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SCIENTIFIC EDITOR: *TOTAL NUTRITION: FROM THE MOUNT SINAI SCHOOL OF MEDICINE*, ST. MARTIN'S PRESS, NY, 1995.

CO-AUTHOR: *THE VITAMIN PUSHERS: THE 'HEALTH FOOD' INDUSTRY SELLS A BILL OF GOODS*, PROMETHEUS, BUFFALO, NY, 1994.

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 BRONX, NEW YORK

September 5, 1996

Dockets Management Branch  
 Food & Drug Administration  
 Department of Health & Human Services, Room 1-23  
 12420 Parklawn Drive  
 Rockville, MD 20857

**FAXED**  
 9-5-96  
 3:15 PM - JH

By mail and FAX to 301-594-3215

The undersigned submits this petition to the Commissioner of Food and Drugs to issue an order in the form of administrative action.

**A. Action requested**

That the FDA insert, in 21 CFR Ch. 1(4-1-93 Edition) §640.3 (d) after the title "*Therapeutic bleedings*," the words:

**"Except for blood withdrawn from persons with iron overload disease, whose blood should not be stigmatized, but should be labeled solely 'volunteer donor' in accordance with 21 CFR Ch. 1(4-1-93 Edition) §606.121(5)."**

**B. Statement of grounds.**

The stigma regarding hemochromatosis is based on the mythology that it was an infectious disease. That mythology ended with the discovery that it was a non-infectious genetic disorder (and the 1996 discovery of a diagnostic test for the hemochromatosis gene).

The purpose of stigmatizing therapeutic phlebotomy blood, including homozygous hemochromatosis blood, is to protect the recipient against transmission of the donor's disease(s).

21 CFR Ch. 1(4-1-93 Edition) §640.3 (d) now states:

*Therapeutic bleedings.* Blood withdrawn in order to promote the health of a donor otherwise qualified under the provisions of this section, shall not be used as a source of Whole Blood unless the container label conspicuously indicates the donor's disease that necessitated withdrawal of the blood.

If, after the title "*Therapeutic bleedings*," the words "Except for blood withdrawn from persons with iron overload disease, whose blood should not be stigmatized, but should be labeled solely 'volunteer donor' in accordance with 21 CFR Ch. 1(4-1-93 Edition) §606.121(5)." are inserted, you will:

1) Save Americans with homozygous or heterozygous hemochromatosis approximately \$20 billion annually in "therapeutic phlebotomy" costs (at ≈ \$200 per phlebotomy). Volunteer donors are not only charged nothing but also are given various inducements to donate blood.

2) Completely eliminate the chronic problem of inadequate volunteer donor blood in the US and among our Armed Forces overseas). The ≈ 1.25 million Americans with homozygous hemochromatosis alone will provide a minimum of 12 donations per year per person, which is 15 million units per year.

It should be noted that the approximately 3 phlebotomies per year desirable for healthy heterozygotes are prophylactic and *not* therapeutic; since healthy heterozygotes have **no disease**. They just have elevated serum ferritin iron, which is especially desirable for most blood recipients. The ≈ 30 million heterozygotes will provide a minimum of 3 donations per year per person, or 90 million units per year. This totals 105 million units annually of American volunteer donor blood.

## REFERENCES:

The above was discussed at the February 26-27, 1996, Iron Overload Expert Panel meeting of the Centers for Disease Control (CDC) in Atlanta, GA, coordinated by Sharon McDonnell, MD, MPH and Ray Yip, MD, MPH, and chaired by CDC's Rick Trowbridge, MD, MPH. Participant Paul R. McCurdy, MD, Director, Blood Resources Program, BRP/DBDR/NHLBI/NIH provided the relevant sections of 21 CFR, Ch. 1.

Enclosed with this mailing is the agenda of the Centers for Disease Control meeting (above) with list of participants, their addresses and telephone numbers. Summaries of the proceedings are available from Dr. Sharon McDonnell of the CDC.

Also see:

- 1) A Simopoulos, V Herbert, B Jacobson: *The Healing Diet* (formerly *Genetic Nutrition*), Macmillan, NYC, 1995.
- 2) V Herbert: Introduction and medicolegal considerations. In: V Herbert, Chair: Symposium: Diagnosis & Treatment of Iron Disorders. *Hosp Practice* 1991;26 (Suppl 3):4-6.
- 3) V Herbert: Everyone should be tested for iron disorders. *J Am Diet Assoc* 1992; 92:1502-1509.
- 4) V Herbert, S Shaw, E Jayatilleke. Vitamin C-driven free radical generation from iron. *J Nutr* 1996;126(Suppl 4):1213S-1220S.

