平成２２年度第３回血液事業部会
運営委員会提出資料

資料５－２

XMRVの疫学に関する主な文献一覧(平成22年5月18日作成、平成22年11月24日改訂)
【前立腺癌関係】

血液事業部会運営委員会委員　岡田　義昭

文献番号	文献名	XMRVの陽性率 前立腺がん	XMRVの陽性率 慢性疲労症候群	XMRVの陽性率 健康人	検出法（組織）	報告国	要約
1	Urisman A, et al., PLoS Pathog. 2006 Mar;2(3):e25. Identification of a novel Gammaretrovirus in prostate tumors of patients homozygous for R462Q RNASEL variant.	9/86 10.5% （遺伝子の型による内訳） QQ 8/20 40%　RQ 0/14　0% RR 1/52 1.9%	-	-	RT-PCR （前立腺）	米国	DNAアレイによって前立腺がん組織から新たなウイルス（XMRV）を発見した。RNaseLにホモ型変異（QQ)にもつ前立腺癌の40%からXMRVが検出されたが、変異がない前立腺癌(RR)では1.9%であった。
2	Fischer N, Hellwinkel O, Schulz C, Chun FK, Huland H, Aepfelbacher M, Schlomm T. J Clin Virol. 2008 Nov;43(3):277-83 Prevalence of human gammaretrovirus XMRV in sporadic prostate cancer	1/87 1.2% （非家族性）	-	1/70 1.42%	RT-PCR （前立腺）	ドイツ	非家族性の前立腺がん組織からXMRVの検出が試みられた。その結果、欧州北部においてはほとんど検出されなかった。但し、本研究において、RNaseLにホモ型変異（QQ)をもつサンプルは6%未満であったことに注意を要する。
3	Hohn O, Krause H, Barbarotto P, Niederstadt L, Beimforde N, Denner J, Miller K, Kurth R, Bannert N. Retrovirology. 2009 Oct 16;6:92. Lack of evidence for xenotropic murine leukemia virus-related virus(XMRV) in German prostate cancer patients	0/589　0% (PCR) 0/146　0% （抗体）	-	0/5　0% （抗体）	PCR、RT-PCR （前立腺） ELISA（血清）	ドイツ	589例(76例の RNaseLホモ型変異型を含む）の前立腺癌組織からDNAとRNAを抽出し、核酸増幅法を用いてXMRVの遺伝子の有無を調べたが検出できなかった。また、血清中からもXMRVに反応する抗体は検出できなかった。
4	Schlaberg R, Choe DJ, Brown KR, Thaker HM, Singh IR. Proc Natl Acad Sci U S A. 2009 Sep 22;106(38):16351-6 XMRV is present in malignant prostatic epithelium and is associated with prostate cancer, especially high-grade tumors	14/233 6.2% PCR 54/233 23% ウイルス抗原	-	2/101 2% PCR 4/101 4% ウイルス抗原	PCR （前立腺） 組織染色 （前立腺）	米国	233例の前立腺癌中14例からPCR法によってXMRV遺伝子が検出できた。RNaseLの変異とは関連がなかった。XMRVのタンパクは上皮細胞に存在していた。
13	Danielson B.P.,Ayala G.E.,and Kimata J.T. JID.2010 Nov.202:1470-77 Detection of xenotropic murine leukemia virus-related virus in normal and tumor tissue of patients from the southern United States with prostate cancer is dependent on specific polymerase chain reaction conditions	32/144　22.2%	-	-	PCR （前立腺）	米国 （南部）	米国の南部にある州での前立腺癌患者からXMRV遺伝子の検出を行なった。前立腺癌の生検検体から DNAを抽出し、PCRを実施（env領域）した。32例が陽性であった。内28例は正常組織と癌組織を独立に検討でき、18例は両方とも陽性であった。XMRV陽性例ではRNASEL遺伝子の変異やgleason score（病理組織分類）との間に有意な差は認められなかった。
14	Aloia AL, Sfanos KS, Isaacs WB, Zheng Q, Maldarelli F, De Marzo AM, Rein A; Cancer Res; Published OnlineFirst October 21, 2010 XMRV: A New Virus in Prostate Cancer?	0/約800 0%	-	-	PCR （前立腺） 組織染色 （前立腺）		約800の前立腺検体について、リアルタイムPCRと免疫組織染色を用い、XMRVの検出を試みた。その結果、前立腺癌にXMRVは見られなかった。XMRVは実際にはヒトには感染を起こしていない可能性がある。もし感染していても、このデータは前立腺癌との因果関係を支持しない。

