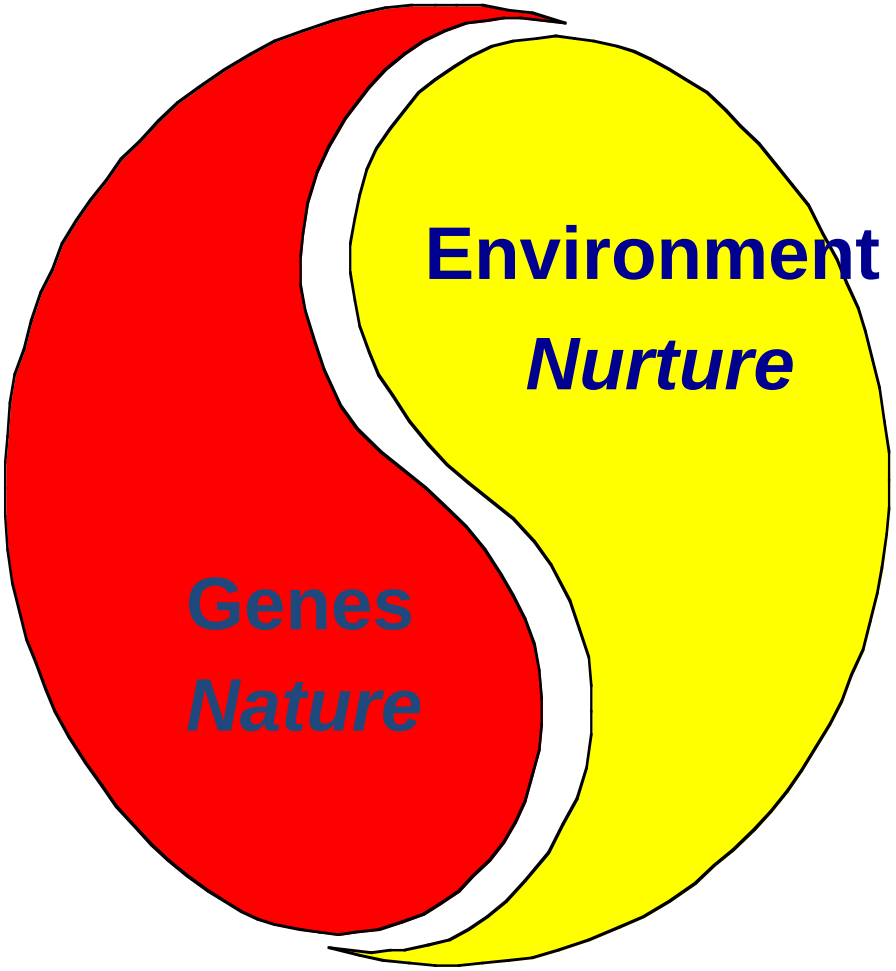
Environmental Factors in Scleroderma

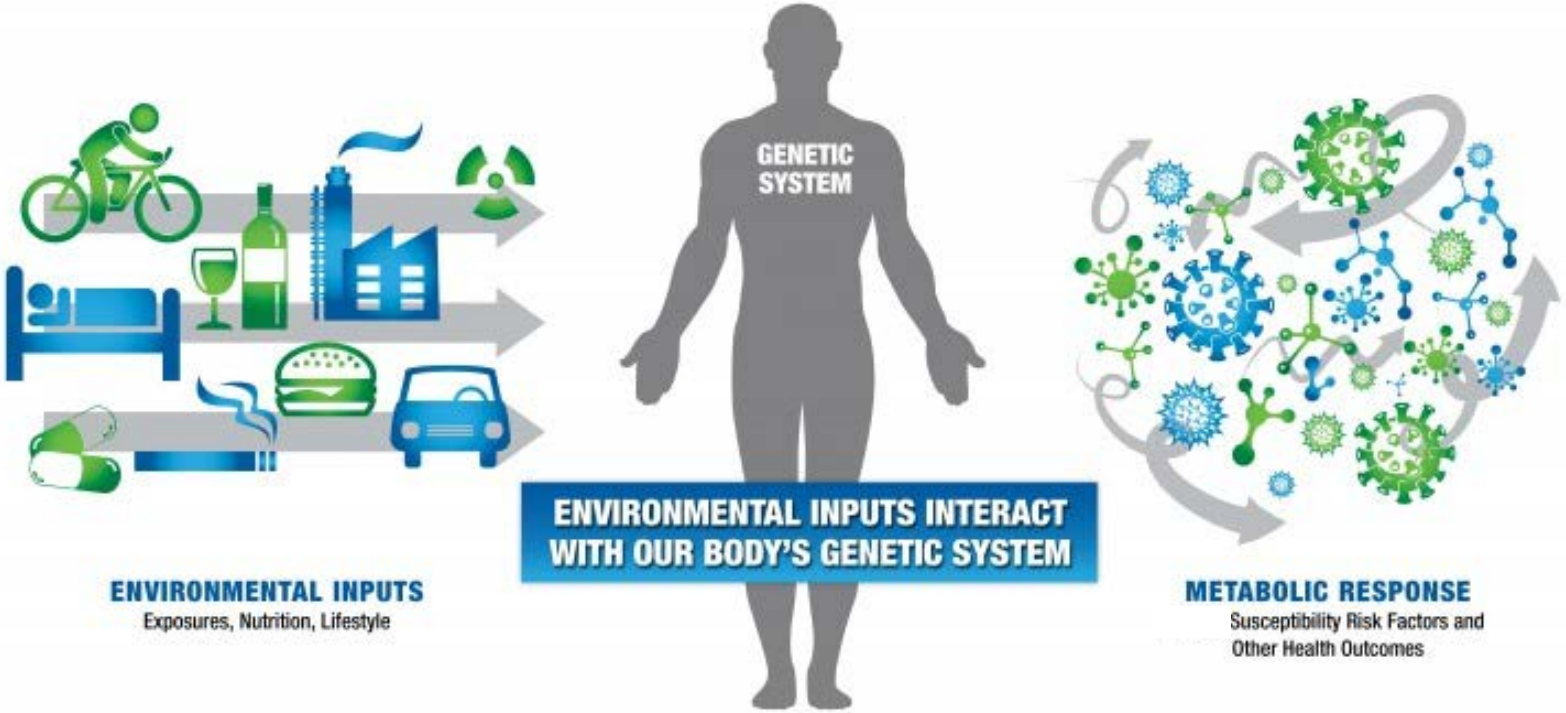
Richard M. Silver, MD
Medical University of South Carolina
Charleston, SC

Environmental Factors

- Gene-Environment interaction
- Diseases that mimic scleroderma
- Diseases with features of scleroderma
- Scleroderma *per se*


