FOOD AND DRUG ADMINISTRATION
GENERAL AND PLASTIC SURGERY DEVICES PANEL
OPEN PUBLIC HEARING
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TESTIMONY BY

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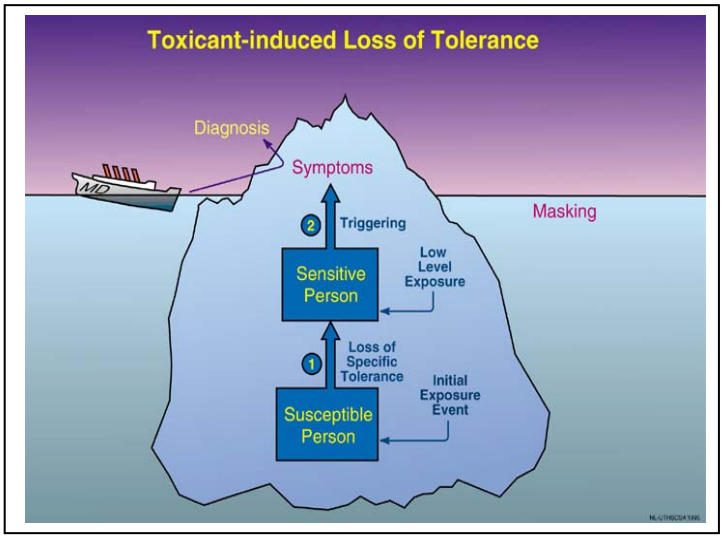
I have no financial interests related to this hearing.

I am a professor of environmental and occupational medicine and a board certified internist, allergist and immunologist at the University of Texas Health Science Center at San Antonio. For more than a decade, my research has focused on people who report developing chronic, multi-system symptoms—headaches, memory and concentration difficulties, depression, fatigue, fibromyalgia, gastrointestinal problems, etc.—following an identifiable environmental exposure, e.g., to pesticides, solvents or chemicals used during the first Gulf War. I have served as a consultant to the Department of Veterans Affairs on the Gulf War veterans' illnesses, the EPA on sick buildings including its own headquarters building, the National Institute of Dental and Craniofacial Research on temporomandibular joint implants (as well as the National Institute of Environmental Health Sciences, the National Toxicology Program, the governments of Canada, Germany, Sweden and others). What unites these seemingly diverse groups—Gulf War veterans, sick building occupants and patients with implants is the fact that following a well-defined exposure event, a subset of individuals appears to lose their prior innate or natural tolerance (much as diabetics lose their tolerance for sugar) for a wide variety of structurally unrelated substances. Thereafter, everyday exposures including commonly eaten foods, medications, alcoholic beverages, caffeine, and chemical inhalants such as fragrances, diesel exhaust and tobacco smoke—exposures that never bothered these individuals before and do not bother most people—trigger



myriad, often disabling symptoms. In environmental medicine, this two-step disease process has come to be known as "Toxicant-induced Loss of Tolerance" or "TILT" (Miller 1997). It does not appear to matter whether the exposure that initiated TILT was exogenous (chemical inhalants) or endogenous (implant). The body's response is remarkably similar.

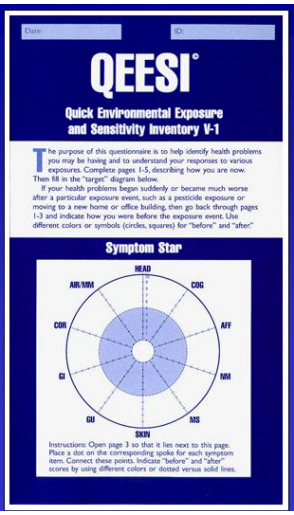
We have studied and reported on 87 people with surgical implants, three-quarters of whom had received breast implants (Miller and Prihoda 1999b). Among the latter, 69% reported rupture of an implant and 78% had had one or more implants removed. Of those who had undergone explantation, only 9% reported their health status as "greatly improved" (36% "somewhat improved;" 13% "unchanged;" 18% "somewhat worsened;" and 24% "greatly worsened").

