cells and is easily isolated from both the subject's plasma and peripheral blood mononuclear cells (**Supplementary Methods**). Her viral load cannot, however, be quantified with a group M–specific commercial assay (Amplicor Monitor v1.5, Roche) or with an academic assay (Generic HIV charge virale, Biocentric[3]) (**Supplementary Fig. 2**). We did not obtain amplification with complementary group M–specific PCRs (**Supplementary Methods**). We initially suspected HIV-1 group O infection, endemic in western central Africa, especially in view of the subject's Cameroonian origin. However, amplification with our usual group O primers failed (**Supplementary Methods** and **Supplementary Table 1**), leading us to search for a divergent virus by using a nonspecific extra-long RT-PCR method. We successfully amplified the viral genome with this approach, allowing us to fully sequence it (**Supplementary Methods**, **Supplementary Fig. 5** and **Supplementary Table 2**).

Evolutionary analysis of the near-complete genome sequence (**Supplementary Methods**) shows that the RBF168 strain is most closely related to SIVgor (**Fig. 1a** and **Supplementary Fig. 3**), and similarity plotting confirms that this relationship is maintained in all regions of the genome (**Fig. 1b**). Before the discovery of strain RBF168, HIV-1 group O was the lineage most closely related to SIVgor, but it is too divergent to be directly derived from current SIVgor strains[4]. As strain RBF168 clusters significantly with SIVgor strains (see support values on tree, **Fig. 1a** and **Supplementary Fig. 3**), the most likely explanation for its emergence is gorilla-to-human transmission of SIVgor (**Supplementary Fig. 4a,b**). Similar to the proposed chimpanzee origin for the HIV-1 group O and SIVgor lineage[4], we cannot rule out the possibility that SIVcpz gave rise to strain RBF168, either indirectly by transmission to gorillas and then to humans (**Supplementary Fig. 4a,b**) or directly by transmission to humans and also to gorillas (**Supplementary Fig. 4c**). Detection of RBF168-like viruses in chimpanzees would be needed to confirm this possibility.

Strain RBF168 thus represents a new HIV-1 variant and is the prototype of a new human lineage that we designate as putative group P, pending the identification of further human cases, in keeping with nomenclature guidelines[6]. The human case described here does not seem to be an isolated incident, as before coming to Paris the subject had lived in the semiurban area of Yaoundé, the capital of Cameroon, and reported no contact with apes or bush meat (**Supplementary Methods**), and the variant's high level of replication *in vivo* and ready isolation in culture indicate that it is adapted to human cells. This efficient replication of RBF168 is rather unexpected, given the absence of an arginine (or lysine) at position 30 in the Gag protein, considered a signature of human-specific adaptation of HIV-1 (ref. 9). Contrary to most HIV-1 strains (apart from group M subtype C), but like SIVgor and all SIV*cpzPtt* strains[9], RBF168 has a methionine at this amino acid position.

The human prevalence of this new lineage remains to be determined. Strain RBF168 shows typical HIV-1 behavior in serological and nonspecific molecular tests, suggesting that it could be circulating unnoticed in Cameroon or elsewhere. HIV screening tests and molecular tools have improved markedly over the past two decades, enabling the distinct HIV types and groups to be detected. This increased sensitivity, however, may paradoxically mask the circulation of divergent strains. Indeed, new variant infections can now be detected only by monitoring discrepancies between immunological status and virological results in molecular assays. Currently, there is no simple detection algorithm based on existing serological and molecular tools, and, therefore, only nucleotide sequencing can identify further HIV-1 group P strains.

In conclusion, our findings indicate that gorillas, in addition to chimpanzees, are likely sources of HIV-1. The discovery of this novel HIV-1 lineage highlights the continuing need to watch closely for the emergence of new HIV variants, particularly in western central Africa, the origin of all existing HIV-1 groups.

Accession codes. The near-full-length sequence of strain RBF168 has been submitted to GenBank under accession number GQ328744.

Note: Supplementary information is available on the Nature Medicine website.

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AUTHOR CONTRIBUTIONS

J.-C.P., M.L. and F.D.O. conceived of and designed the experiments. M.L., F.D.O. and V.L. performed the molecular and serological experiments. J.E.D. and D.L.R. performed the computational analysis. P.C. managed the subject and collected epidemiological data. J.-C.P., V.L. and F.D. monitored the subject's virologic status. J.-C.P., M.L., J.E.D., F.D.O., D.L.R. and F.S. wrote the paper.

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1. Gao, F. *et al. Nature* **397**, 436–441 (1999).
2. Keele, B.F. *et al. Science* **313**, 523–526 (2006).
3. Van Heuverswyn, F. *et al. Nature* **444**, 164 (2006).
4. Takehisa, J. *et al. J. Virol.* **83**, 1635–1648 (2009).
5. Simon, F. *et al. Nat. Med.* **4**, 1032–1037 (1998).
6. Robertson, D.L. *et al. Science* **288**, 55–56 (2000).
7. Gueudin, M. *et al. J. Acquir. Immune Defic. Syndr.* **36**, 639–641 (2004).
8. Rouet, F. *et al. J. Acquir. Immune Defic. Syndr.* **45**, 380–388 (2007).
9. Wain, L.V. *et al. Mol. Biol. Evol.* **24**, 1853–1860 (2007).

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研究報告の概要

○乳児への食物の噛み与え行為：HIV伝播のリスク要因の可能性

目的：一部の保護者は乳児に食物を噛んで与えているが、一般的に、当該行為と離乳期間におけるHIV伝播とは関連付けられていなかった。我々は、この行為に関連すると考えられる米国のHIV伝播3症例について述べる。

患者と方法：9、15、39ヵ月齢の小児においてHIV感染3症例が診断された。臨床症状の発症により検査を実施し、他の伝播経路を除外するため詳細な調査を行った。また、envのC2V3C3またはgp41領域とgag領域をコードするp17を用いて、症例および疑わしい感染源から得られたウイルスの系統発生学的比較を行った。

結果：2症例は、HIVに感染した母親から授乳は行われず、米国のHIV検査ガイドラインによってHIVの周産期伝播は否定されていた。第3の症例では、小児の世話を手伝った叔母がHIVに感染していたが、母親は感染していなかった。3例ともHIV感染者が世話をし、食物を噛んで与えていた。2例では、食物を噛み与えた大人に口腔内出血があったことが報告された。系統樹解析により、3例中2例において、世話をしていたHIV感染者からの噛み与えにより感染したという疫学的結論が支持された。

結論：この報告症例は、噛み与えとHIV感染とを関連づける有力な証拠を提供するものである。これは、重大な世界的影響を有する未報告の伝播ルートであり、これまで授乳によると考えられてきた乳児の生後HIV伝播報告の説明となり得る。噛み与えリスクおよび歯周病などの修飾因子についての理解が深まるまでは、HIV感染あるいはリスクのある保護者や出産を控えた親に対して、噛み与え行為について質問し、安全性が高く実行しやすい離乳食を指導するよう医療提供者に勧める。