Environment
Nurture
Genes
Nature

Causes of Autoimmune Disease



Genes and Autoimmune Disease

- For some autoimmune diseases, disease concordance in identical twins is higher than in most other diseases studied.

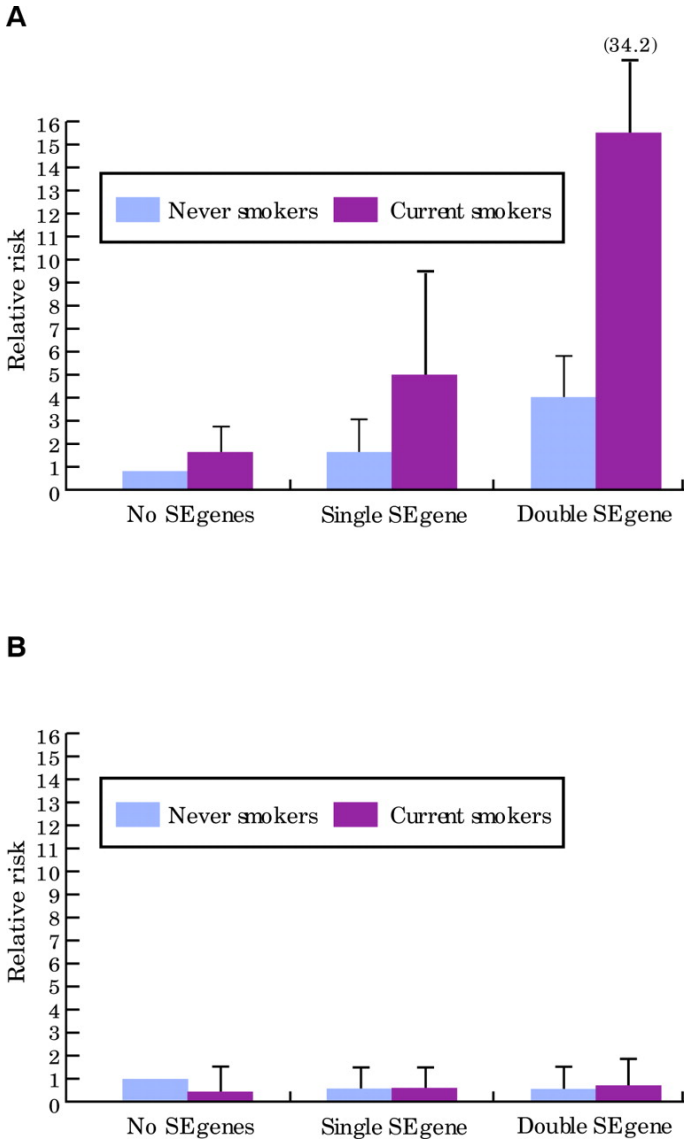
- For other autoimmune diseases, the genetic component is relatively small.