Using a validated screening questionnaire for TILT (the Quick Environmental Exposure and Sensitivity Inventory [QEESI]; sensitivity 92%; specificity 95%), we found that the symptom severity scores of implant recipients rivaled those of the environmentally exposed groups we were studying. Compared to controls, implant recipients also reported many more, and more severe, adverse responses to everyday chemical exposures. Further, implant

Study of Individuals with Surgical Implants

- Of the women who had had one or more breast implants removed:
  - 9% reported their health status as "greatly improved"
  - 36% as "somewhat improved"
  - 13% as "unchanged"
  - 18% as "somewhat worsened"
  - 24% as "greatly worsened"

Source: Miller CS, Prihoda TJ. Tox Industr Health 15:386-397, 1999



High validity, reliability for assessing chemical intolerance

Sensitivity 92%, specificity 95%

Source: Miller CS, Prihoda TJ. Tox Industr Health 15:370-385, 1999

Symptom Severity Scores (0-10)

Symptoms	Implant Recipients	Controls
Musculoskeletal	9.0****	2.9
Airway/mucous membrane	7.7****	2.5
Heart/chest-related	6.4****	1.1
Gastrointestinal	7.8****	1.7
Cognitive	8.4****	1.6
Affective (mood-related)	7.9****	2.1
Neuromuscular	7.8****	1.4
Head-related (e.g., headaches)	7.7****	1.9
Skin	6.7****	1.7
Genitourinary	6.9****	1.3
Totals (0-100)	75.3****	18.0

**** $p \leq 0.0001$ as compared to controls

Source: Miller CS, Prihoda TJ. Tox Industr Health 15:386-397, 1999

recipients reported far more severe reactions to a wide variety of foods, medications, alcoholic beverages, caffeine, and other common exposures than did controls.

Toxicant-induced Loss of Tolerance is a new paradigm for environmentally-induced disease that differs from classical toxicity and allergy in important ways (Miller 2001). TILT helps explain:

- why affected individuals remain sick years after their initial exposure—as a consequence of subsequent triggering by everyday exposures.
- why symptoms wax and wane in such a bewildering fashion—as triggering exposures change over time and their effects overlap.

Ironically, affected individuals (and their physicians) may be completely unaware of the intolerances resulting from TILT because of a phenomenon called "masking": if an individual reacts adversely to multiple chemicals, foods and drugs, and (s)he is exposed to these substances, one after another, during the day, then symptoms resulting from these exposures overlap in time. As a consequence, there is so much background "noise" that patients cannot identify any specific triggers for their symptoms. They just feel bad most of the time, with chronic fatigue or flu-like symptoms that won't go away.

Recent Canadian studies indicate that genetic polymorphisms may determine who is more vulnerable to developing TILT (Mckeown-Eyssen et al. 2004). At the present time, however,

Severity of Chemical Intolerances (0-10)

Chemical Intolerances	Implant Recipients	Controls
Diesel or gas exhaust	6.5****	2.3
Tobacco smoke	6.7****	3.5
Insecticide	7.1****	2.7
Gasoline	6.5****	1.7
Paint or paint thinner	6.9****	2.5
Cleaning products (disinfectants, bleach)	6.9****	1.9
Fragrances	6.8****	2.2
Tar or asphalt	5.8****	1.9
Nail polish or hairspray	6.3****	1.4
New furnishings (carpet, shower curtain)	5.7****	1.4
Totals (0-100)	63.7****	21.3

**** $p \leq 0.0001$ as compared to controls

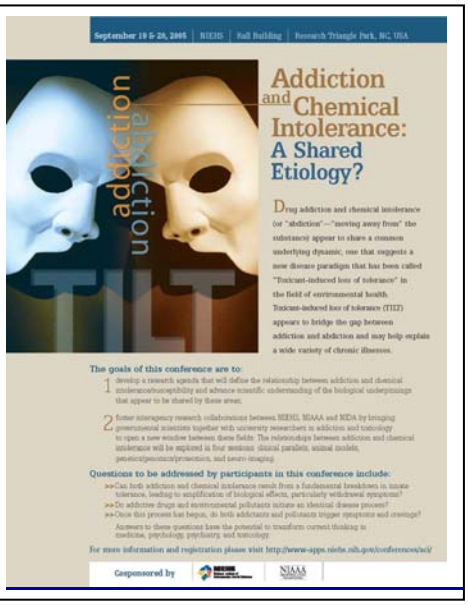
Source: Miller CS, Prihoda TJ. Tox Industr Health 15:386-397, 1999

