

18 January 2001
Testimony before the
FDA Transmissible Spongiform Encephalopathies Advisory Committee
Bethesda, Maryland

Bess Beliveaux
Executive Director
Lions Eye Bank of Central Texas
Austin, Texas 78705
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I am Bess Beliveaux, Executive Director for Lions Eye Bank of Central Texas, Austin, Texas. For more than twenty years, I have worked with and for medical examiner's offices and with and for donor programs. Throughout these years, I have spoken hundreds of times with family survivors in regards to the death of one or more family members. Though well intentioned, my experiences have proven that the majority of those interviewed are limited in their abilities to provide accurate medical and social information. What I have to share with you today is anecdotal; and, still, important for you to know.

Examples of medical and social history provided by "informed" family members include:

1. "The only time he's been sick is when he was born brain dead. . . but the doctors fixed him."
2. In a small Texas town, a 70-year-old Fire Chief collapsed during a fire fight and was transported to the local emergency department. All life saving measures failed and cause of death was listed as Myocardial Infarction. The decedent's wife wanted him to become a donor and provided medical and social information significant only for hypertension and heart disease. While performing the external body exam, eye bank technicians learned the decedent was wearing pink ladies underwear and had numerous, recent penile and scrotal piercings. The recent piercings being obvious contraindications to donation.
3. "When she was a child, she had screamin' mighty Jesus." – this is a colloquialism for spinal meningitis, though the correct medical diagnosis was unfamiliar to family members.
4. A father reported to an organ bank that his late-teens child had no tattoos, piercings, etc. After organ recovery, the external exam performed by the eye bank technician revealed the decedents back was nearly covered with fresh tattoos.

5. Family members told the staff at a local Emergency Department that their mother had a past medical history positive for some disease that began with an "H". The ER staff recorded this as hepatitis. Later conversation with the decedent's primary care physician revealed the "H" actually should have been recorded as hemorrhoids. Because the PCP was not readily available, corneal tissues were destroyed because we were unable to determine the validity of past medical history positive for hepatitis. Of note: all serology testing was non-reactive.
6. A father and mother reported their son, a suicide victim, had wished to be a donor and, reported no contraindicating medical or social history. Follow up with the medical examiner's office revealed the donor had an incarceration history recent enough and long enough to be a contraindication to donation.
7. In a face-to-face meeting with spouse and other family members, medical and social history provided for the deceased spouse/father was clear of contraindications. When the eye bank coordinator left the room, the spouse followed and stated that all was not well; and, that she had not wanted the children to know their father had engaged in promiscuous behavior with prostitutes. In many settings, the spouse may not have had an opportunity or inclination to make such confessions.

I am not implying all medical and social interviews are so blatantly misleading. For the most part, the misconceptions are very subtle and can easily be overlooked. Family members do not typically intend to provide misleading or incorrect information. Perhaps it is that our society has become far more mobile and far more distanced from the family nucleus than ever before that misleading or incorrect information can so easily be provided. Also, many family members simply are not savvy enough regarding medicine and/or social contraindications. It is my experience and belief that the medical/social interview is rarely, if ever, of true value in evaluating the usability of donor tissues. Especially, I am concerned that we are considering this source of information as a defining factor for determining the suitability of donated non-vascular corneal tissues. Additionally, I believe a donor that has the advantage of medical examiner investigation and forensic autopsy is one that comes with infinitely more accurate medical and social information.

I appreciate your role in promulgating rules to provide for public health and safety. It is with this in mind, therefore, that I ask this advisory committee to explore options other than medical/social interviews of a decedent's next-of-kin for determining a potential donor's risk for transmitting spongiform encephalopathy or any other prion disease.

Also, I am providing this committee with letters from corneal surgeons, a forensic pathologist and a neuropathologist regarding this matter of screening potential donors for transmissible spongiform encephalopathies and other prion diseases.

Thank you for your time and consideration.

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INFORMATION](#)[INVESTOR RELATIONS](#)**#2490: Creutzfeldt-Jakob Disease DetectR™****COMPONENTS**

Name	Method	Reference Range	Units
14-3-3 Beta Isoform	IB	Not detected	

SPECIMEN REQUIREMENTS

No	Type	Volume	Temperature
1	CSF	1.0 (0.5) mL	Frozen

GENERAL INFORMATION

Setup Schedule	Monday-Friday
Turn-Around Time	3-10 days
Fee	\$224.00
CPT Code	84182
Notes	Detects 14-3-3 Protein Beta-Isoform.

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For test information, please call *Specialty's* Client Services at 800-421-4449.

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William F. McCormick, M.D.
120 Niles Wheelock Road
Jonesborough, Tennessee 37659
10-14-99

EBAA -- Medical Advisory Board
c/o Edward J. Holland, M.D.
University of Minnesota
Dept. of Ophthalmology
UHMC Box 493
420 Delaware Street, SE
Minneapolis, MN 55455

Dear Dr. Holland,

The idea behind the proposed new medical standard regarding corneal donation is good -- prevent direct transmission of prion (C-J) disease. However, it will have the "real" undesired VS "ideal" consequence of significantly decreasing available corneas far in excess of its potential to eliminate the very rare prion-diseased donor.