報告企業の意見	今後の対応	使用上の注意記載状況・その他参考事項等
・HIVに感染した保護者が食物を噛み与えることによって乳児がHIVに感染したことが、系統樹解析により支持されたとの報告である。 ・これまで、本製剤によるHIV感染の報告はない。また本製剤の製造工程には、平成11年8月30日付医薬発第1047号に沿ったウイルス・プロセスバリデーションによって検証された2つの異なるウイルス除去・不活化工程が含まれている。さらに最終製品についてHIV-NAT陰性であることを確認している事から本製剤の安全性は確保されていると考える。	今後も情報の収集に努める。なお、日本赤十字社ではHIV抗体検査にこれまでの凝集法と比べてより感度の高い化学発光酵素免疫測定法（CLEIA）を導入したことに加え、20プールNATについてもHIV-2及びHIVグループOの検出が可能な新NATシステムを導入し、陽性血液を排除している。	赤十字アルブミン20 赤十字アルブミン25 赤十字アルブミン20%静注4g/20mL 赤十字アルブミン20%静注10g/50mL 赤十字アルブミン25%静注12.5g/50mL 血液を原料とすることに由来する感染症伝播等

(9)

Practice of Feeding Premasticated Food to Infants: A Potential Risk Factor for HIV Transmission

WHAT'S KNOWN ON THIS SUBJECT: Although some caregivers are known to premasticate food for infants, usually during the weaning period, HIV transmission has not been linked to this practice.

WHAT THIS STUDY ADDS: The reported cases provide compelling evidence linking premastication to HIV infection, a route of transmission not previously reported that has important global implications including being a possible explanation for some of the reported cases of "late" HIV transmission in infants, so far attributed to breastfeeding.

ABSTRACT

OBJECTIVES: Although some caregivers are known to premasticate food for infants, usually during the weaning period, HIV transmission has not been linked to this practice. We describe 3 cases of HIV transmission in the United States possibly related to this practice.

PATIENTS AND METHODS: Three cases of HIV infection were diagnosed in children at ages 9, 15, and 39 months; clinical symptomatology prompted the testing. A thorough investigation to rule out alternative modes of transmission was conducted. In addition, phylogenetic comparisons of virus from cases and suspected sources were performed by using the C2V3C3 or gp41 region of *env* and the p17 coding region of *gag*.

RESULTS: In 2 cases, the mothers were known to be infected with HIV, had not breastfed their children, and perinatal transmission of HIV had previously been ruled out following US HIV testing guidelines. In the third case, a great aunt who helped care for the child was infected with HIV, but the child's mother was not. All 3 children were fed food on multiple occasions that had been premasticated by a care provider infected with HIV; in 2 cases concurrent oral bleeding in the premasticating adult was described. Phylogenetic analyses supported the epidemiologic conclusion that the children were infected through exposure to premasticated food from a caregiver infected with HIV in 2 of the 3 cases.

CONCLUSIONS: The reported cases provide compelling evidence linking premastication to HIV infection, a route of transmission not previously reported that has important global implications including being a possible explanation for some of the reported cases of "late" HIV transmission in infants, so far attributed to breastfeeding. Until the risk of premastication and modifying factors (eg, periodontal disease) are better understood, we recommend that health care providers routinely query children's caregivers and expecting parents who are infected with HIV or at risk of HIV infection about this feeding practice and direct them to safer, locally available, feeding options. *Pediatrics* 2009; 124:658–666

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KEY WORDS
HIV, feeding, premastication, prechewed, child

ABBREVIATIONS
MTCT—mother-to-child transmission
CDC—Centers for Disease Control and Prevention
PCR—polymerase chain reaction
EIA—enzyme immunoassay
EBV—Epstein-Barr virus

The views in this article are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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The availability of antiretroviral medications, the appropriate use of cesarean delivery, and the avoidance of breastfeeding have dramatically reduced the incidence of mother-to-child transmission (MTCT) of HIV in the United States and other developed nations. Every diagnosis of HIV infection in a child, especially in the developed world, should prompt us to identify missed opportunities for diagnosis and intervention to prevent MTCT.[1,2] Although the practice of premasticating food for children, usually during the weaning period, has been described in various parts of the world,[3–8] including the United States, HIV transmission has not been linked to this practice. We report 3 cases of pediatric HIV infection that are likely to have resulted from a child, who was not infected with HIV, receiving premasticated (prechewed) food from an adult who was infected with HIV.

PATIENTS AND METHODS

Local health departments investigated the 3 cases through interviews with the available involved adults and through review of medical charts. Blood specimens from the children, available family caregivers, and the sexual partner of a deceased caregiver were sent to the Centers for Disease Control and Prevention (CDC) for HIV nucleic acid extraction, polymerase chain reaction (PCR) amplification, and genetic sequencing of the C2V3C3 or gp41 coding regions of *env* and the p17 coding region of *gag*.[9] These regions are commonly used for phylogenetic comparison of HIV sequences to determine relatedness between strains when transmission is suspected. Phylogenetic analysis has been widely used in transmission cases, both epidemiologic and forensic, and both person-to-person and transmission chains.[9] In brief, sequences were edited with Sequencher 3.1 software (Gene Codes, Madison, WI) and aligned with the SE-AI 1.0 sequence alignment editor.[10] The Modeltest 3.04 program[11] was used with each alignment to test for a statistically justified model of DNA substitution for use in the phylogenetic tree-building program by using neighbor-joining methodology implemented in *PAUP**.[12] Because of the epidemiologic focus of this report, phylogenetic analysis has been used to either support or fail to support the conclusions of the epidemiologic investigations. Available family caregivers consented to specimen collection and participation in the investigation. In addition, consent to report deidentified case details was obtained from the mothers of the children in cases 1 and 3. Case 1, who is now an adolescent, provided his assent as well. Unfortunately, Case 2 and his mother, as well as the great-aunt of case 1, have died.

RESULTS

Case 1 (Miami, FL)

In 1993, a previously healthy 15-month-old black boy was seen by a pediatrician for recurrent diarrhea and otitis media. The results of a first-generation HIV-1 antibody test (enzyme immunoassays [EIAs]) (Bio-Rad Laboratories, Hercules, CA) and Western blots performed on specimens from the child at 15, 16, and 19 months of age were positive. PCR-based tests for HIV were not available for clinical care at that time. The results of EIAs performed on specimens from the mother (21 years old) at these same 3 intervals were negative.