Severity of Other Intolerances (0-10)

Other Intolerances	Implant Recipients	Controls
Chlorinated tap water	4.2*	0.4
Foods or food additives	6.1*	1.3
Food cravings or feeling ill if meal missed	5.9*	1.8
Feeling ill after meals	4.6*	1.3
Caffeine	4.3*	1.1
Feeling ill if stop or decrease caffeine	3.2*	2.3
Alcohol in small amounts	4.8****	0.9
Fabrics, jewelry, creams, and cosmetics that touch skin	5.0****	1.2
Adverse reactions to drugs or medications	7.1****	1.4
Classical allergic reactions (pollen, dust, mold, dander, insect stings)	6.6****	3.6
Totals (0-100)	49.4*	15.2

* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$ as compared to controls

Source: Miller CS, Prihoda TJ. Tox Industr Health 15:386-397, 1999



no one is able to predict which individuals will be affected. This fall (September 19-20, 2005), I will be chairing a meeting on TILT sponsored by two NIH institutes (the National Institute of Environmental Health Sciences [NIEHS], and the National Institute on Alcohol Abuse and Alcoholism [NIAAA]). Invited scientists will explore clinical observations, animal models, neuroimaging and genetic approaches for understanding this emerging new disease paradigm. I invite you to attend.

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BIOSKETCH
FOR
CLAUDIA S. MILLER, M.D., M.S.

Claudia S. Miller, M.D., M.S., is a tenured Professor in Environmental and Occupational Medicine in the Department of Family and Community Medicine of the University of Texas Health Science Center at San Antonio (UTHSCSA), where she serves as Deputy Chair of Community Medicine. She also directs the South Texas Environmental Education and Research Center (STEER), which features a one-month elective for health professions students which focuses on environmental medicine, community health, public health, and international health at the U.S.-Mexico Border.

Dr. Miller co-authored the landmark New Jersey Report on Chemical Sensitivity (for which the New Jersey Department of Health received the World Health Organization's Macedo Award), a professionally acclaimed book—Chemical Exposures: Low Levels and High Stakes (Second edition, John Wiley and Sons, Inc., New York, 1998), and numerous book chapters and peer-reviewed publications on the health effects of low level chemical exposures.

Dr. Miller has held appointments to federal advisory committees including the National Advisory Committee on Occupational Safety and Health, the Department of Veterans Affairs Persian Gulf Expert Scientific Committee, and the National Toxicology Program Board of Scientific Counselors. She has been a consultant to the Texas Department of Health, the Environmental Protection Agency, the Agency for Toxic Substances and Disease Registry, the Canadian Government, and the Department of Veterans Affairs on the unexplained illnesses of Gulf War Veterans. She also served on the San Antonio Mayor's Brooks Opportunities Task Force, helping to develop the Brooks City Base concept and to establish the International Consortium for the Environment. From 2000-2001, she was on an National Institutes of Health (NIH) sabbatical, working in the office of the Deputy Director of the National Institute of Environmental Health Sciences (NIEHS) in Research Triangle Park, North Carolina.

Board-certified in Allergy/Immunology and Internal Medicine, Dr. Miller holds a staff appointment at University Hospital in San Antonio and served as a consultant to the Chief-of-Staff of the Houston VA for its Persian Gulf Regional Referral Center. She received her B.A. in Molecular Biology from The University of Wisconsin, Madison, Wisconsin, and her M.S. in Environmental Health from The University of California School of Public Health, Berkeley, California. After receiving her M.D. from UTHSCSA, she completed her internship and residency in Internal Medicine at Brackenridge Hospital in Austin, Texas, and her fellowship in Allergy/Immunology at UTHSCSA. Prior to medical school, she worked as an industrial hygienist for 12 years and directed occupational health training for compliance officers at the Occupational Safety and Health Administration's National Training Institute in Chicago.