markers (HBsAg), using tests for HBsAg (Abbott Auxyme Monoclonal EIA).
Results: The presence of markers for Hepatitis B (HBsAg) were found in 89 (0.97%) blood donors. In 2001 the presence of HBsAg was found in 12 blood donors, 2002 – in 20 blood donors, 2003 in 14 blood donors, 2004 in 17 blood donors, 2005 in 14 blood donors, 2006 in 12 blood donors. With A blood group were 42 (47.2%) blood donors, with 0 blood group were 28 (31.4%) blood donors, with B blood group were 10 (11.2%) blood donors and with AB blood group were nine (10.2%) blood donors.
Conclusion: The obligatory testing of the donors blood is of exceptional importance to prevent the transmission of diseases. Moreover, a significant ring in the chain for ensuring safe blood is the selection of a qualitative donor, that is a donor who donates blood volontarily, freely, anonymously and periodically.

P-616

## OCCULT HEPATITIS B VIRUS INFECTION IN BLOOD DONORS FROM CENTRAL PORTUGAL

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Background: The detection of HBV DNA in serum without HBsAg and with/without the presence of antibodies (anti-HBc/anti-HBs), defines the state of the occult hepatitis B virus infection. The prevalence in endemic areas varies from 7% to 19%, while in the west countries varies from 0% to 9%, being greater in people with anti-HBc and/or anti-HBs. Low serum HBV DNA titers, in the range of 100–1000 copies/mL, are typical in occult HBV infection. A high prevalence of occult HBV has been reported in hepatocellular carcinoma (HCC).
Aims: The appearance of the nucleic acid testing (NAT) with great sensibility allows us to identify a population with HBsAg negative but with low levels of HBV DNA in serum. In our Centre all donors are screened for HBV DNA, HIV RNA and HCV RNA.
Methods: In the screening of the hepatitis B serologic markers we have used ELISA and quimioluminiscence tests. In the screening of the HBV DNA we have used the Transcription Mediated Amplification (TMA) technology, in single testing, with predicted HBV detection rate of 50% and 95% of 3.1 and 7.4 IU/mL, respectively.In the screening of HBV viral load we have used PCR technology, with detection limit of 60 IU/mL.
Results: The Regional Blood Centre (Coimbra) started the screening of the HBV DNA to all donors in October 2006. Until November 2007, we have studied 20.881 donors. We found three cases of occult hepatitis B virus infection.
Conclusions: Some aspects need to be investigated, especially the relationship between the occult hepatitis B virus infection and the infectivity of the different blood components. The sensibility of the NAT is very important in the precocious detection of the HBV DNA in blood donors.

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## PREVALENCE OF HEPATITIS E VIRUS INFECTION IN BLOOD DONORS IN DIFFERENT CITIES OF CHINA

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Background: Hepatitis E virus (HEV) is a single strand and non-enveloped RNA virus. HEV infection is normally transmitted via the faeco-oral route. However HEV recently emerged as a transfusion-transmitted pathogen. Several transfusion-transmitted HEV infections have been reported in

 

HEV-hyperendemic or nonhyperendemic countries. In China, neither HEV antibodies nor HEV RNA are systematically tested in blood donors. Alanine aminotransferase (ALT) in serum/plasma has been tested in all blood donors since 1960s in China, before hepatitis B surface antigen screening. With the introduction of specific anti-HCV and viral nucleic acid testing (NAT), ALT test is no longer used in routine donor screening in many countries. However, ALT measurement is still retained as a screening tool for blood donors in China, in consideration that viral hepatitis is endemic in China, although ALT has low specificity for detecting individuals with transfusion-transmitted virus infection risk and its value is controversial.

Aims: To evaluate the prevalence of HEV infection among blood donors in four cities of China and to evaluate the value of ALT measurement for eliminating HEV infectious blood in blood donors.

Methods: Donor samples with negative results in routine screening (anti-HCV, anti-HIV1/2, HBsAg, syphilis and ALT) and samples with ALT elevated alone were collected from four blood centers in four Chinese cities, Beijing (North), Urumchi (Northwest), Kunming (Southwest), and Guangzhou (South) in 2005 and were frozen at -40?. A total of 6665 blood donor samples were tested for anti-HEV IgG, anti-HEV IgM and HEV Antigen (Ag) by enzyme-linked immunoassays (WANTAI Biological Enterprise Co. Ltd, Beijing, China) in 2007. Repeated positive results defined as a positive result. The Person Chi-Squared test or Fisher's exact test were used for the statistical analysis.