The mother reported that when the child was aged 9 to 14 months, she and the infant had lived with a maternal great-aunt (33 years old) infected with HIV. During this time, the great-aunt helped care for the child and fed him food that she had premasticated. The mother noted that on more than 1 occasion, the great-aunt's gingiva were bleeding when she premasticated the child's food, and the mother saw blood mixed with the prechewed food; however, at that time, the mother was unaware of the great-aunt's HIV diagnosis. The great-aunt died of sepsis and pneumonia related to *Streptococcus pneumoniae* when the child was ~14 months of age (~1 month before the child's first positive EIA test result). She was not reported to be on antiretroviral medications and had an absolute CD4 count of ~270 cells per μL on more than 1 occasion during the 6 months before her death.

The great-aunt had been in a 12-year sexual relationship with a male intravenous drug user who was HIV-infected. The mother stated that he did not use intravenous drugs in the house while she and the child resided there. She did not recall seeing needles in the house (and thus did not believe that the child could ever have been stuck by one) and did not believe that the child had ever been sexually abused by her great-aunt's sexual partner. In addition, there was no history of him ever feeding the child premasticated food.

HIV phylogenetic analysis was performed on the HIV-1 sequences of the great-aunt's sexual partner because clinical specimens from the great-aunt had not been banked before her death. Phylogenetic analysis of the HIV-1 sequences from the child and the great-aunt's sexual partner showed no phylogenetic clustering, suggesting that these 2 viral strains were not epidemiologically linked (Fig 1). However, the history of premastication in the absence of known risk factors for HIV transmission and the possibility that the great-aunt's HIV strain was from a source other than her sexual partner suggested that the great-aunt was the possible source of the child's HIV infection.

Case 2 (Miami, FL)

A black child born to a mother (36 years old) infected with HIV was followed up in the University of Miami

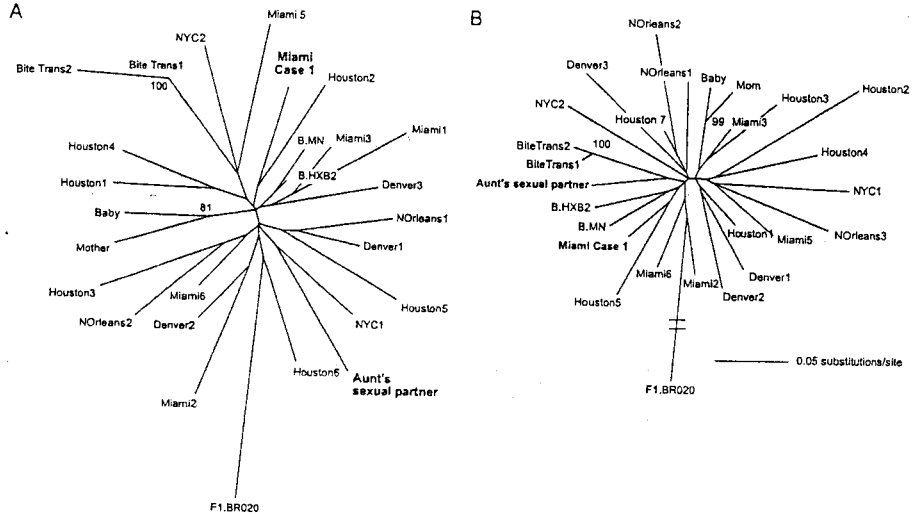

FIGURE 1

Case 1 (Miami). A, Phylogenetic relationship of the HIV sequences derived from case 1 and the great-aunt's sexual partner, 5 unrelated subtype B strains from Miami (Miami 1–3, 5, and 6), 15 unrelated subtype B strains from US cities other than Miami (Denver 1–3, Houston 1–6; New Orleans 1 and 2; New York City 1 and 2, B.MN, and B.HXB2), 1 subtype F strain (F1.BR020), and 2 epidemiologically related transmission pairs (bite transmission 1 and 2; infant and mother). Shown is a neighbor-joining tree of the gp17 region of *gag*; only bootstrap values of >70% are indicated. B, Phylogenetic relationship of the HIV sequences derived from case 1 and the great aunt's sexual partner, 4 unrelated subtype B strains from Miami (Miami 2, 3, 5, and 6), 16 unrelated subtype B strains from US cities other than Miami (Denver 1–3, Houston 1–5 and 7, New Orleans 1–3, New York City 1 and 2, B.MN, and B.HXB2), 1 subtype F strain (F1.BR020), and 2 epidemiologically related transmission pairs (bite transmission 1 and 2; infant and mother). Shown is a neighbor-joining tree of the C2V3C3 region of *env*; only bootstrap values of >70% are indicated. In A and B, US subtype B sequence strains were used as references along with subtype F as an outgroup. Sequences from 2 epidemiologically related transmission pairs were also included (bite transmission 1 and 2; infant and mother). Phylogenetic analysis shows no clustering or epidemiological relatedness between the virus from case 1 (Miami) and the virus from the great aunt's sexual partner.

Pediatric HIV Screening Clinic until 1993, when HIV-1 infection was ruled out on the basis of negative results from first-generation HIV-1 antibody test (EIAs) (Bio-Rad Laboratories) performed when the child was aged 20 and 21 months. PCR-based tests for HIV were not available for clinical care at that time. The child had normal immunoglobulin levels and a normal CD4 count (absolute count: 1700 cells per μL) at the time of the negative EIA results. Neither the mother nor child received perinatal antiretroviral prophylaxis. In 1995, at age 39 months, the child was seen by a pediatrician for anemia and recurrent submandibular lymphadenitis with abscess caused by *Mycobacterium fortuitum*. The mother's history of AIDS and intranasal cocaine abuse without intravenous drug abuse, combined with the child's clinical presentation, prompted the pediatrician to order an HIV-1 EIA (Bio-Rad Laboratories), a confirmatory Western blot, and p24 antigen testing for the child; all results were positive. A concurrent CD4 count of 24 cells per μL (1%) indicated severe immunosuppression.

The mother reported feeding the child premasticated table food but could not recall details regarding the child's age or her own oral health during the time she prechewed the child's food.

Phylogenetic analysis of the mother's and the child's HIV-1 sequences supported the epidemiologic conclusion that the mother was the source of the child's HIV-1 infection (Fig 2).