In forty-plus years of practice as a physician, pathologist, forensic pathologist, and neuropathologist, I have seen in my own autopsy material (more than 10,000), and in referred material, a half dozen cases of C-J (and other prion) disease(s). All of these cases were in clearly symptomatic hospitalized patients; none were in ambulatory, non-hospitalized "well" individuals who died as a result of violent death.

Even given its (their) rarity (1:1,000,000), the lethal nature of prion disease would warrant their absolute exclusion from the donor cornea population: (1) if it were possible, and (2) if we were still able to obtain corneas for the great (relative) number that need them. The proposed "interview" is impractical -- it will not work in the real world. The time required to find knowledgeable next of kin, relative, etc. is too great for transplant purposes. The key word here is knowledgeable.

The use of some markers such as 14-3-3 β -isoform would require the local hospital (laboratory) to be able to do the test accurately, in a timely fashion, and in a cost effective manner, with the second the greatest problem.

I would estimate that the use of laboratory tests and next of kin interviews would prevent cornea procurement in at least one half of the now-available donor population for the potential prevention of one-to-two cases of prion disease/year/USA. I would not require their (interview and labs) use in the vast majority of forensic pathology derived cases, but would urge medical examiners and forensic pathologists to exclude most debilitated and aged potential donors and obviously any with known dementia.

Sincerely,



William F. McCormick, M.D.
Deputy Chief Medical Examiner
State of Tennessee

I personally obtained authorization by telephone from William F. McCormick, MD, on 16 January 2001 at 7 p.m. CST, to provide copies of this letter to members of the FDA Transmissible Spongiform Encephalopathies Advisory Committee.

A handwritten signature in cursive script that reads "Bess Beliveaux".

Bess Beliveaux
Executive Director
Lions Eye Bank of Central Texas
Austin, Texas 78705

Robert L. Rock, M.D.
H. Grady Rylander, M.D.
George C. Thorne, M.D.
Gary R. Rylander, M.D.



Janet A. Lindsey, M.D.
K. Randy Pierce, M.D.
Gregory L. Hemphill, M.D.
Mark A. Plunkett, M.D.

January 15, 2001

Food and Drug Administration
Transmissible Spongiform Encephalopathies
Advisory Committee

Dear Committee Members:

I have been a corneal surgeon in the state of Texas for twenty-one years and am distressed to hear that the Food and Drug Administration (FDA) will be adding a series of questions regarding Creutzfeldt-Jakob disease (CJD) to medical screening standards for all donor corneas. This requirement will significantly affect the number of tissues currently being obtained by legislative consent.

Texas and the US have greatly benefited by having available these young, healthy donor corneas recovered through the cooperative efforts of medical examiners. Medical examiner laws have been instrumental in helping to eliminate the waiting lists of patients in need of sight restoring corneal transplantation; and, has successfully and safely provided donor corneal tissues (in Texas) since 1977. This important legislation provides 50 - 60 % of the donor corneal tissues for our community.

I appreciate the position the FDA has taken to develop and maintain strict medical standards and screening devices to help ensure a safe supply of donor corneal tissues. However, with the annual incidence of CJD at one case per million population (with most cases being present in patients 60 years of age or older) and the calculated risk of a prion-infected corneal donor at .005%, imposing these screening steps which will terminate this important law is unnecessary.

I ask that you please consider the issues surrounding this important matter.

Sincerely,

George C. Thorne, M.D.

Robert L. Rock, M.D.
H. Grady Rylander, M.D.
George C. Thorne, M.D.
Gary R. Rylander, M.D.



Janet A. Lindsey, M.D.
K. Randy Pierce, M.D.
Gregory L. Hemphill, M.D.
Mark A. Plunkett, M.D.

January 16, 2001

Food and Drug Administration
Transmissible Spongiform Encephalopathies
Advisory Committee

Dear Committee Members:

I have recently been informed about a potential new screening criteria for Creutzfeldt-Jakob disease, which could dramatically limit our access to young, healthy corneal tissue for corneal transplantation. If the information is accurate and the new screening process negates the effectiveness of our current medical examiner laws I would ask that you reconsider the situation. As a corneal surgeon I would hope to be able to use the healthiest donor material with the smallest risk of disease transmittance. The risk of disease transmittance via corneal transplantation will never be zero unless such a procedure is abandoned. The risk of transmittance of Creutzfeldt-Jakob disease via corneal transplantation is theoretically small enough that I and most of my patients can live with it in order to continue a readily available supply of young donor material.

Please reconsider the impact of the new screening criteria on our future availability of healthy young corneal donor material.