Results: Of the 6665 blood donors tested, the prevalence of anti-HEV IgG, anti-HEV IgM and HEV Ag were 24.23% (1615/6665), 1.08% (72/6665) and 0.03% (2/6665) respectively. The prevalence of anti-HEV IgG, anti-HEV IgM and HEV Ag were all higher in 487 donors with elevated ALT alone (30.80%, 2.05% and 0.21%, respectively) than in 6178 donors with negative results in routine screening (23.71%, 1.00% and 0.02%)

Table HEV Seroprevalence in blood donors

| Samples | Cities | Numbers Tested | Anti-HEV IgG : % | Anti-HEV IgM % | HEV Ag (%) |
|---|---|---|---|---|---|
| Samples with negative results in routine screening | Beijing | 2378 | 458 (19.26%) | 30 (1.26%) | 0 (0.00%) |
| | Urumchi | 1910 | 341 (17.85%) | 14 (0.73%) | 1 (0.05%) |
| | Kunming | 1170 | 431 (36.84%) | 11 (0.94%) | 0 (0.00%) |
| | Guangzhou | 720 | 235 (32.64%) | 7 (0.97%) | 0 (0.00%) |
| | Total | 6178 | 1465 (23.71%) | 62 (1.00%) | 1 (0.02%) |
| Samples with elevated ALT alone | Beijing | 72 | 16 (22.22%) | 2 (2.78%) | 0 (0.00%) |
| | Urumchi | 247 | 45 (18.22%) | 1 (0.40%) | 0 (0.00%) |
| | Kunming | 152 | 84 (55.26%) | 6 (3.95%) | 0 (0.00%) |
| | Guangzhou | 16 | 5 (31.25%) | 1 (6.25%) | 1 (6.25%) |
| | Total | 487 | 150 (30.80%) | 10 (2.05%) | 1 (0.21%) |
| Total | | 6665 | 1615 (24.23%) | 72 (1.08%) | 2 (0.03%) |

Data were shown as "numbers of positive samples (positive rate)"

($P < 0.05$). Of the two HEV Ag positive donors, one had negative results in routine screening and had average HEV Ag ELISA S/CO ratio of 3.4, anti-HEV IgG (-), anti-IgM (-); the other had elevated ALT alone and had average HEV Ag ELISA S/CO ratio of 18.0, anti-HEV IgG (+) with average S/CO ratio of 10.8, anti-HEV IgM (-). The following table shows the more detailed results.

Conclusions: Hepatitis E virus is endemic in China. Among blood donors with negative results in routine screening in China, about 1% are anti-HEV IgM (+) or HEV Ag (+) and may be HEV infectious. ALT screening may have some role in eliminating HEV infectious blood in China.

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~~Abstract withdrawn.~~

P-619

## POLYMORPHISM OF HLA-DRB1 OF THE UYGHURS IN CHRONIC HEPATISIS B IN KHOTAN AREA XINJIANG CHINA

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This abstract is read by title only.

P-620

## IMPACT OF PHOTOCHEMICAL TREATMENT OF PLATELET COMPONENTS (INTERCEPT™) ON PLATELET AND RBC COMPONENT USE BY HEMATOLOGY PATIENTS DURING 3 YEARS OF ROUTINE PRACTICE

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Background: In 2003 the Blood Transfusion Center (BTC), Cliniques Universitaires Mont Godinne (CUMG) initiated universal use of pathogen inactivated INTERCEPT Platelets (I-P, Cerus Europe BV, Amersfoort, Netherlands) for transfusion (txn) support of thrombocytopenia. Hematology patients require intensive txn support.

Aims: To examine the impact of I-P adoption on platelet (PLT) and red blood cell concentrate (RBC) use by hematology patients, the duration of support, the number of PLT txn per patient, total PLT dose per patient, and total RBC units per patient were compared for 3 years before I-P adoption, when only conventional PLT (C-P) were used, and for 3 years after adoption of I-P. RBC use served as a surrogate for hemostasis efficacy of PLT txn and was evaluated during periods of PLT support and periods without PLT txn support.

Methods: In both periods, PLT were collected by apheresis in reduced plasma concentration with process leukocyte reduction. For C-P, T-Sol (Fenwal, La Chatre, France) with a ratio to plasma of 70:30% was used. For I-P, Intersol (Cerus) with a ratio to plasma of 65:35% was used. I-P components (2.5–6.0–E11 PLT) were treated with amotosalen (150 μmol/L) plus UVA (3 J/cm sq) to inactivate pathogens and leukocytes. I-P replaced gamma irradiation, bacteria detection, and CMV serology. I-P and C-P were available for issue the day after collection. Days of txn support were calculated from the first PLT txn until 5 days after the last PLT txn. An