Case 3 (Memphis, TN)

In 2004, a 9-month-old black girl was seen in an emergency department because of fever, jaundice, nosebleed, oral thrush, and failure to thrive. HIV-1 infection was diagnosed based on an ultrasensitive HIV-1 RNA PCR of >100 000 copies per mL (Cobas Amplicor HIV-1 Monitor 1.5 test [Roche Molecular Systems, Inc, Branchburg, NJ]; dynamic range of detection: 50–100 000 copies per mL). Given the mother's history of chronic HIV infection since 1995, this child had previously been screened for perinatal infection. Three

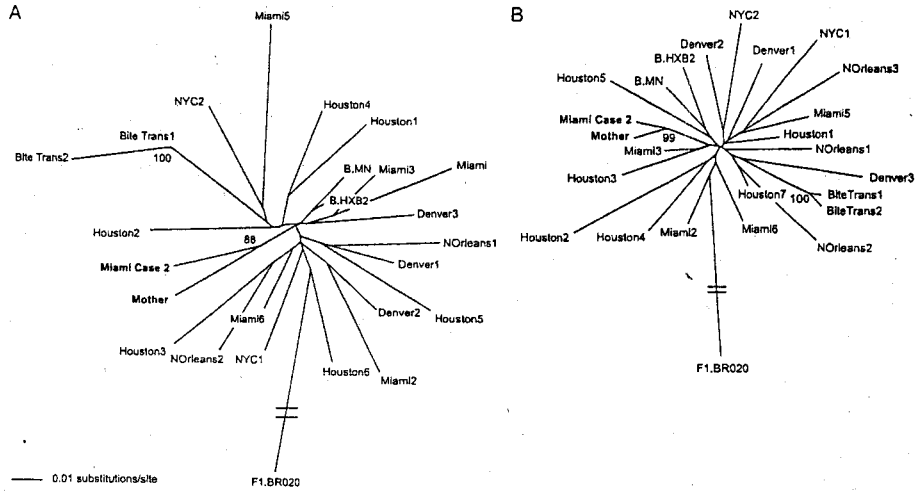

FIGURE 2

Case 2 (Miami). A, Phylogenetic relationship of the HIV sequences derived from the mother-infant pair of case 2, 5 unrelated subtype B strains from Miami (Miami 1–4 and 6), 15 unrelated subtype B strains from US cities other than Miami (Denver 1–3, Houston 1–6, New Orleans 1 and 2; New York City 1 and 2, B.MN, and B.HXB2), 1 subtype F strain (F1.BR020), and 1 epidemiologically related human bite-transmission pair (bite transmission 1 and 2). Shown is a neighbor-joining tree of the gp17 region of *gag*; only bootstrap values of >70% are indicated. In A and B, US subtype B sequences were used as reference strains along with a subtype F as an outgroup. Sequences from an epidemiologically related transmission pair were also included (bite transmission 1 and 2). Phylogenetic analysis shows strong clustering, with an 88% bootstrap support for the epidemiological relatedness between the virus from case 2 (Miami) and the child's mother. B, Phylogenetic relationship of the HIV sequences derived from the mother-infant pair of case 2 from Miami, 4 unrelated subtype B strains from Miami (Miami 2, 3, 5, and 6), 16 unrelated subtype B strains from US cities other than Miami (Denver 1–3, Houston 1–5 and 7, New Orleans 1–3, New York City 1 and 2, B.MN, and B.HXB2), 1 subtype F strain (F1.BR020), and 1 epidemiologically related human bite-transmission pair (bite transmission 1 and 2). Shown is a neighbor-joining tree of the C2V3C3 region of *env*; only bootstrap values of >70% are indicated. Phylogenetic analysis shows strong clustering with a 99% bootstrap support for the relatedness between the virus from case 2 (Miami) and the child's mother.

standard quantitative HIV RNA viral loads (Cobas Amplicor HIV-1 Monitor 1.5 test; dynamic range of detection: 400–750 000 copies per mL) were performed at 41, 60, and 118 days of life. Results of all 3 tests were negative (no copies of HIV RNA detected).

The mother (31 years old) had not adhered to highly active antiretroviral therapy during pregnancy. During pregnancy, she was started on nevirapine, stavudine, and lamivudine and was later switched to once-a-day ritonavir-boosted atazanavir and tenofovir because of poor compliance. Her viral load on the day before delivery was 35 100 copies per mL. The child was delivered at 35 weeks' gestation via cesarean delivery because of the mother's high blood pressure and edema. The mother received intravenous zidovudine before her cesarean delivery. The mother reported that she gave the infant oral zidovudine during the first 6 weeks of life and that the infant did not breastfeed.

At ~8 months of age, the child was seen for low-grade fever and was diagnosed with oral candidiasis and a nonspecific viral infection. In the following week, a red blotchy rash developed on the child's face, arms, and legs; the pediatrician ascribed the rash to allergic dermatitis.

A clinician who routinely queried caregivers about infant care feeding practices, including premastication, determined that the mother had intermittently offered the child prechewed meats from ~120 days of life until the child's current illness. The mother reported that during the period that she prechewed the child's food, she had intermittently bleeding gums and mouth sores that later resolved spontaneously or with medications for oral thrush. During this same period, the mother's adherence to highly active antiretroviral therapy was poor, her HIV viral load was 499 000 copies per mL, and her CD4 count was 100 cells per μL (6%).

Phylogenetic analysis of the mother's and the child's HIV-1 sequences sup-

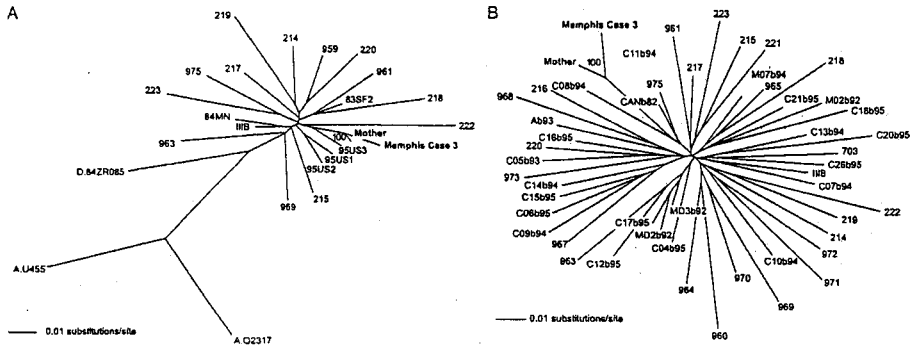

FIGURE 3

Case 3 (Memphis). A, Phylogenetic relationship of the HIV sequences derived from the mother-infant pair of case 3 and unrelated subtype strains from the United States (19 subtype B, 2 subtype A, and 1 subtype D). Shown is a neighbor-joining tree of the gp17 region of *gag*; US subtype B sequences and 1 subtype D sequence were used as reference strains in the tree, and 2 subtype A sequences were used as an outgroup. Only bootstrap values of >70% are indicated for the subtype B branching order. This phylogenetic analysis shows strong clustering, with a 100% bootstrap support for the epidemiological relatedness of the virus from case 3 (Memphis) and the child's mother. B, Phylogenetic relationship of the HIV sequences derived from the mother-infant pair of case 3 from Memphis and 49 unrelated subtype B strains from the United States. Shown is a neighbor-joining tree of the gp41 region of *env*, only bootstrap values of >70% are indicated. US subtype B sequences were used as reference strains in this unrooted tree. Phylogenetic analysis shows strong clustering with a 100% bootstrap support for the relatedness between the virus from case 3 (Memphis) and the child's mother.

ported the epidemiologic conclusion that the mother was the source of HIV-1 infection in the child (Fig 3).