	Identical Twin Concordance
rheumatoid arthritis	0 - 15%
multiple sclerosis	10 - 25%
hyperthyroidism	15 - 20%
type 1 diabetes	15 - 40%
lupus	25 - 35%
systemic sclerosis	4%

- Genetic susceptibility is an important determinant of autoimmune disease - but it's not the only determinant.

Gene-Environment Interaction Rheumatoid Arthritis

Relative risk (RR) for development of rheumatoid arthritis (RA) in current smokers (with different numbers of copies (0–2) of the shared epitope (SE) of HLA-DR) compared with never smokers. (A) RR for seropositive RA and (B) RR for seronegative RA.

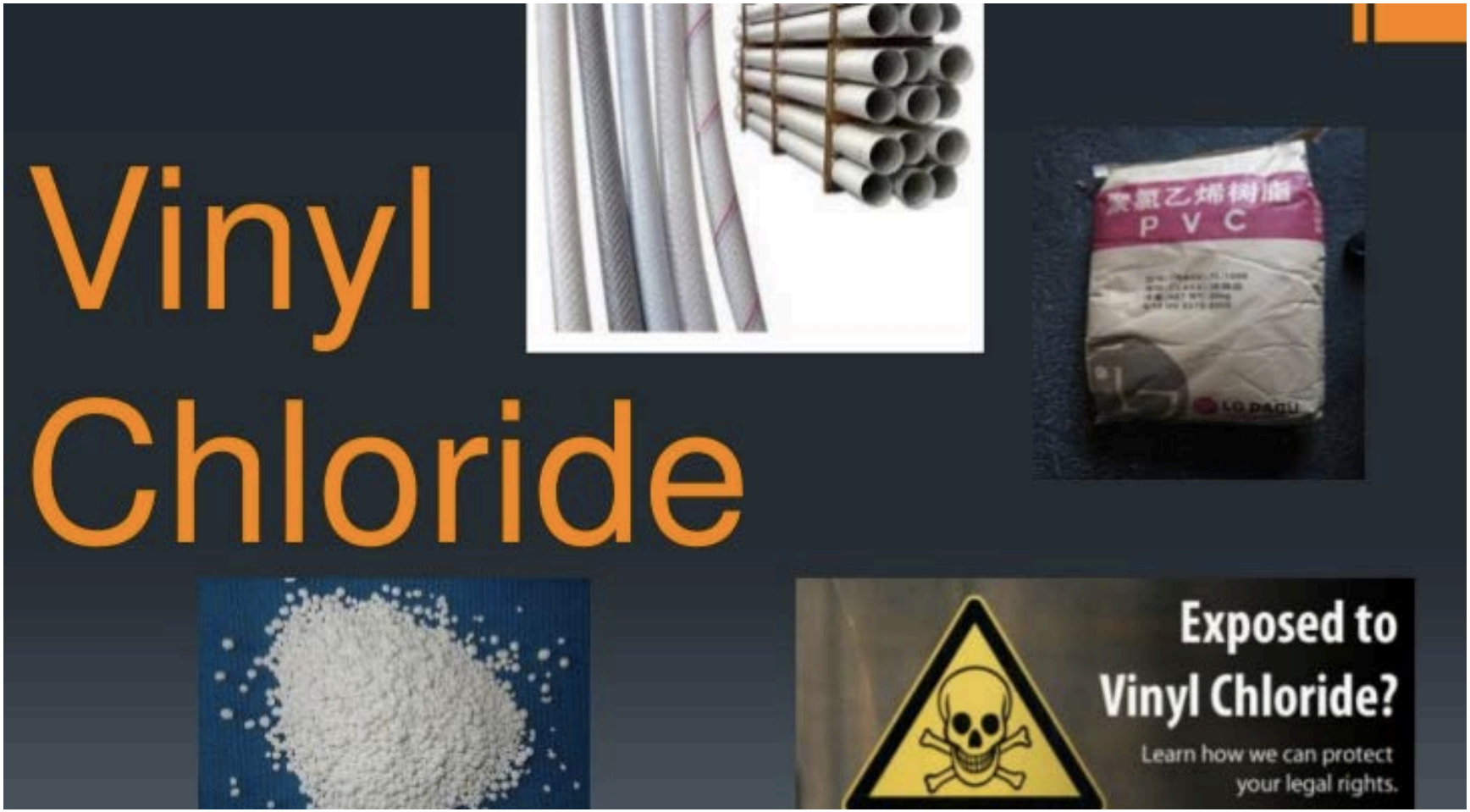


Klareskog L et al. Ann Rheum Dis 2004;63:ii28-ii31

Environmental Exposures and Diseases that Mimic Scleroderma

- Vinyl Chloride Disease
- Toxic Oil Syndrome
- Eosinophilia-Myalgia Syndrome
- Nephrogenic Systemic Fibrosis

Vinyl Chloride Disease



Toxic Oil Syndrome

- Spain, 1981
- Linked to adulterated rapeseed oil sold as “olive oil”
- 20,000 affected
- 1,200 deaths

Eosinophilia-Myalgia Syndrome

- United States, 1989-1990
- L-Tryptophan supplements
- 1,500 cases
- 27 deaths

Nephrogenic Systemic Fibrosis

- Initial report in 2000
- Associated with exposure to Gadolinium as MRI contrast agent in patients with renal impairment

Environmental and Occupational Exposures and Diseases with Features of Scleroderma

- Pulmonary Fibrosis
- Pulmonary Arterial Hypertension
- Raynaud's Phenomenon

Environmental and Occupational Exposures and Diseases with Features of Scleroderma

- Pulmonary Fibrosis