XMRVの疫学に関する主な文献一覧(平成22年5月18日作成、平成22年11月24日改訂)
【慢性疲労症候群関係】

血液事業部会運営委員会委員　岡田　義昭

文献番号	文献名	XMRVの陽性率			検出法（組織）	報告国	要約
		前立腺がん	慢性疲労症候群	健康人			
5	Lombardi VC, Ruscetti FW, Das Gupta J, Pfost MA, Hagen KS, Peterson DL, Ruscetti SK, Bagni RK, Petrow-Sadowski C, Gold B, Dean M, Silverman RH, Mikovits JA. Science. 2009 Oct 23:326(5952):585-9 Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome	-	68/101 67%	8/218 3.7%	PCR (末梢単核球)	米国	慢性疲労性症候群（CFS）患者の67%からXMRV遺伝子が検出され、XMRVに感染したCFS患者の細胞や血漿中に感染性ウイルスが存在した。また、一部の症例ではウイルスと抗体が共存していた。　健常人の3.7%からもXMRVが検出された。CFS由来のXMRVは塩基配列が前立腺癌由来のものとクラスターを形成していた。
6	Erlwein O, Kaye S, McClure MO, Weber J, Wills G, Collier D, Wessely S, Cleare A. PLoS One. 2010 Jan 6;5(1):e8519. Failure to detect the novel retrovirus XMRV in chronic fatigue syndrome	-	0/186 0%	-	PCR (全血)	イギリス	慢性疲労性症候群186例を対象に全血から核酸増幅法によるXMRV遺伝子の検出を行ったが、検出できなかった。
7	Groom HC, Boucherit VC, Makinson K, Randal E, Baptista S, Hagan S, Gow JW, Mattes FM, Breuer J, Kerr JR, Stoye JP, Bishop KN. Retrovirology. 2010 Feb 15;7:10 Absence of xenotropic murine leukaemia virus-related virus in UK patients with chronic fatigue syndrome	-	0/136 0% DNA 0/140 0% RNA	0/95 0% DNA 0/141 0% RNA	PCR（全血） RT-PCR（血清）	イギリス	全血及び血清から核酸を抽出し、核酸増幅法を用いてXMRVの遺伝子を検出したが、慢性疲労性症候群及び健常人から検出されなかった。
8	van Kuppeveld FJ, de Jong AS, Lanke KH, Verhaegh GW, Melchers WJ, Swanink CM, Bleijenberg G, Netea MG, Galama JM, van der Meer JW. BMJ. 2010 Feb 25;340:c1018 Prevalence of xenotropic murine leukaemia virus-related virus in patients with chronic fatigue syndrome in the Netherlands: retrospective analysis of samples from an established cohort	-	0/32　0% RNA	0/43 0% RNA	RT-PCR (末梢単核球)	オランダ	1991～1992年に凍結保存されていた末梢単核球からRNAを抽出し、核酸増幅法によってXMRV遺伝子を検出したが、慢性疲労性症候群及び健常人から1例も検出されなかった。
9	Switzer WM, Jia H, Hohn O, Zheng HQ, Tang S, Shankar A, Bannert N, Simmons G, Hendry RM, Falkenberg VR, Reeves WC, Heneine W; Retrovirology 2010, 7:57 Absence of evidence of Xenotropic Murine Leukemia Virus-related virus infection in persons with Chronic Fatigue Syndrome and healthy controls in the United States	-	0/51　0% DNA	0/56　0% DNA	PCR (末梢単核球) 免疫学的試験	米国	米国カンザス州とジョージア州のCFS患者51名とコントロール56名の血清について、PCRと抗体検査が行われた。その結果、いずれからもXMRVは検出されなかった。この結果は、XMRVとCFSの関係を支持しない。
10	Lo SC, Pripuzova N, Li B, Komaroff AL, Hung GC, Wang R, and Alter H.J.PNAS.2010,107.1470-77 Detection of MLV-related virus gene sequences in blood of patients with chronic fatigue syndrome and healthy blood donors	-	32/37　86.5% DNA (XMRVとは異なるウイルス)	3/44　6.8% DNA (XMRVとは異なるウイルス)	PCR (末梢単核球)	米国	既に報告されているgag領域のプライマーを用いて37人のCFS末梢血を解析したところ、32人からマウス白血病に類似したレトロウイルスが検出された。塩基配列からは、XMRVよりもpolytropic（多種指向性）マウス内因性レトロウイルスに類似していた。
11	Barnes E.,Flanagan P.,Brown A.,Robinson N.,Brown H.,McClure M.,Oxenius A.,Collier J.,Weber J.,Gunthard H.F.,Hirschel B.,Fidler S.,Phillips R.,and Frater J.　JID.2010 Failure to detect xenotropic murine leukemia virus-related virus in blood of individuals at high risk　of blood-borne viral infection	-	0/151　0% DNA 0/79　0% RNA	-	PCR (末梢単核球) RT-PCR (血漿)	英国 西ヨーロッパ	英国と西ヨーロッパの HIV-1感染者163人（慢性期84人、急性期79人）とHCV感染者67人（慢性期）において、慢性感染者からは DNA、急性期にある感染者からはRNAを抽出し、 NAT検査を実施したが、XMRVの遺伝子は検出できなかった。さらにgagに対するT細胞の反応性も63人で検討したが、反応性は認められなかった。以上から、英国や西ヨーロッパでは血液や性的感染リスクを持つヒトでのXMRV感染率は高くなかった。
12	Hnrich T.J.,Li J.Z.,Felsenstein D.,Kotton C.N.,Plenge R.M.,Pereyra F.,Marty F.M.,Lin N.H.,Grazioso P.,Crochiere D.M.,Eggers D.,Kuritzkes D.R.,and Tsibris A.M.N.JID.2010 Xenotropic mueine leukemia virus-related virus prevalence in patients with chronic fatigue syndrome or chronic immunomodulatory conditions	-	0/198　0% DNA	0/95　0% DNA	PCR (末梢単核球)	米国	ボストン周囲にある大学病院において、XMRV感染の頻度を調べるためにCFS32人、 HIV感染者43人、幹細胞及び臓器移植患者26人、関節リュウマチ（RA)患者97人、RAのコントロールの患者95人計230人から DNAを抽出しNAT検査を行なった。XMRVの遺伝子は検出できなかった。