In all 3 cases, additional follow-up interviews with caregivers and physical examinations of the children did not reveal other modes of potential HIV transmission (eg, percutaneous injuries, transfusion or receipt of transplanted tissues, other parenteral exposures or other high-risk contacts [including sexual abuse] with persons infected with HIV in the household).

DISCUSSION

The cases described suggest that HIV may be transmitted through consumption of food that has been premasticated by a person infected with HIV. To our knowledge, this route of HIV transmission has not been reported previously. Bleeding in the oral cavity of the adult infected with HIV, who prechewed the food as documented in cases 1 and 3, was likely the primary source of HIV. The caregivers' lack of access to or lack of adherence to perinatal HIV prophylaxis or antiretroviral therapy probably decreased the suppression of their HIV-1 viral loads. This factor in addition to the children's compromised oral mucosa because of teething or intercurrent oral illness such as candidiasis (reported in case 1) likely facilitated HIV transmission. In addition, tonsillar epithelial factors[13] may have facilitated HIV infection because the tonsils come into contact with blood-tinged food and saliva.

In reviewing the cases, it is important to understand why the first 2 cases were not reported earlier. In cases 1 and 2, the clinicians first contacted the local health department soon after each child's HIV diagnosis. The local and state health departments collaborated with the CDC to conduct an epidemiological investigation. These 2 cases were not reported immediately to the general public for several reasons. Only one of the two possible transmission events was supported by phylogenetic data. Prechewing as a mode of HIV transmission had not been described, and ample data at the time indicated that routine household contact and kissing were not associated with a significantly increased risk of oral HIV transmission. In case 1, transmission through child sexual abuse, a known mode of pediatric HIV transmission that is difficult to establish, and needle-stick exposures were denied but could not be absolutely ruled out. The report of a third possible case, supported by laboratory data, provided the impetus for this report.

Although the practice of premasticating food for children has been described in various parts of the world,[5–8,14–16] including the United States, the extent of this practice is not well known. In the late 1980s, a first-year medical student's observation of this practice prompted a survey of black patients at a primary care pediatrics clinic at the University of Nebraska Medical Center.[7] Although the reports of several infant-feeding surveys conducted at about this time did not mention the practice of premastication, 45 (65%) of 68 adult caregivers in the Nebraska survey acknowledged prechewing food for their infants, and 90% reported knowledge of this practice.[7] More recently, a study of oral health in a random sample of Alaska Native children (aged 12–36 months) and their caregivers documented that 86.2% of caregivers were currently prechewing or had prechewed food for their infants.[8]

From October 2005 to May 2007, the US Food and Drug Administration, in conjunction with the CDC and other federal agencies, conducted the Infant Feeding Practices Study II,[17] which collected data from responses to questionnaires mailed to a sample of US women who had given birth to term or near-term infants. After learning about the cases reported here and because of the lack of information about the prevalence of this behavior in the United States, researchers added the question, "In the past 2 weeks, have you chewed up food and then given it to your infant, so the food was already chewed up before you fed it to your infant?" Separate questionnaires were mailed to parents when the infants were aged 4, 5, 6, 7, 9, 10.5, and 12 months.

Unpublished data from the Infant Feeding Practices Study II[17] indicate that the prevalence of premastication rose from 0.77% (17 of 2203 respondents) at 4 months of age to 10.5% (189 of 1794 respondents) at 10 months of age (Sara Fein, PhD, and Laurence Grummer-Strawn, PhD, written personal communication, 2007). Among the subset of black respondents, the prevalence of premastication was higher than that among other racial and ethnic subgroups and increased as children aged: 5 (6%) of 87 respondents premasticated food for children aged 4 months; 33 (50%) of 66 respondents premasticated food for children aged 10 months. Although the sample was skewed toward white respondents with more education and higher income, the findings suggest a much higher prevalence of premastication than expected and the need for clinical care providers in the United States to be cognizant of this practice.

In a study of complementary infant-feeding practices in China, 62.5% of 104 respondents in various cities reported ever having prechewed food for their children.[16] Among those respondents practicing premastication, 21.5% did so often or very often. They started prechewing food when the child was a median of 8 months old (range: 1–24 months) and stopped at a median of 24 months (range: 5–48 months). Prechewing was also more common when someone other than the parent was involved in feeding the infant.

The association between prechewing food and the transmission of infectious organisms has been documented or hypothesized. The transmission of group A streptococci[18] and hepatitis B virus[15] through premasticated food has been documented; however, both organisms are considerably more infectious than HIV, and as noted, multiple reports have indicated that the risk of oral HIV transmission under ordinary circumstances, such as kissing or sharing household items, is extremely low.[19,20] The feeding of premasticated foods by mothers to infants has been associated with increased risk of *Helicobacter pylori* infection in infants in Burkina Faso[21] and with dental caries in children in southern Asia.[22] Similar transmissions of human herpesvirus 8 in rural Tanzania[23] and Epstein-Barr virus (EBV) in Uganda[24] have been hypothesized. In EBV-endemic regions, some authors have suggested that prechewing food may foster viral transmission to toddlers and may explain, in part, local elevations in the incidence of EBV-associated Burkitt lymphoma in children.[25]

Eating prechewed food, however, may provide health benefits. The premastication of food was protective in univariable but not multivariable analysis against respiratory syncytial virus infection for Alaska Native children aged <6 months.[26] It has also been hypothesized that the feeding of premasticated iron-rich foods may prevent iron deficiency during the first 6 to 12 months of life in resource-limited countries where other sources of iron supplementation are not available during the breastfeeding period.[16] Although the prechewing of food increased bacterial counts in the weaning foods given to infants in northern Thailand, it was suggested that the mother's immunoglobulin A in saliva mixed with the food may reduce the infectivity of these bacteria.[4]