  - Silica dust, asbestos, beryllium
  - Radiation
  - Drugs - Bleomycin, Amiodarone, Nitrofurantoin, Methotrexate, etc.
  - Herbicides

Environmental and Occupational Exposures and Diseases with Features of Scleroderma

- Pulmonary Arterial Hypertension
  - Appetite suppressants
  - Cocaine
  - HIV infection
  - Jamaican bush tea

Environmental and Occupational Exposures and Diseases with Features of Scleroderma

- Raynaud's Phenomenon
  - Hand/Vibration Syndrome
  - Drugs
    - Migraine and ADHD Rx
    - Beta blockers
  - Solvents

Raynaud's Phenomenon in Medical Laboratory Workers Who Work with Solvents

GORDON L. PURDIE, DIANNE J. PURDIE, and ANDREW A. HARRISON

Conclusion. We found that exposure to solvents may be associated with the development of RP, supporting previous work indicating that solvent exposure may be an etiological factor in systemic sclerosis. J Rheumatol 2011;38:1940–6.

Environment and Autoimmune Disease

- Two examples of environmental exposures that may increase the risk for SSc
    - Silica dust
    - Solvents

Association of SSc with Silica Exposure and Silicosis

1914	Scottish stonemasons
1957	S. African gold miners
1967	American coalminers
1985	German coalminers
1995	Italian workers

Silica Exposure and SSc

Compensable Occupational Disease in Some Countries

Interim Report to the Workers' Compensation Board on Scleroderma

Findings and Recommendations

FINDINGS

The Panel finds a probable connection between systemic sclerosis and occupational exposure to silica.