平成２２年度第３回血液事業部会
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諸外国における慢性疲労症候群罹患者に対する献血制限について

平成 22 年 11 月現在

１．現時点において、XMRV 感染リスクに対する予防的措置として、既往歴も含め、慢性疲労症候群罹患者に対する献血制限の実施が確認されている国

カナダ（除くケベック州）・・別添１
オーストラリア・・別添２
ニュージーランド・・別添３

なお、イギリスは、現時点では慢性疲労症候群と XMRV との関係を示す疫学的エビデンスはないとした上で、ドナーの健康確保の観点から、既往歴も含めた献血制限を実施している（別添４）。

２．献血時に健康であることを前提とした上で、現時点において、慢性疲労症候群の既往歴まで含めた献血制限は勧告・実施していない国

米国（FDA）（注）・・別添５
カナダ・ケベック州・・別添６
日本

（注）なお、AABB（米国血液銀行協会）は、慢性疲労症候群の既往がある方の献血の辞退を促すよう、会員に対し自主的に勧告している。（別添７）

その他の欧州諸国については、現在調査中。

（血液対策課調べ）

別添1

Indefinite Deferral for History of Chronic Fatigue Syndrome

Canadian Blood Services is undertaking a deferral to protect blood product recipients from any potential risk that could come from a link between Xenotropic Murine Leukemia Virus-Related Virus (XMRV) and Chronic Fatigue Syndrome (CFS). XMRV is a type of retrovirus originating in mice ("murine" relates to mice).

Although the media is reporting that XMRV may be a threat to the blood supply, the deferral Canadian Blood Services is undertaking at this point relates to those patients with a history of CFS only. At this point there is no evidence that XMRV causes any disease in humans. This new information has reported association, but not causality.

Today, donors who have a history of CFS and who are well again are allowed to donate blood. Under the new deferral, it is this group that will no longer be able to donate blood at Canadian Blood Services' clinics. Blood donors with a history of CFS represent a very small segment of Canadian Blood Services' donor base, so the impact on the blood supply will be minimal.

Donors with active cases of CFS don't usually come in to donate blood because they are not feeling well. Historically, however, Canadian Blood Services has allowed people with a history of the illness to donate. This is what will change with the new deferral.

Health Canada, the body that regulates Canadian Blood Services, has approved this deferral. Implementation will occur in late April.

It is important to note that the available data related to the link between XMRV and CFS is conflicting. While it has been reported to have a strong association in American patients, the finding has not been substantiated in patients in the UK or the Netherlands, suggesting some geographic differences in the pattern of virus spread. Furthermore, there are as yet no data confirming that XMRV causes disease. So at this time, it is not possible to quantify the risk a donor with a history of CFS could pose to a blood recipient.