Although our evidence argues in favor of premastication-related HIV transmission facilitated by blood in the mouth of the caregiver and compromised oral mucosa in the child, we acknowledge some limitations. In case 1, phylogenetic evidence linking infection in the child and infection in the premasticating caregiver was lacking because no blood sample was available for the latter. However, the history of premastication and the absence of other modes of transmission are compelling. The possibility of late perinatal seroconversion, for cases 2 and 3 whose mothers were infected with HIV, is extremely unlikely because the results of sequentially performed highly specific tests were negative: in case 3, HIV RNA PCR was performed thrice in the first 6 to 18 weeks of life,[27,28] and in the child of case 2, HIV enzyme-linked immunosorbent assays were performed twice after 18 months of age.[29] HIV-1 RNA testing is reliable for early diagnosis of HIV in infants.[30] Finally, in light of the findings of the Infant Feeding Practices Study II, which indicate that prechewing is common, one might question why, in >10 years, only 3 cases in the United States have been linked to this practice and why no

cases have been reported in resource-limited settings such as Africa, where premastication may be more common than in the United States. A possible explanation is that transmission through breastfeeding makes it difficult to detect premastication-related HIV transmission in resource-limited countries such as Africa; the absence of breastfeeding transmission has allowed us to detect premastication-related transmission in the United States. Premastication-related HIV transmissions are probably rare, requiring a convergence of risk factors affecting both the caregiver and the child. In addition, health care providers are unaware of the practice and have not considered it a potential cause of "late" HIV infection in infants. To our knowledge, no HIV-related MTCT studies with breastfeeding populations have specifically queried caregivers about premastication.[31] The 3 reported cases raise the question as to whether some cases of late pediatric HIV infection reported in MTCT studies and attributed to breastfeeding might have been due in part to the coexisting practice of premastication. Eliciting a history of premastication requires that health care providers be aware that premastication exists and that they are culturally sensitive in asking questions about it. It is crucial to educate caregivers who are infected with HIV about prechewing, because they may be unaware of its potential health risks and may perceive it as a routine, safe, and culturally acceptable practice.

CONCLUSIONS

We hope that our results will prompt additional investigation and the reporting of other potential cases of premastication-related perinatal HIV transmission. Until the risk of prechewing and modifying factors (eg, periodontal disease) are better understood, we recommend that health care providers routinely query children's caregivers and expecting parents who are infected with HIV or at high risk of HIV infection about the practice of premasticating food, that they advise against premastication and that they direct parents and other caregivers to safer, locally available, and accessible feeding options. Translating these recommendations into practice will require cognizance of culturally sensitive issues and potential nutritional consequences linked to premastication. Health care providers should identify the extent to which premastication is practiced in their communities and should notify public health authorities of cases of HIV infection that are potentially linked to premastication. In the United States, such cases should be reported to local health departments according to state surveillance guidelines for HIV/AIDS reporting.

We recognize the potential global implications of our findings. Because infants are fed prechewed food worldwide, we understand that a recommendation against premastication by caregivers infected with HIV should not be made lightly, especially in areas where alternative methods of food preparation are limited and sociocultural beliefs may favor this practice. For example, even in developed nations, providing alternative means for preparing infant food safely, such as blenders, may not eliminate premastication if it has traditional or cultural roots. In resource-limited settings, a risk/benefit analysis will be needed and should take into account the availability of safe feeding practices. Finally, it will be important to determine not only the prevalence of premastication but its contribution to HIV infection in children worldwide in the context of other well-described prenatal, intrapartum, and postnatal risk factors, including breastfeeding.

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REFERENCES

1. D'Ippolito M, Read JS, Korelitz J, Joao EC, Mussi-Pinhata M, Rocha N. Missed opportunities for prevention of mother-to-child transmission of human immunodeficiency virus type 1 in Latin America and the Caribbean: the NISDI Perinatal Study. *Pediatr Infect Dis J*. 2007;26(7):649–653
2. McDonald C, Lambert J, Nayagam D, et al. Why are children still being infected with HIV? Experiences in the prevention of mother-to-child transmission of HIV in south London. *Sex Transm Infect*. 2007;83(1):59–63
3. Hennart P, Vis HL. Breast-feeding and post partum amenorrhoea in Central Africa. 1. Milk production in rural areas. *J Trop Pediatr*. 1980;26(5):177–183
4. Imong SM, Jackson DA, Rungruengthanakit K, et al. Maternal behaviour and socioeconomic influences on the bacterial content of infant weaning foods in rural northern Thailand. *J Trop Pediatr*. 1995;41(4):234–240
5. Neander WL, Morse JM. Tradition and change in the Northern Alberta Woodlands Cree: implications for infant feeding practices. *Can J Public Health*. 1989;80(3):190–194
6. Radbill SX. Infant feeding through the ages. *Clin Pediatr (Phila)*. 1981;20(10):613–621
7. Walburn JN, Pergam JM, Perry SH, Jensen J. Black child care practices in the Midwest. *Pediatrics*. 1988;82(5):789–790
8. Lewis CW, Riedy CA, Grossman DC, Domoto PK, Roberts MC. Oral health of young Alaska Native children and their caregivers in Southwestern Alaska. *Alaska Med*. 2002;44(4):83–87
9. Robbins KE, Weidle PJ, Brown TM, et al. Molecular analysis in support of an investigation of a cluster of HIV-1-infected women. *AIDS Res Hum Retroviruses*. 2002;18(15):1157–1161
10. Rambaut A. *Se-Al: Sequence Alignment Editor* [computer program]. Version 1.0. Oxford, United Kingdom: distributed by the author; 1996
11. Posada D, Crandall KA. Modeltest: testing the model of DNA substitution. *Bioinformatics*. 1998; 14(9):817–818
12. *PAUP*, Phylogenetic Analysis Using Parsimony* [computer program]. Version 4.0b8. Sunderland, MA: Sinauer Associates, Inc; 2001
13. Moutsopoulos NM, Nares S, Nikitakis N, et al. Tonsil epithelial factors may influence oropharyngeal human immunodeficiency virus transmission. *Am J Pathol*. 2007;171(2):571–579
14. Imong SM, Rungruengthanakit K, Ruangyuttikarn C, Wongsawasdii L, Jackson DA, Drewett RF. The bacterial content of infant weaning foods and water in rural northern Thailand. *J Trop Pediatr*. 1989;35(1):14–18
15. Huang MJ. An epidemiological study on prevalence and risk factors of hepatitis B virus (HBV) infection in preschool children [in Chinese]. *Zhonghua Liu Xing Bing Xue Za Zhi*. 1990;11(3): 129–132
16. Zhang Y. *The Role of Premastication in the Evolution of Complementary Feeding Strategies: A Bio-Cultural Analysis* [honors thesis]. Ithaca, NY: Cornell University; 2007. Available at: http://ecommons.library.cornell.edu/bitstream/1813/7810/1/Zhang,%20Yuanyuan.pdf. Accessed January 30, 2009
17. Fein SB, Grummer-Strawn LM, Raju TN. Infant feeding and care practices in the United States: results from the Infant Feeding Practices Study II. *Pediatrics*. 2008;122(suppl 2):S25–S27
18. Steinkuller JS, Chan K, Rinehouse SE. Prechewing of food by adults and streptococcal pharyngitis in infants. *J Pediatr*. 1992;120(4 pt 1):563–564
19. Centers for Disease Control and Prevention. Human immunodeficiency virus transmission in household settings: United States. *MMWR Morb Mortal Wkly Rep*. 1994;43(19):347, 353–356
20. Centers for Disease Control and Prevention. Transmission of HIV possibly associated with exposure of mucous membrane to contaminated blood. *MMWR Morb Mortal Wkly Rep*. 1997;46(27): 620–623
21. Taylor DN, Blaser MJ. The epidemiology of *Helicobacter pylori* infection. *Epidemiol Rev*. 1991;13: 42–59
22. Harrison R, Benton T, Everson-Stewart S, Weinstein P. Effect of motivational interviewing on rates of early childhood caries: a randomized trial. *Pediatr Dent*. 2007;29(1):16–22
23. Mbulaiteye SM, Pfeiffer RM, Whitby D, Brubaker GR, Shao J, Biggar RJ. Human herpesvirus 8 infection within families in rural Tanzania. *J Infect Dis*. 2003;187(11):1780–1785
24. Mbulaiteye SM, Walters M, Engels EA, et al. High levels of Epstein-Barr virus DNA in saliva and peripheral blood from Ugandan mother-child pairs. *J Infect Dis*. 2006;193(3):422–426
25. Callahan CM, Vincent AL, Greene JN, Sandin RL. Infections in oncology: infectious causes of malignancy. *Cancer Control* [serial online]. 1999;6(3). Available at: www.moffitt.org/site.aspx?spid=70F1A2340DC748F6ACE061475B65B9F6. Accessed January 30, 2009