The Panel recommends the following rule:

ELIGIBILITY RULE:

A) Workers suffering from systemic sclerosis [scleroderma] with occupational exposure to silica for a minimum of three years are entitled to compensation

or

B) Claims from workers with less than three years exposure shall be considered on their own merits. Claims from workers who have experienced high intensity exposure to silica shall be given special consideration.

Crystalline Silica (Silicon Dioxide)

- Crystalline silica (quartz) - abundant mineral in sand, rock, clay
- Respirable silica can result in chronic, progressive lung disease (silicosis)
- Traditional “dusty trades” include mining, construction, ceramic manufacturing, pottery; grinding
- Silica serves as an “Adjuvant” - generalized stimulation of immune response
- Silica is different from silicone

Occupational Exposure to Silica Dust

IS OCCUPATIONAL ORGANIC SOLVENT EXPOSURE A RISK FACTOR FOR SCLERODERMA?

PAUL J. NIETERT, SUSAN E. SUTHERLAND, RICHARD M. SILVER, JANARDAN P. PANDEY, REBECCA G. KNAPP, DAVID G. HOEL, and MUSTAFA DOSEMECI

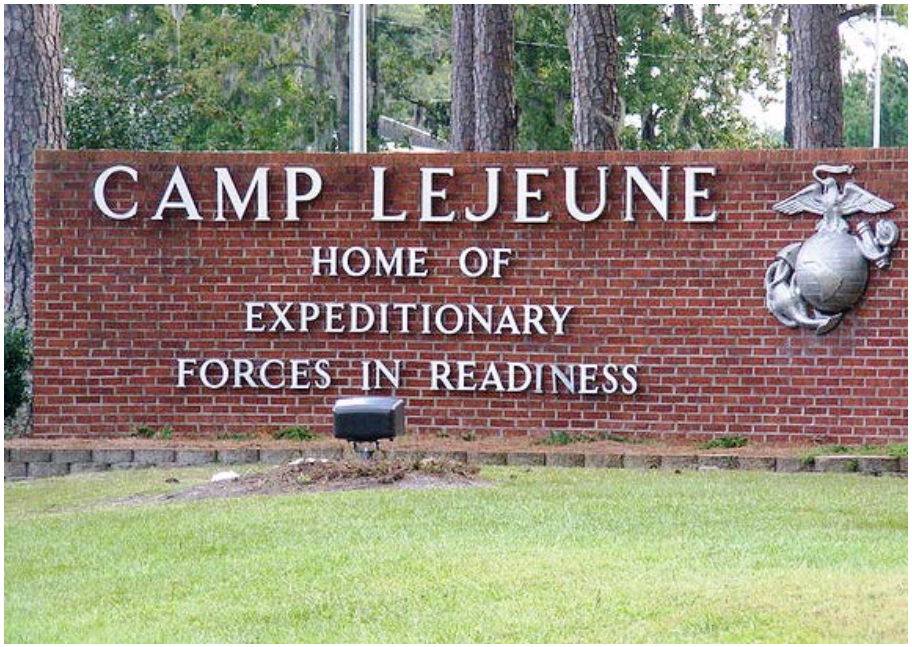
ARTHRITIS & RHEUMATISM
Vol. 41, No. 6, June 1998, pp 1111–1118

Table 4. Exposure to solvents stratified by systemic sclerosis (SSc) subclassification among men only*

Solvent, exposure type	Limited SSc		Diffuse SSc	
	% exposed (n = 18)	OR (95% CI)†	% exposed (n = 19)	OR (95% CI)†
Any				
Max. intensity	50	2.1 (0.7–6.6)	63	3.6 (1.2–11.2)‡
Cum. intensity	61	3.2 (0.9–11.3)	58	2.6 (0.8–8.7)
Max. probability	28	1.3§	32	1.6 (0.5–5.3)
TCE				
Max. intensity	28	3.0§	32	3.7 (1.0–14.2)
Cum. intensity	22	1.2§	42	3.3 (1.0–10.9)‡
Max. probability	11	2.9§	21	7.1§‡
Benzene				
Max. intensity	22	1.8§	32	3.1 (0.9–11.0)
Cum. intensity	33	1.5 (0.4–5.1)	37	1.7 (0.5–5.4)
Max. probability	22	2.0§	26	2.5§
CCl_4				
Max. intensity	6	0.6§	5	0.6§
Cum. intensity	28	1.3§	42	3.0 (0.9–9.8)
Max. probability	6	1.0§	16	3.8§
TCA				
Max. intensity	17	2.2§	21	3.2§
Cum. intensity	22	1.3§	42	3.1 (1.0–10.0)
Max. probability	11	2.9§	11	3.9§