Once the scientific community understands more about the role of XMRV or other viruses in relation to chronic fatigue, Canadian Blood Services will revisit the deferral decision to determine whether the deferral is still warranted. Canadian Blood Services is part of an inter-agency North American task force led by the American Association of Blood Banks (AABB) that is investigating the XMRV issue.

How Canadian Blood Services currently handles potential threats to the blood supply system:

Canadian Blood Services operates one of the safest blood systems in the world. An essential element of our commitment to safety is our multilayered approach to ensuring that our blood products meet the highest level of safety available.

Before they donate, donors are asked an extensive list of questions about their behaviour and about their health status. People, who are unhealthy, including those with symptomatic diseases, are deferred from donation.

The organization then subjects each and every donation to a variety of blood screening tests for pathogens that are known to be transmissible by blood transfusion including HIV and the hepatitis B and C viruses.

Canadian Blood Services also maintains strong international networks with other blood systems to monitor the behaviour of possible pathogenic threats to the blood supply, so that if a new pathogen appears we can be ready to respond to the threat.

Canadian Blood Services
Société canadienne du sang

別添２

Australian Red Cross
BLOOD SERVICE

Published on *Australian Red Cross Blood Service* (http://www.donateblood.com.au)

Blood Service updates CFS donor policy

23/04/2010
The Blood Service has decided to indefinitely defer donors with Chronic Fatigue Syndrome (CFS).

The Australian Red Cross Blood Service will indefinitely defer donors who have been diagnosed with Chronic Fatigue Syndrome (CFS).

This follows recent research, describing a possible link between chronic fatigue, and a retrovirus called Xenotropic Murine leukaemia virus-related Virus (XMRV).

As the Blood Service currently defers donors who have CFS, this change will delay their return to donating until there is more scientific literature on the possible viral link.

The number one priority of the Blood Service remains the safety of Australia's blood supply.

Blood Service specialist, Dr Tony Keller, said eligibility to donate is always a balance between risk and benefit.

"There is at present no test available for CFS or XMRV, but our donor questionnaire alerts us when someone has CFS. Very few donors will be affected by this decision," Dr Keller said.

"The science on this internationally is unclear. The recent North American research findings haven't been supported by research undertaken in Europe, and there is currently no Australian research on XMRV.

"We will review our decision in two years time, when further studies into the virus have been done."

The Blood Service currently has 570,000 donors a year. In the past two years, there have been only 70 donors deferred due to Chronic Fatigue Syndrome.

We are writing to a small number of donors to notify them of this change.

National News & Events

別添３

Detailed Eligibility Criteria and FAQ's

Antibiotics - I am taking antibiotics. Can I donate?

Accidents – I was involved in an accident and had stitches or other treatment. Can I donate?

Acne – I have active acne. Can I donate?

Acupuncture - I have just had acupuncture. Can I donate?

Addiction – Drugs. Can I donate if I have every injected or taken drugs?

Age - How does age affect my ability to donate?

Alcohol - I had several alcoholic drinks before going to give blood. Can I donate?

Allergy - I am allergic to one of the following: dust / a food / a medicine / an insect sting / other. Can I donate?

Anaemia - I have been anaemic. Can I donate?

Angioplasty – I have had an angioplasty. Can I donate?

Antibiotics - I am taking antibiotics. Can I donate?

Antidepressants - I take an antidepressant. Can I donate?

Arrhythmia – I have abnormal heart beats or I am being treated for an abnormal heart beat. Can I donate?

Arthritis – I have arthritis. Can I donate?

Asthma – I have asthma. Can I donate?

Bleeding disorder – I have been diagnosed with a bleeding condition/disorder. Can I donate?

Blood borne diseases - what is tested for?

Blood pressure - I take high blood pressure medicine. Can I donate?

Blood transfusion - I have had a blood transfusion. Can I donate?

Blood volume - What is the volume of blood in a person's body?

Body piercing - I have just had a part of my body pierced. Can I donate?

Breast-feeding - I am breast-feeding. Can I donate?

Cancer - I had cancer. Can I donate?

Chicken pox - I have chicken pox. Can I donate?

Childbirth - How long after the birth of my baby. Can I donate?

Cholecystectomy – I have had my gall bladder removed. Can I donate?

Cholecystitis – I have had cholecystitis recently. Can I donate?