## C. Impact

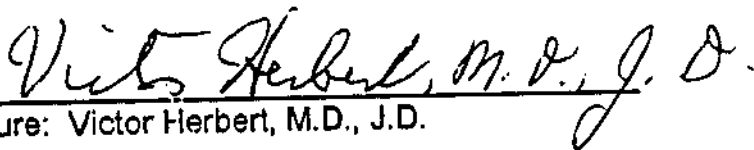
1) Save Americans with homozygous or heterozygous hemochromatosis approximately \$20 billion annually in "therapeutic phlebotomy" costs (at ≈ \$200 per phlebotomy). Volunteer donors are not only charged nothing but also are given various inducements to donate blood.

2) Completely eliminate the chronic problem of inadequate volunteer donor blood in the US and among our Armed Forces overseas). The ~ 1.25 million Americans with homozygous hemochromatosis alone will provide a minimum of 12 donations per year per person, which is 15 million units per year.

The ~ 30 million heterozygotes will provide a minimum of 3 donations per year per person, or 90 million units per year. This totals 105 million units annually of American volunteer donor blood.

#### **D. Certification**

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.



Signature: Victor Herbert, M.D., J.D.

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cc: Sharon McDonnell, MD, MPH; Ray Yip, MD, MPH, Rick Trowbridge, MD, MPH, CDC  
Paul McCurdy, MD, Director, Blood Resources Program, NIH  
Roberta Crawford, Sandra Thomas, David Snyder, Randy Alexander,  
Iron Overload Diseases Association (IODA)  
Margaret Krikker, Hemochromatosis Research Foundation, Inc.  
The Hon. Sen. Edward M. Kennedy  
The Hon. Congressman John D. Dingell  
John W. Rowe, MD, President, Mount Sinai Medical Center, NYC  
Kenneth Kizer, MD, Dept. of Veterans Affairs, VA Central Office, Washington, DC  
The Hon. Donna Shalala, Secretary, DHHS  
Phillip R. Lee, MD, Ass't. Secretary for Health, USPHS  
Harold Varmus, MD, Director, NIH  
Director, Armed Services Blood Bank Program, Tacoma, WA

Centers for Disease Control  
and Prevention**Centers for Disease Control and Prevention  
National Prevention Programs and Guidelines****Agenda****Panel on Iron Overload****February 26-27, 1996**

The Centers for Disease Control and Prevention (CDC) has invited a panel of scientific experts and other interested parties to assist us in thinking through key issues in the development of National guidelines and programs for iron overload diseases. This includes iron overload in its earliest stages, a mere phenotypic expression with some abnormal laboratory findings to overt penetrance, with full-blown clinical expression and grave illness.

As an agency, we are considering recommending universal screening for iron overload of all adults every ten years. We ask this group to help us weigh issues relating to the science, the policy and the problems inherent in such a far-reaching recommendation.

We recognize we have a work in progress with our current guidelines and that consensus among the group on many issues is unlikely. We do however, hope for a fair hearing of all sides of many issues.

The facilitator, Dr. Rick Trowbridge will keep the meeting moving between and within sessions. For all sessions questions will be posed to the panel members. Time for observers to ask or answer questions will be provided and in some circumstances the input of a specific observer will be sought because of their expertise. All presentations will be held to 10 minutes so that sessions have time for discussion.

The sessions are divided into topics. Within topics we have tried to pose very specific questions that might help panel members consider the issue in depth and help us gain the input of their experience. One risk of this process is that the overlap of clinical science and research with public health may sometimes feel awkward. We are aware that individual exceptions to the guidelines and community standards will always occur. Each clinician or researcher will have a case that breaks the rule or doesn't fit with guidelines. However, it is our job to extrapolate an idea or program into every situation, including county health units, community hospitals and large research institutions. Our needs and viewpoint in public health may be very different than what you as a panel member or observer may normally consider. We hope you find this perspective fun and interesting. Your input is deeply appreciated and will be of great use to our agency and we hope to all persons with the disease whether they are aware of it yet or not.

If you have any questions about these issues or the attached agenda feel free to call me. Please do consider this agenda preliminary and over the next week some changes are expected.