Table 5. Exposure to solvents among systemic sclerosis patients who tested positive for the anti–Scl-70 antibody, stratified by sex*

Solvent, exposure type	Anti–Scl-70 positive women		Anti–Scl-70 positive men	
	% exposed (n = 19)	OR†	% exposed (n = 10)	OR†
Any				
Max. intensity	5	0.9	70	4.6‡
Cum. intensity	21	2.4	70	[illegible]
Max. probability	11	2.5	40	2.0
TCE				
Max. intensity	11	1.8	40	4.8‡
Cum. intensity	26	4.0‡	40	[illegible]
Max. probability	11	2.2	20	5.0
Benzene				
Max. intensity	5	1.3	50	5.8‡
Cum. intensity	16	4.6	50	[illegible]
Max. probability	5	1.9	30	2.6
CCl_4				
Max. intensity	0	–	20	[illegible]
Cum. intensity	5	0.8	60	5.2‡
Max. probability	0	–	0	–
TCA				
Max. intensity	0	–	30	[illegible]
Cum. intensity	11	1.9	60	5.8‡
Max. probability	0	–	0	–

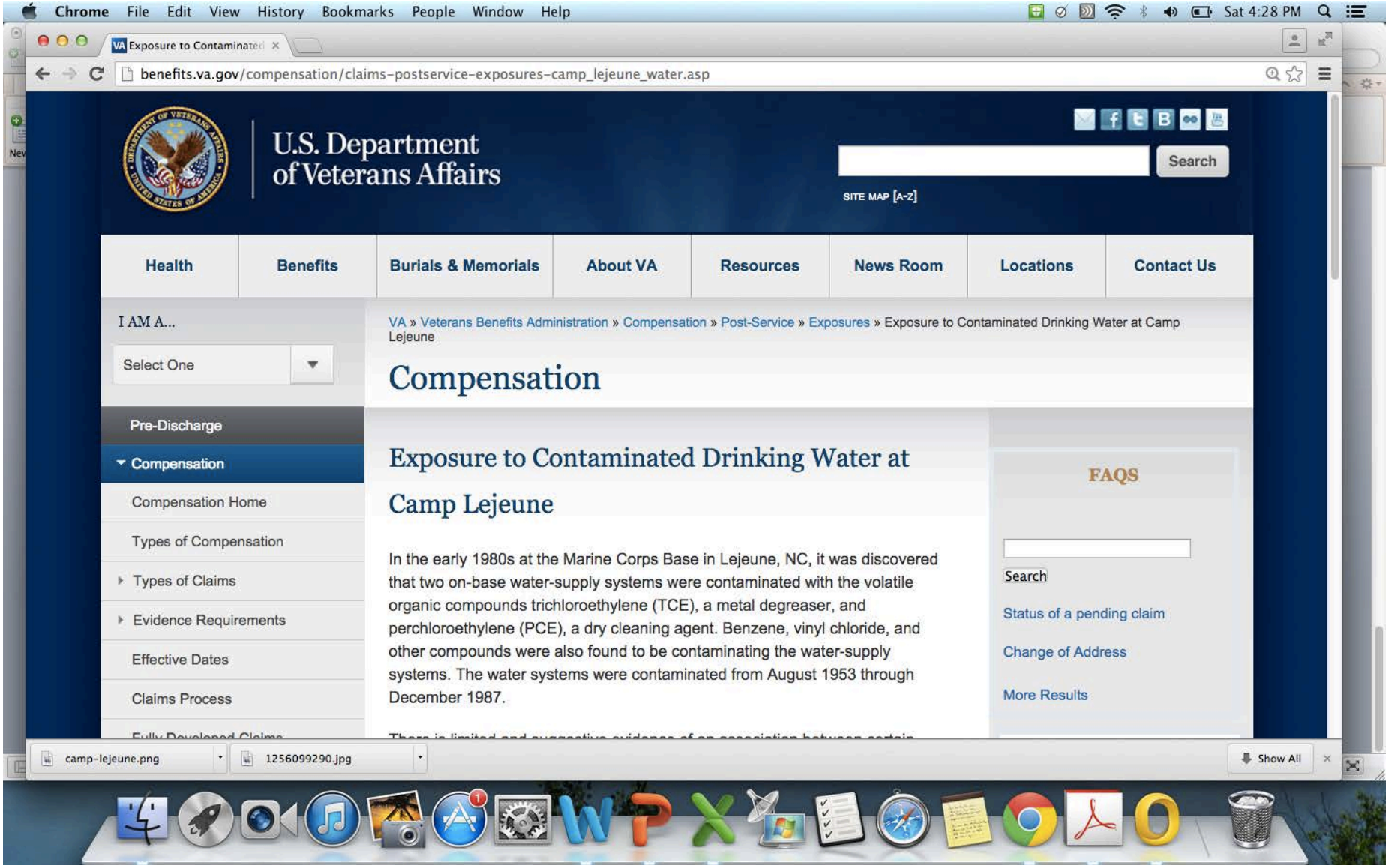


- In early 1980s, 2 water-supply systems found to be contaminated.
- Exposures occurred 1957 - 1985, then the wells were closed.
- Off-base dry-cleaner contaminated groundwater collected by on-base supply wells with PCE.
- Other contaminants included TCE, DCE, benzene, toluene and VC.
- TCE max level in drinking water was 1,400 ppb in May 1982. Current limit for TCE in drinking water is 5 ppb.

Contaminated Water Supplies at Camp Lejeune Assessing Potential Health Effects

- Cancer
  - Esophageal, Lung, Breast, Bladder, Kidney
- Blood Diseases
  - Adult Leukemia, Multiple Myeloma, MDS
- Renal Toxicity
- Hepatic Steatosis
- Female Infertility, Miscarriage
- Neurobehavioral Effects
- **Scleroderma**