Cholesterol - I take medication for cholesterol reduction. Can I donate?

Chronic fatigue syndrome - I have/had chronic fatigue syndrome, Can I donate?

People with a diagnosis of Chronic Fatigue Syndrome are permanently deferred from donating blood in New Zealand.

Coeliac Disease – I have Coeliac Disease. Can I donate?

Cold sores - Can I donate if I have a cold sore?

Colds- I have a cold. Can I donate?

Concussion – I was knocked unconscious. Can I donate?

Condoms What if I use Condoms Every Time?

Conjunctivitis – I have conjunctivitis. Can I donate?

Contraceptive pill - I take birth control pills. Can I donate?

Corneal Graft – Corneal transplant. I have had a corneal transplant. Can I donate?

Correctional institutions - Why doesn't the NZ Blood Service collect blood from inmates of correctional institutions?

Crohn's Disease – I have Crohn's Disease. Can I donate?

Cystitis – I have had cystitis recently. Can I donate?

Cytomegalovirus (CMV) infection – I have been diagnosed with cytomegalovirus infection. Can I donate?

Deep vein thrombosis (DVT) – I have had a deep vein thrombosis in a leg. Can I donate?

Dengue fever - I had dengue fever. Can I donate?

Dental treatment - I have just been to the dentist. Can I donate?

Depression – I am being treated for depression. Can I donate?

Dermatitis – I have dermatitis. Can I donate?

Diabetes - I am diabetic. Can I donate?

Diarrhoea - I have diarrhoea. Can I donate?

Disability – I have a physical disability. Can I donate?

Diverticulitis/diverticulosis – I have diverticulitis or diverticulosis. Can I donate?

Drug use (recreational) - Can I still donate blood even if I have taken recreational drugs?

Ear piercing - I have just had my ears pierced. Can I still donate blood?

別添４

Media Statement

8 November 2010

MS033/10

ME/CFS sufferers permanently deferred from giving blood

From 1 November 2010, people with Myalgic Encephalitis/Chronic Fatigue Syndrome (ME) were permanently deferred from giving blood in the UK.

The change to donor selection guidelines, which applied across all four UK Blood Services, was as a result of recommendations by the UK Blood Services Standing Advisory Committee on the Care and Selection of Donors, and Joint Professional Advisory Committee (JPAC).

In the past, donors with a history of ME/CFS could give blood, provided they had completely recovered and were feeling well.

However, as ME/CFS is a condition where people can relapse and become ill again, donor selection guidelines were changed as a precaution to protect the donor's safety by ensuring the condition is not made worse by donating blood. There is no evidence that a donation from a donor with this condition could in any way harm a patient.

This change brought donor selection guidelines for ME/CFS into line with other conditions where individuals are permanently excluded from blood donation to protect their own health.

Ends

For further information, please contact the NHSBT press office on 0117 969 2444, at pressoffice@nhsbt.nhs.uk or out of hours on 07659 133583.

Notes to Editors

- Donor selection guidelines relating to donor safety are recommended by the UK Blood Services Standing Advisory Committee on the Care and Selection of Donors, and Joint Professional Advisory Committee (JPAC)
- The change to donor selection guidelines for ME/CFS applies across all four UK Blood Services – NHS Blood and Transplant (NHSBT) for England and North Wales; the Scottish National Blood Transfusion Service (SNBTS); the Welsh Blood Service (WBS); and the Northern Ireland Blood Service (NIBTS)

- NHS Blood and Transplant (NHSBT) is a Special Health Authority in the NHS. It is the organ donor organisation for the UK and is responsible for matching and allocating donated organs. Its remit also includes the provision of a reliable, efficient supply of blood and associated services to the NHS in England and North Wales
- In October 2009 a study from the United States suggested a link between the virus XMRV and Chronic Fatigue Syndrome. This was reviewed and discussed in the relevant advisory committees. Further studies by the Centres for Disease Control in the US and a number in Europe have failed to demonstrate a link between XMRV infection and CFS. Currently there is no epidemiological evidence of a link between XMRV and CFS in the UK. The research on XMRV has been considered by the relevant UK Blood Services/DH advisory committees; there is no current evidence of a threat to public health in the UK; and this will be kept under review by those committees in the light of any new evidence.