Effect of I-P Adoption on Platelet and RBC Use

| Parameter | CP | IP | P |
|---|---|---|---|
| Platelet Use (mean/median) | | | |
| Patients supported | 272 | 276 | |
| Days of PLT support | 31.6/15 | 33.1/15 | 0.70 |
| PLT txn/pt | 20.8/10 | 24.2/11 | 0.17 |
| Total PLT dose ($10^{11}$)/pt | 87.3/41 | 100.8/43 | 0.19 |
| RBC Use During Platelet Support (mean/median) | | | |
| Patients transfused | 222 | 244 | |
| Total RBC units/pt | 16.4/8.0 | 17.6/7.0 | 0.64 |
| RBC Use Outside of Platelet Support (mean/median) | | | |
| Patients transfused | 237 | 235 | |
| Total RBC units/pt | 12.7/8.0 | 12.7/8.0 | 0.99 |

別紙様式第2-1

No. 30

# 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 | 新医薬品等の区分 | 機構処理欄 |
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| | | | | 2008. 7. 22 | 該当なし | |

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**研究報告の概要**

○米国医師会がゲイ男性の供血5年延期を「容認できる」との考え
米国医師会(AMA)は、男性同性愛行為を行った供血者の供血延期期間を生涯から5年間に変更するとした連邦の方針を支持するという声明を採択した。この声明は2008年のAMA年次総会で採択され、「AMAは、現在の科学的エビデンスとリスク分析モデルに基づき、MSMに対する5年間の供血延期は容認できる(supportable)と認める」と述べている。AMAによると、「容認できる」という言葉は、基本的に、FDAに対して新しい方針を通知し「実施に協力する」ことを意味している。また、AMAは今回の変更に対して反対を主張しない。
FDAは1977年以降、採血事業者に対し、MSMの供血を生涯延期とすることを求めてきた。AMAの声明は、血液事業者団体が主張する1年間の供血延期により近いものとなっている。血液事業者は、供血延期は金銭や薬物と引き替えのセックスなどハイリスク行為に対して実施すべきであると主張してきた。また、最近ではゲイ・グループによる反対運動、政府機関や大学での議論も行われ、一部の大学では構内での移動採血を中止しようとする動きが出ていた。

| 報告企業の意見 | 今後の対応 |
|---|---|
| 米国医師会は、男性同性愛行為を行った供血者の供血延期期間を生涯から5年間に変更するとした連邦の方針を支持するという声明を採択したとの報告である。MSMのHIV等ウイルス感染率は高く、日本においても1年間の献血延期の他、検査目的の献血禁止などの対策を引き続き行っていく必要がある。 | 日本赤十字社は、輸血感染症対策として、男性と性的接触を持った男性は1年間献血不適としている。今後も引き続き情報の収集に努める。 |

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2008 #26 July 4, 2008

INSIDE:



## AMA Deems Five-Year Blood Donor Deferral for Gay Men "Supportable"

The American Medical Association (AMA) has adopted a statement indicating it may support changing the federal policy imposing a lifetime deferral for potential blood donors who have had sex with men to a five-year deferral.

The statement, adopted by the AMA House of Delegates at the 2008 AMA Annual Meeting June 14-18 in Chicago, reads: "*The AMA recognizes that based on existing scientific evidence and risk assessment models, a shift to a five-year deferral policy for blood donation from men who have sex with men (MSM) is supportable.*"

According to the AMA, the word "supportable" basically means the organization will notify the Food and Drug Administration of its new policy and "will be open to work with groups to advance the policy." In addition, the AMA will not speak up against efforts to examine changing the federal deferral requirement.

The FDA requires blood collectors to permanently defer men who have had sex with men (MSM) since 1977 from blood donation. The AMA statement, recommended by its Council on Science and Public Health, hews closer to the one-year deferral for MSM called for in a joint recommendation by America's Blood Centers, AABB, and the American Red Cross. The organizations said such a policy is more consistent with deferrals for other high-risk activities, such as receiving money or drugs for sex. They have argued that public education and the development of sensitive nucleic acid amplification tests have significantly reduced the residual risk of sexually transmitted diseases entering the blood supply.

In recent years, the controversial federal policy has sparked a number of protests by gay groups, who say it was inspired by and promotes unfair stereotypes, and arguments among government officials and academics, who say it is violates non-discrimination policies. This year alone, California's San Jose State University decided to ban blood drives on its 30,000-student campus over discrimination concerns. At Sonoma State University in Santa Rosa, a professor suggested ending blood drives there because the lifetime deferral violates the university's non-discrimination policy, though after a protracted debate involving faculty and students the university decided to allow blood collection to continue. The Santa Clara County Board of Supervisors in February voted unanimously to oppose the federal policy and encourage federal lobbyists to work to overturn the ban.

(continued on page 2)