Natl Acad Sci's National Research Council, 2009

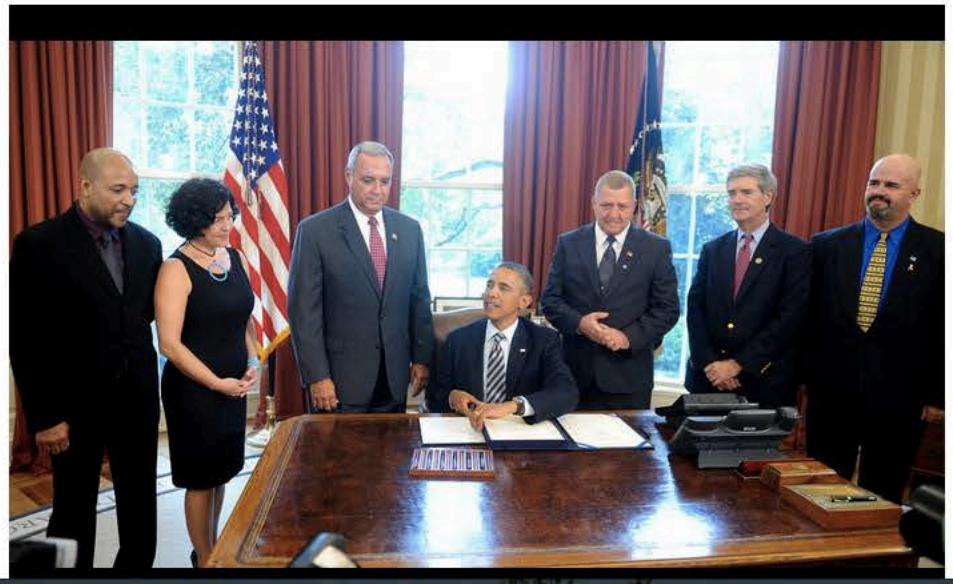

Chrome File Edit View History Bookmarks People Window Help
Sat 4:28 PM
Exposure to Contaminated
benefits.va.gov/compensation/claims-postservice-exposures-camp_lejeune_water.asp
U.S. Department of Veterans Affairs
Search
SITE MAP [A-Z]
Health
Benefits
Burials & Memorials
About VA
Resources
News Room
Locations
Contact Us
I AM A...
Select One
Pre-Discharge
Compensation
Compensation Home
Types of Compensation
Types of Claims
Evidence Requirements
Effective Dates
Claims Process
VA » Veterans Benefits Administration » Compensation » Post-Service » Exposures » Exposure to Contaminated Drinking Water at Camp Lejeune
Compensation
Exposure to Contaminated Drinking Water at Camp Lejeune