別添５

Vaccines, Blood & Biologics

New study on the detection of murine leukemia virus-related virus gene sequences in the blood of patients with chronic fatigue syndrome (CFS) and healthy blood donors - Questions and Answers

Questions and Answers

1. What are murine leukemia viruses?

Murine leukemia viruses (MLV) are retroviruses known to cause cancer in certain mice. In 2006, investigators found that a type of MLV, called xenotropic murine leukemia virus-related virus (XMRV), could potentially infect humans. XMRV is one of a number of MLVs that appear to be transmitted to humans.

2. What is CFS?

Chronic fatigue syndrome (CFS) is a debilitating disorder defined solely by clinical symptoms and the absence of other causes. It's unknown what causes CFS.

3. Has MLV or XMRV previously been associated with CFS or other disease?

A previous study, published in the journal [Lombardi et. al. *Science* October 23, 2009 326: 585], reported finding XMRV in a high percentage of CFS patients and a small percentage of healthy blood donors. However, other studies conducted in the U.S., Netherlands, and UK did not detect evidence of XMRV or other MLV-related viruses in CFS patients.

XMRV was first identified in tissue samples from some prostate cancer patients in 2006. However, one subsequent study failed to find XMRV in prostate cancer tissues, and another study found the virus only rarely in such tissues.

4. What did the new study evaluate?

Investigators from the Food and Drug Administration's (FDA) Center for Biologics Evaluation and Research, the National Institutes of Health (NIH) Clinical Center, and Harvard Medical School have published a study in the scientific journal *Proceedings of the National Academy of Sciences* that examines the presence of MLVs in blood collected from two groups -- patients diagnosed with CFS and healthy blood donors.

This study tested blood samples collected from the New England area in the mid-1990s from 37 patients diagnosed with CFS, as well as samples from 44 healthy blood donors collected in the Clinical Center Blood Bank, NIH, between 2003 and 2006. Investigators performed DNA sequencing on each sample that produced positive product for verification of MLV-like gene sequences. Diverse MLV gene sequences, similar to that of the recently discovered XMRV, were identified in samples from 32 of the 37 patients with CFS (86.5%) and 3 of the 44 (6.8%) healthy blood donors that were tested.

Follow-up samples were collected from 8 of the CFS patients in 2010, and 7 of these again tested positive for MLV-like gene sequences.

5. What did the new study conclude?

This study supports a previous investigation[Lombardi et al. *Science* October 23, 2009 326: 585]that showed XMRV, a genetic variant of MLV-like viruses, to be present in the blood of people with CFS. The study demonstrates a strong association between a diagnosis of CFS and the presence of MLV-like virus gene sequences in the blood. The study also showed that MLV-like viral gene sequences were detected in a small fraction of healthy blood donors. Although the statistical association with CFS is strong, this study does NOT prove that these retroviruses are the cause of CFS. Further studies are necessary to determine if XMRV or other MLV-related viruses can cause CFS.

6. Are there studies that support different conclusions?

Some previous studies from the United States (including a study by the Centers for Disease Control and Prevention), the United Kingdom and the Netherlands reported finding no evidence of XMRV or other MLV-related infections in people with CFS. These different findings could be caused by a variety of factors (for example, difference in study populations), and underscore the need for additional studies and standardized methods.

7. Can MLV or XMRV be transmitted by blood or tissue products?

Additional research is needed to investigate the possibility that these MLV-related viruses and XMRV may be transmitted by blood or human tissue and are capable of causing disease. Investigators at FDA, NIH, CDC and other scientific institutions are in the process of conducting studies to verify the capabilities of the tests used by the different laboratories for the detection of XMRV or MLV-related viruses in blood. These studies are intended to develop and standardize a highly sensitive and specific XMRV test to better study its association with disease, as well as the possibility that XMRV can be transmitted to blood or tissue recipients.

8. What are the implications for blood donors?

At present, FDA does not have a donor policy specific to XMRV or other MLVs. There is currently no evidence that XMRV or MLVs are transmitted by transfusion in humans or that XMRV or other MLVs cause human disease. FDA regulations require that donors be in good health at the time of donation.

9. Does FDA agree with the AABB recommendation to discourage donation by people with history of CFS?

FDA does not object to the AABB recommendation. The AABB recommendation is consistent with a long-standing position of the Chronic Fatigue and Immune Dysfunction Syndrome (CFIDS) Association of America that individuals with CFS voluntarily should not donate blood.

