- 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.

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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.

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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

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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)