In the early 1980s at the Marine Corps Base in Lejeune, NC, it was discovered that two on-base water-supply systems were contaminated with the volatile organic compounds trichloroethylene (TCE), a metal degreaser, and perchloroethylene (PCE), a dry cleaning agent. Benzene, vinyl chloride, and other compounds were also found to be contaminating the water-supply systems. The water systems were contaminated from August 1953 through December 1987.
FAQS
Search
Status of a pending claim
Change of Address
More Results
camp-lejeune.png
1256099290.jpg
Show All

POLITICS & GOVERNMENT AUGUST 6, 2012

Obama signs law giving health care to Lejeune tainted water victims

HIGHLIGHTS

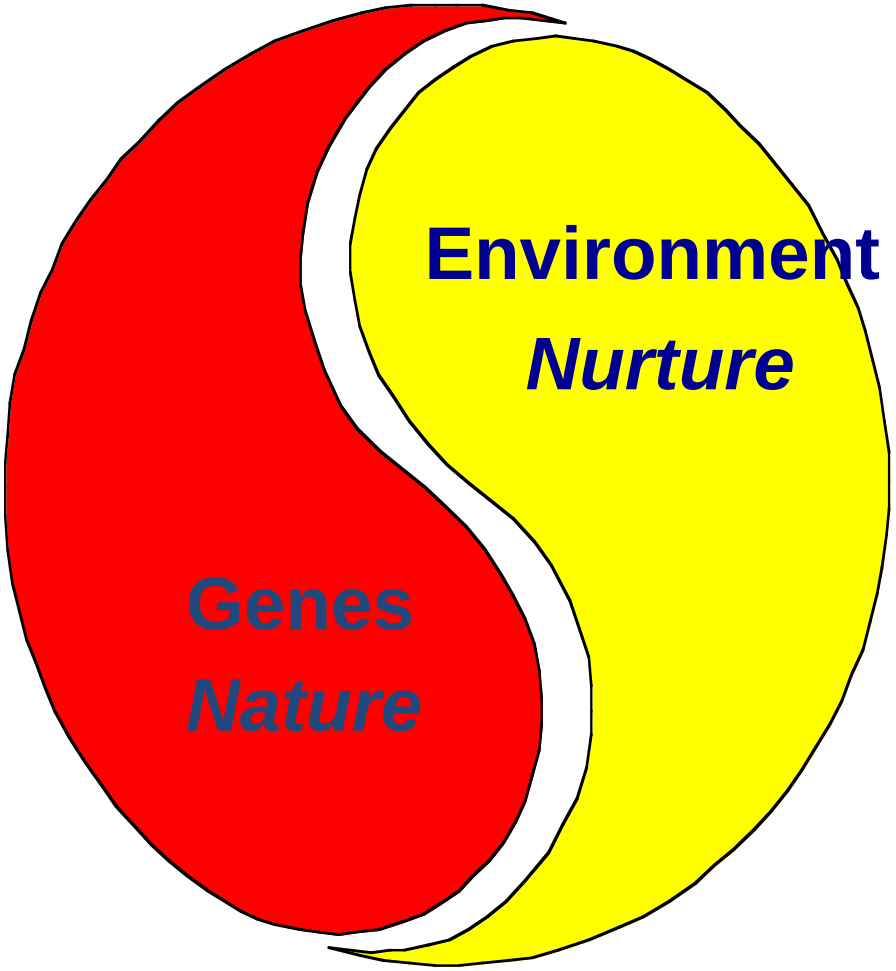
President Barack Obama signed into law on Monday legislation to provide health care to thousands of sick Marine veterans and their families who were exposed to contaminated water at Camp Lejeune.



VIDEOS

about 10 hours ago

Obama is proud of SCOTUS marriage


Environment
Nurture
Genes
Nature