10. How are the differences between the CDC and FDA study results being evaluated?

Differences in the results could reflect differences in the patient populations that provided the samples. Alternatively, undefined differences in the method of sample preparation could be contributing to the discordant test results. All of the scientists involved are working collaboratively to design experiments to quickly answer this scientifically puzzling question. An independent investigator at the National Heart, Lung, and Blood Institute (NHLBI) set up a test set of 36 samples, including known positives and presumed negatives. Both the FDA/NIH and CDC labs participated in this test, and the results showed that both labs were able to detect XMRV present at low levels in blinded samples. Additionally, the CDC laboratory provided 82 samples from their published negative study to FDA, who tested the samples blindly. Initial analysis shows that the FDA test results are generally consistent with CDC, with no XMRV-positive results in the CFS samples CDC provided (34 samples were tested, 31 were negative, 3 were indeterminate).

11. What do these findings mean to CFS patients and clinicians who treat them?

Although this study found MLV-like viral gene sequences in a high percentage of CFS patients, this does not prove that these retroviruses are the cause of CFS or of any other disease. Moreover, other studies have not found evidence of such retroviruses in patients with CFS. Further studies are necessary to determine if XMRV or other MLV-like viruses are reproducibly associated with CFS, and if so whether the virus is a causative agent or a harmless co-traveler. The different findings from various studies reinforce the need for more research--including careful analysis of other cohorts of CFS patients from different geographic regions, studies of larger populations of healthy people, and testing of transmissibility of the agents through blood transfusions in animal models. FDA, NIH, and CDC have and will continue to collaborate with other agencies and groups involved in this research.

別添6

Hema-Quebec 86th Board meeting summary on XMRV

Tuesday, June 15, 2010

8.6.1 XMRV

The Vice-President, Medical Affairs presented the recommendation of the SAC and the RRAC. For many years now, Héma-Québec has accepted donors with a history of chronic fatigue syndrome (CFS) if they feel well on the day of the donation. As a result of the recent report of an association between CFS and XMRV (xenotropic murine leukemia virus-related virus), Héma-Québec management has decided to re-examine this criteria. The diagnostic criteria for CFS were described briefly. This syndrome is not new. Its manifestations have been reported for a long time. However, its etiology remains unknown. XMRV was also described. Its epidemiology and means of transmission remain unknown at present. A recent study identified a good proportion of people suffering from CFS as carriers of the XMRV. Subsequently, three other studies were unable to find positive subjects. In scientific circles, the first study is contested. Furthermore, the conflicting results of these studies cannot be clearly explained. These conflicting results were then discussed. It was also noted that there is no medical evidence demonstrating that CFS is transmitted by transfusion. However, some organizations have already taken measures in this respect. Specifically, the AABB recommends indefinitely prohibiting donors who have been diagnosed as infected with the XMRV. In the United States, the CFS Advisory Committee recommended prohibiting blood donors with CFS, although no measure has been announced by the FDA. As for the CBS, it has decided to prohibit donors with a history of CFS on a permanent basis (only if the information is provided spontaneously by the donor; no question is asked systematically). Australia and New Zealand have adopted the same measures as the CBS. The risk management options have been reviewed by the advisory committees and, for the reasons mentioned below, the option of the status quo is recommended by the SAC and the RRAC:

- **CFS is not an emerging disease.**
- **Although several micro-organisms have been studied, no etiological link has been established between them and CFS.**
- **Specifically in terms of XMRV, only one of the four studies found a link with CFS.**
- **Symptomatic donors (with an active illness) are already prohibited.**
- **There is no evidence that CFS is transmitted through transfusion.**

It was also mentioned that the Management Committee tracks XMRV at each meeting.
It was moved, duly seconded and unanimously resolved **to maintain the selection criteria for chronic fatigue syndrome (CFS), namely to accept donors with a history of CFS if they feel well on the day of the donation.**

http://www.hema-quebec.qc.ca/hema-quebec/profil/conseil-administration/compte-rendus/2010/juin10/index.en.html

別添７

Recommendation on Chronic Fatigue Syndrome and Blood Donation

The AABB Interorganizational Task Force on Xenotropic Murine Leukemia Virus-Related Virus reviewed the risk of transfusion transmission of XMRV by individuals with chronic fatigue syndrome (CFS). The task force presented its recommendations to the AABB Board of Directors, which approved an interim measure intended to prevent patients with a current or past diagnosis of CFS from donating blood or blood components.

AABB released an Association Bulletin today recommending that, as an interim measure until further definitive data are available, its member blood collectors, through the use of donor information materials available at the donation site, actively discourage potential donors who have been diagnosed by a physician with CFS [also known as chronic fatigue and immune dysfunction syndrome (CFIDS) or myalgic encephalomyelitis (ME)] from donating blood or blood components.