Sincerely,


Gary R. Rylander, MD

Subj: Re: FDA Hearing regarding TSE and CJD
Date: 1/15/2001 12:48:06 PM Central Standard Time
From: sfulcher@mailbox.sw.org (S.F. Fulcher)
BBeliveaux@aol.com

Dear Bess,

I hope the following helps:

To Whom it May Concern,

I am writing this letter in support of the use of corneal tissue obtained from Medical Examiner cases for corneal transplantation. In the State of Texas, the existence of Medical Examiner laws allowing for the use of such tissue has greatly enhanced the quality of life for countless individuals who have undergone corneal transplantation. These laws have significantly enhance the availability and quality of tissue for transplantation that would otherwise be wasted. I strongly support the continued use of such tissue, as the benefits far outweigh and exceed any risks associated with tissue transplantation, and therefore benefits society as a whole. I personally have NEVER encountered one single adverse event associated with donor tissue in the 12 years that I have performed corneal transplants. To change the regulations to prohibit the use of Medical Examiner approved tissue would seem to me to be over regulatory exuberance and overkill. Again, I urge those responsible to judiciously allow the continued use of Medical Examiner tissue for corneal transplantation in the interest of the overriding public benefit.

Sam Fulcher M.D.

Subj:

Date: 10/5/1999 3:28:59 PM Central Daylight Time

From: Stephen.Cina@59MDW.WHMC.AF.MIL (Cina, Stephen)

To: lebct@io.com (lebct@io.com)

Memorandum:

As we discussed on the telephone today, 10/5/99:

1. CJ is a highly infectious neurodegenerative disorder. Transplantation of any tissues from a known infected person would most likely be contraindicated.
2. Most patients dying of CJ would follow a clinical course that would suggest this diagnosis. It is possible that a person with very early CJ could die of trauma and be autopsied without knowledge of this infection.
3. I have performed 1000 autopsies and not encountered an occult CJ infection in a traumatic death.
4. I have been involved with 3000 other forensic autopsies. Of these, the diagnosis of CJ was suspected twice. I am not aware of a traumatic death in which CJ was diagnosed at autopsy.

I hope you find this information useful.

Stephen J. Cina, MD
Forensic Pathologist

----- Headers -----

Return-Path: <Stephen.Cina@59MDW.WHMC.AF.MIL>

Received: from rly-yd05.mx.aol.com (rly-yd05.mail.aol.com [172.18.150.5]) by air-yd05.mail.aol.com (vx) with ESMTP; Tue, 05 Oct 1999 16:28:59 -0400

Received: from deliverator.io.com (deliverator.io.com [199.170.88.17]) by rly-yd05.mx.aol.com (v61.13) with ESMTP; Tue, 05 Oct 1999 16:28:46 -0400

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by deliverator.io.com (8.9.3/8.9.3) with ESMTP id PAA19375
for <lebct@io.com>; Tue, 5 Oct 1999 15:28:45 -0500

Received: from 59mdw.whmc.af.mil (59mdw.whmc.af.mil [206.39.75.77])
by mx2.io.com (8.9.1a/8.9.1a) with ESMTP id PAA30452
for <lebct@io.com>; Tue, 5 Oct 1999 15:28:43 -0500

Received: by 59mdw.whmc.af.mil with Internet Mail Service (5.5.2448.0)
id <S43B3VJT>; Tue, 5 Oct 1999 15:24:05 -0500

Message-ID: <86724839085AD211AB4E08002BE51EBD09D97D@59mdw.whmc.af.mil>

From: "Cina, Stephen" <Stephen.Cina@59MDW.WHMC.AF.MIL>

To: "lebct@io.com" <lebct@io.com>

Subject:

Date: Tue, 5 Oct 1999 15:24:04 -0500

MIME-Version: 1.0

X-Mailer: Internet Mail Service (5.5.2448.0)

Content-Type: text/plain;
charset="iso-8859-1"



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BESS BELIVEAUX, CEBT
Executive Director

Certified Member



And member of the
Eye Bank Association of Texas

Monday, January 15, 2001

Food and Drug Administration
Transmissible Spongiform Encephalopathies
Advisory Committee

Dear Sirs,

I would like to respectfully submit to the Transmissible Spongiform Encephalopathies Advisory Committee an item to consider regarding issues and questions pertaining to Creutzfeldt-Jakob disease and other Transmissible Spongiform Encephalopathies.

Developing questions to ask a potential donor's family must meet several requirements. One of the first hazards is to avoid the use of terminology that is unfamiliar to the person answering questions (Spilker B, Schoenfelder J, Data Collection Forms in Clinical Trials. New York: Raven, 1991, page 27). Unfortunately, the questions pertaining to the symptomatology of CJD and other TSE's that have been proposed for widespread implementation greatly exceed the vocabulary of most individuals.

The validity of a medical-social interview must be based on the assumption that those being interviewed know the meanings of required medical terminology. Demographers often suggest that respondents chosen from the general population will answer most accurately if eighth graders can understand the questions (Aday LA, Designing and Conducting Health Surveys. San Francisco: Jossey-Bass, 1996, page 193). When the wording was tested to screen for CJD on software checks in a word processing program, the readability and grammar failed.

We feel that CJD-TSE interview questions are inappropriate and are above the educational level of most respondents. This could result in the unnecessary deferral of otherwise acceptable donors. We strongly recommend that the TSE Advisory Committee hire a consultant who is skilled in survey methodology and demography before implementing any interviewing screening criteria for Transmissible Spongiform Encephalopathies.

Respectfully,

Gary R. Warner OPA-C, CST
Chief Operating Officer
Lions Eye Bank of Central Texas