Sincerely,

Sharon McDonnell MD MPH

CDC, Division of Nutrition and Physical Activity, NCCDPHP

**Monday February 26, 1996**

- 12:30 pm: Opening statements and welcome to panel and participants by Frederick Trowbridge MD MPH, Director Division of Nutrition and Physical Activity, CDC.
- 12:40 pm: Session I: An Overview of the CDC guidelines:
- a) How and why CDC came to this point. Plans from here. Ray Yip MD MPH.
  - b) Overview of hemochromatosis issues. Linda Bradley PhD
  - c) The proposed screening, diagnostic and treatment algorithm. Sharon McDonnell MD MPH
  - d) A cost effectiveness analysis of the CDC protocol. Anne Haddix PhD
  - e) Discussion:
    - i) Problems with this approach or compelling reasons for change?
    - ii) Is there a way to enhance the effectiveness of screening?
    - iii) What criteria should be used for interpretation (men, women, age groups).
    - iv) Limitations of tests and concerns about performance ie biologic, physiologic and pathologic variability.
- 2:40 pm: Break and curbside coordination
- 3:00pm: Session III: Laboratory issues in planning for Universal screening and lessons learned from Cholesterol and lead screening programs- Eric Sampson PhD
- a) Discussion
    - i) Do we have the laboratory standards, accuracy, reliability in the "real" world to support the test(s) of choice?
    - ii) What background information and preparation needed regarding laboratory practices and variation before we can recommend universal screening?
  - b) Presentations
    - i) Anne Looker PhD -- Preliminary laboratory data reporting from NHANESIII.
    - ii) Comments by Elaine Gunter MS on NHANESIII methods
  - c) New laboratory methods in consideration and practice
    - i) David Witte MD - UIBC
    - ii) Victor Herbert MD- holoferritin

Discussion

5:30pm: Break

**Tuesday February 27, 1996**

8:30 am: Session IV: Diagnosis -- what is needed?

- a) An elevated fasting TS -- what workup is needed for presumptive hemochromatosis? Focus on younger asymptomatic patients.
- b) The Kaiser experience. Vincent Felliti MD
- c) Specific Questions for discussion:
  - i) The liver biopsy when, why, and why not?
  - ii) Phlebotomy as a diagnostic tool.
  - iii) Is there a place for other types of imaging MRI and CT to answer the same or different questions?
- d) The potential for the gene test as confirmation - New Developments in genetics. More help from Mice. Barry Rothenberg ~~MD~~ PhD

10:10 am Break

10:30 am Session IV: Overview on Management

- a) Treatment parameters for continuous phlebotomy -- end points -- Symptoms, serum ferritin, anemia.
- b) What should patients be advised to do or not do?
- c) Continuous phlebotomy, what are the side effects and how to prevent them?
- d) Blood -- a treatment, a benefit or a cost. Potential concerns and possibilities for change in policy. Paul McCurdy MD, NIH
- e) How is a pint of blood from healthy hemochromatotic different biochemically than non-hemochromatotic. A case for the "super-donor" and an improved cost-benefit analysis.

12:00 pm: Lunch

1:30 pm Session V: Issues and inputs

- a) General and specific comments on the CDC guidelines
- b) Outstanding issues in iron overload that need to be addressed
  - i) The public health point of view.
  - ii) The clinical evaluation point of view.
  - iii) The clinical management point of view.
- c) Recommendations to CDC

- i) for research and development
- ii) for development and promotion of a National program

2:45 pm: Break

3:00 pm: Session VI: Implications of screening-- Economic and social issues.

- a) Costs to patients for treatment, insurability and stigma.
- b) Subjective costs and preparing society for more people with a diagnosis.

Comments from the floor

4:00 pm: End meeting

**Panel members and Participants  
Iron overload Expert Committee  
February 26-27, 1996  
Atlanta GA**

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**CDC and Audience members to be present:**

- Ray Yip MD MPH (770)488-4719
- Ibrahim Parvanta MS (770)488-4335
- Sharon McDonnell MD MPH (770)488-4788
- Rick Trowbridge MD MPH (770)488-4721
- Larry Grummer-Strawn PhD (770)488-4971
- Geraldine Perry (770)488-4215
- Bettylou Sherry (770)488-4806
- Indu Alawalhia (770)488-4865
- Caryn Bern (770)488-4914

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Laboratory Sciences

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