The task force includes representatives from the blood community, patient advocacy representatives, XMRV subject matter experts and liaisons from several government agencies, including the Office of the Assistant Secretary for Health, the Centers for Disease Control and Prevention, the Food and Drug Administration and the National Institutes of Health.

AABB member institutions are required to follow all federal regulations regarding donor eligibility. At present, there are no specific regulations for deferral of individuals with diseases or syndromes that have been linked to XMRV.

AABB appreciates all individuals who want to donate blood but strongly urges that only those who are eligible and healthy do so.

Last updated: June 18, 2010

RESOURCES

- AABB XMRV Fact Sheet
- CDC XMRV Fact Sheet
- Association Bulletin #10-03 - Chronic Fatigue Syndrome and Blood Donation (member content)

平成２２年度第３回血液事業部会
運営委員会提出資料

「慢性疲労症候群」（Chronic Fatigue Syndrome ; CFS）について

関西福祉科学大学　倉恒弘彦

【概要】

慢性疲労症候群（Chronic Fatigue Syndrome; CFS）とは、健康に生活していた人が風邪などに罹患したことがきっかけとなり、それ以降原因不明の強い全身倦怠感とともに、微熱、頭痛、筋肉痛、思考力の低下、抑うつ、不安などが長期に続いて健全な生活が送れなくなるという病態であり、CDC（米国疾病対策センター）により 1988 年に提唱された比較的新しい疾患概念である。

【患者数】

1999 年の厚生労働省研究班（班長：木谷照夫、大阪大学医学部）による疫学調査（名古屋地区 4000 名を対象、有効回答数 3015）では一般地域住民の約 0.3%がＣＦＳに該当していた。2004 年の文部科学省研究班（代表研究者：渡辺恭良、大阪市立大学）による疫学調査（大阪地区の一般地域住民を対象、有効回答数 2742）でも約 0.3%がＣＦＳに該当しており、日本における 15-65 歳のＣＦＳ患者数は約 24 万人と推定される。

【症状】

慢性的な疲労感とともに、発熱、リンパ節腫大、咽頭痛などの感染症様症状、頭痛、筋肉痛、関節痛、脱力感などの膠原病様症状、睡眠障害、思考力低下、抑うつ、不安などの精神・神経症様症状などの多彩な症状が認められる。

【原因】

種々の生活環境ストレスによって引き起こされた神経・内分泌・免疫系の変調に基づく病態であり、免疫力の低下に伴って種々のウイルスの再活性化が惹起され、これを制御するために産生されたインターフェロン（IFN）などのサイトカインが脳・神経系の機能障害を生じていると思われる。

【治療】

確実に有効な治療法は確立していないが、以下の治療法が試みられる。

抗酸化療法（ビタミンＣ大量、CoQ10 など）、免疫賦活療法（漢方薬など）、向精神薬（SSRI、抗うつ薬、抗不安薬など）、精神療法（認知行動療法）

日本における CFS と XMRV との関係について

関西福祉科学大学　倉恒弘彦

目的：昨年より米国で問題になってきた CFS と XMRV 感染症との関係を日本においても明らかにするため、以下の検討を行った。

対象：大阪市立大学医学部疲労クリニカルセンターに通院中の CFS 患者 100 名
（木谷研究班 CFS 診断基準、CDC の CFS 診断基準を満たす患者）

方法：

1. 抗体検査：XMRV のウイルス粒子（タンパク質）を抗原として、検体中の抗体の有無をイムノブロッティング法により解析した。
2. DNA 検査：末梢血単核球から DNA を抽出し、XMRV DNA の有無を genomic-PCR 法により解析した。
3. 上記解析は、京都大学ウイルス研究所の 2 カ所の研究部門（宮沢先生、小柳先生)、大阪府赤十字血液センター研究部（古田先生）の 3 カ所に血液検体を送付して実施した。

結果：

1. CFS 患者において XMRV の Gag カプシド蛋白に対する抗体が 100 例中 2 名に認められたが（陽性率　2.0%)、健常者 500 名の陽性率 1.6%と比較して有意な差は認めなかった。また、その他のウイルス蛋白に対する抗体は認められなかった。

2. XMRV DNA については、上記 PCR 解析で陽性例は認めなかった。

結論：

現時点の調査結果からは、日本においての CFS と XMRV 感染症との関係は認めなかった。しかし、今回用いた検査法の感度を高めると検出される可能性も否定できないため、引き続き調査研究を行う必要がある。