26. Bulkow LR, Singleton RJ, Karron RA, Harrison LH; Alaska RSV Study Group. Risk factors for severe respiratory syncytial virus infection among Alaska native children. *Pediatrics*. 2002;109(2):210–216
27. Read JS; American Academy of Pediatrics, Committee on Pediatric AIDS. Diagnosis of HIV-1 infection in children younger than 18 months in the United States. *Pediatrics*. 2007;120(6). Available at: www.pediatrics.org/cgi/content/full/120/6/e1547
28. Nesheim S, Palumbo P, Sullivan K, et al. Quantitative RNA testing for diagnosis of HIV-infected infants. *J Acquir Immune Defic Syndr*. 2003;32(2):192–195
29. Moodley D, Bobat RA, Coutsoudis A, Coovadia HM. Predicting perinatal human immunodeficiency virus infection by antibody patterns. *Pediatr Infect Dis J*. 1995;14(10):850–852
30. Working Group on Antiretroviral Therapy and Medical Management of HIV-infected Children. *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*. July 23, 2008. Available at: http://aidsinfo.nih.gov/contentfiles/PediatricGuidelines.pdf. Accessed January 30, 2009
31. Taha TE, Hoover DR, Kumwenda NI, et al. Late postnatal transmission of HIV-1 and associated factors. *J Infect Dis*. 2007;196(1):10–14

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研究報告の概要

○東海地域におけるHIV-2感染疑い症例の遺伝子学的解析

【目的】HIV-2は西アフリカを中心に感染者数の多い疾患である。HIV-1のように世界的規模で感染は拡大しておらず、本邦では、これまで数例が報告されているのみである。今回、我々は名古屋医療センターにおいて新たにHIV-2の感染が疑われた4例を対象に遺伝子学的診断と分子疫学的解析を実施した。

【方法】血清学的にHIV抗体陽性かつ血中HIV-1 RNAコピー数が検出限度以下を示した4例を対象とした。4例のプロファイルは、外国籍の男性が3例、日本国籍の女性が1例であった。患者末梢血白血球より抽出したDNAを鋳型にnested PCRによりgag (778 bps)およびenv (496 bps)領域の遺伝子増幅を試みた。標的遺伝子の増幅に成功した症例についてはダイレクトシークエンス法で塩基配列を決定したのち、リファレンス株と共に系統樹解析を実施した。

【結果】4例中3例で標的遺伝子の増幅に成功し、遺伝子配列よりHIV-2であることが確認された。これら3例は、全て外国籍の男性症例であり、日本国籍の女性では、いずれの領域も増幅産物を得ることができず確定診断には至らなかった。HIV-2は遺伝子学的にサブタイプAからHの8種類のサブタイプに分類されるが、解析に成功した3例のうち1例はgag、env領域ともにリファレンス株のサブタイプA株と同じ枝に分岐し、サブタイプA株と判定し得た。残り2例は、gag領域ではサブタイプBの近傍への分岐を示し、env領域の解析でも独立した系統群を形成し、両遺伝子領域のみではサブタイプ判定には至らなかった。

【結論】活発化する国際交流は感染症の拡大における地理的な障壁の閾値を低下させている。東海地域において見出されたHIV-2感染症例3例について報告したが、これは我が国においてもHIV-2のスクリーニングを強化しなければならないことを示唆している。

使用上の注意記載状況・その他参考事項等

赤十字アルブミン20
赤十字アルブミン25
赤十字アルブミン20%静注4g/20mL
赤十字アルブミン20%静注10g/50mL
赤十字アルブミン25%静注12.5g/50mL

血液を原料とすることに由来する感染症伝播等

報告企業の意見	今後の対応
東海地域においてHIV抗体陽性かつ血中HIV-1 RNAコピー数が検出限度以下を示し、HIV-2感染が疑われた症例4例を分析したところ、3例でウイルス遺伝子の増幅に成功し、HIV-2感染が確認されたとの報告である。 これまで、本製剤によるHIV感染の報告はない。また本製剤の製造工程には、平成11年8月30日付医薬発第1047号に沿ったウイルス・プロセスバリデーションによって検証された2つの異なるウイルス除去・不活化工程が含まれている。さらに最終製品についてHIV-NAT陰性であることを確認している事から本製剤の安全性は確保されていると考える。	今後も情報の収集に努める。なお、日本赤十字社ではHIV抗体検査にこれまでの凝集法と比べてより感度の高い化学発光酵素免疫測定法(CLEIA)を導入したことに加え、20プールNATについてもHIV-2及びHIVグループOの検出が可能な新NATシステムを導入し、陽性血液を排除している。また、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。

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P-101　血液培養より *Histoplasma capsulatum* を分離したHIV感染症の1例―細菌学的所見を中心に―

東邦大学医療センター大森病院臨床検査部[1]，
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東邦大学医療センター大森病院病院病理部[5]，
千葉大学真菌医学研究センター[6]
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渋谷和俊[5]，佐野文子[6]，亀井克彦[6]，山口恵三[1,2,3]

【目的】ヒストプラズマ症は輸入真菌症のひとつであり，培養陽性率が低いとされている．今回，血液培養より *Histoplasma capsulatum* を分離したHIV感染症の1例を経験したため報告する．

【症例】39歳，タイ人男性．主訴は発熱，発疹，歯肉出血．15年前にタイより来日．4週間前より39～40℃台の発熱が出現，1週間前から歯茎より出血を認め，3日前から出血傾向が増悪したため当院救急外来を受診．精査加療目的にて入院となった．

【入院後経過】HIV抗体陽性．BALFから *Candida albicans* が検出され，β-Dグルカン値の上昇もみられた．IPM，CPFX，FLCZにより治療が開始されたが全身状態は増悪．第6病日に骨髄生検を施行し，病理学的所見で細胞質内に小型類円形の構造物が多数認められ，ヒストプラスマ症が強く疑われた．第8病日よりAMPHにより治療開始したがDICとなり，第25病日，消化管出血のため死亡された．

【血液培養検査】入院時に2セットのボトルが提出された．血培装置で1週間培養を行ったが陰性であったため，ボトルより抽出した培養液沈渣のサブカルチャーを試みた．培養17日目にサブロー寒天に集落の発育を認め真菌陽性との報告をした．同定は27℃と35℃の温度差で二形性を示すこと，集落の形態よりヒストプラズマ属を推定し，血培採取後50日目に報告した．最終的に千葉大学真菌医学研究センターに依頼し，*H. capsulatum* と同定された．一方，ボトルは血培装置で計3週間培養を行ったが陰性であった．

【考察】本症例は臨床側からヒストプラズマ症疑いの情報があったため執拗に培養を行ったことから分離に成功したと思われる．ヒストプラズマ属の培養は27℃で4週間まで観察することが推奨されているが，一般細菌用の血培ボトルは5～7日しか培養を行わないため本菌をはじめとする培養に時間を要する真菌を疑うときは繰り返し血培装置に充填するか，培養液沈渣を用いてサブカルチャーを行う必要があると考えられた．

P-102　東海地域におけるHIV-2感染疑い症例の遺伝子学的解析

名古屋医療センター臨床研究センター感染免疫研究部
○伊部史朗，横幕能行，服部純子，間宮均人，
杉浦　亙

【目的】HIV-2は西アフリカを中心に感染者数の多い疾患である．HIV-1のように世界的規模で感染は拡大しておらず，本邦では，これまで数例が報告されているのみである．今回，我々は名古屋医療センターにおいて新たにHIV-2の感染が疑われた4例を対象に遺伝子学的診断と分子疫学的解析を実施した．

【方法】血清学的にHIV抗体陽性かつ血中HIV-1 RNAコピー数が検出限度以下を示した4例を対象とした．4例のプロファイルは，外国籍の男性が3例，日本国籍の女性が1例であった．患者末梢血白血球より抽出したDNAを鋳型にnested PCRによりgag（778 bps）およびenv（496 bps）領域の遺伝子増幅を試みた．標的遺伝子の増幅に成功した症例についてはダイレクトシークエンス法で塩基配列を決定したのち，リファレンス株と共に系統樹解析を実施した．

【結果】4例中3例で標的遺伝子の増幅に成功し，遺伝子配列よりHIV-2であることが確認された．これら3例は，全て外国籍の男性症例であり，日本国籍の女性では，いずれの領域も増幅産物を得ることができず確定診断には至らなかった．HIV-2は遺伝子学的にサブタイプAからHの8種類のサブタイプに分類されるが，解析に成功した3例のうち1例はgag，env領域ともにリファレンス株のサブタイプA株と同じ枝に分岐し，サブタイプA株と判定し得た．残り2例は，gag領域ではサブタイプBの近傍への分岐を示し，env領域の解析でも独立した系統群を形成し，両遺伝子領域のみではサブタイプ判定には至らなかった．

【結論】活発化する国際交流は感染症の拡大における地理的な障壁の閾値を低下させている．東海地域において見出されたHIV-2感染症例3例について報告したが，これは我が国においてもHIV-2のスクリーニングを強化しなければならないことを示唆している．

No. 19

：別紙様式第2-1

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	総合機構処理欄
			2009. 7. 9	該当なし	
一般的名称	人血清アルブミン，	研究報告の公表状況	47 news. Available from: http://www.47news.jp/CN/20090906/CN2009062701000591.html.	公表国 日本	
販売名（企業名）	赤十字アルブミン20（日本赤十字社） 赤十字アルブミン25（日本赤十字社） 赤十字アルブミン20%静注4g/20mL（日本赤十字社） 赤十字アルブミン20%静注10g/50mL（日本赤十字社） 赤十字アルブミン25%静注12.5g/50mL（日本赤十字社）				使用上の注意記載状況・その他参考事項等 赤十字アルブミン20 赤十字アルブミン25 赤十字アルブミン20%静注4g/20mL 赤十字アルブミン20%静注10g/50mL 赤十字アルブミン25%静注12.5g/50mL 血液を原料とすることに由来する感染症伝播等

研究報告の概要

○白血病ウイルス感染者108万人（推計）：大都市圏で割合増
母乳を通じて母子感染し、白血病などを引き起こす可能性がある成人T細胞白血病ウイルス（HTLV-1）について厚生労働省研究班が約20年ぶりに実施した調査で、感染者の地域別割合がもともと高かった九州で減少し、関東や中部、近畿の大都市圏で増加したことが27日、分かった。国内の感染者数は約108万人と推計。旧厚生省研究班が1988～90年度にまとめた調査の約120万人と比べ大きな変化はなかった。これまで全国的な対策は取られておらず、子供への感染を防ぐ取り組みが急務となりそうだ。
研究班班長の山口一成国立感染症研究所客員研究員は大都市圏での割合増加について、感染者が多い九州からの人の移動が背景にあると指摘。「妊婦への抗体検査や授乳指導を実施している自治体は一部に限られ、感染者総数もあまり減少していない」と話した。
HTLV-1はATLと呼ばれるタイプの白血病や、歩行障害などが出る脊髄症（HAM）の原因となる。ATLの発症率は3～5%。根本的な治療法はなく、年間約千人が亡くなっている。
今回の調査は、2006～07年に初めて献血した全国の約119万人を対象に実施、3787人の感染が確認された。感染者の地域別割合は、九州が前回調査の50.9%から41.4%に減少。一方、関東は17.3%（前回10.8%）、中部8.2%（同4.8%）、近畿20.3%（同17.0%）で、いずれも前回より増加した。

報告企業の意見

2006～07年に初めて献血した人を対象に行った調査の結果、全国の成人T細胞白血病ウイルスの感染者数は約108万人と推計され、感染者の地域別割合はもともと高かった九州で減少し、関東や中部、近畿の大都市圏で増加したことが分かったとの報告である。
これまで、本製剤によるHTLV-1感染の報告はない。本製剤の製造工程には、平成11年8月30日付医薬発第1047号に沿ったウイルス・プロセスバリデーションによって検証された2つの異なるウイルス除去・不活化工程が含まれている。本製剤の安全性は確保されていると考える。

今後の対応

今後も引き続き、新たなウイルス等による感染症の発生状況等に関する情報の収集に努める。

(11)