Presentation 13 – Bill Meggs

Environmental Medicine & Gulf War Illnesses: Does the map fit the territory?

Research Advisory Committee on Gulf War Illnesses
July 2007

William Joel Meggs, MD, PhD, FACMT, FACEP
Current Practice: Academic Medical Toxicologist
Does not practice environmental medicine

Case Report

- 32 year old woman
- Presents to medical school allergy clinic
- Referred by her internist
- Opinion requested: use of IV nutrients (especially IV magnesium) to treat asthma
- Huge stack of medical records

Past Medical History

- Severe asthma
  - Multiple hospitalizations
  - Multiple medications
  - Frequent courses of IV and parenteral corticosteroids
- Severe bipolar disorder
  - Multiple psychiatric hospitalizations
  - Treatment with lithium, anti-psychotics, anti-depressants

Family History

- Summarized by patient as “Bad genes.”
- “I will never have children.”

Treatment at Environmental Health Center -- Dallas

- Rotation diet with elimination of many common foods
- Organically grown foods
- Bottled spring water
- Housed in environmental control unit
  - Building materials selected to minimize outgassing
  - Activated charcoal filtered air and bath water

Adjuncts to Food & Chemical Avoidance

- Provocative-neutralization skin testing and antigen injection therapy
- Low flow oxygen using ceramic mask
- Sauna detoxification
- IV nutrients

State of health at clinic visit

- Bipolar disorder in remission
- Asthma in remission
- On no medications
- No hospitalizations or acute visits since treatment at EHCD
- Suffers from food intolerances and chemical sensitivities

Severe limitations on every day life

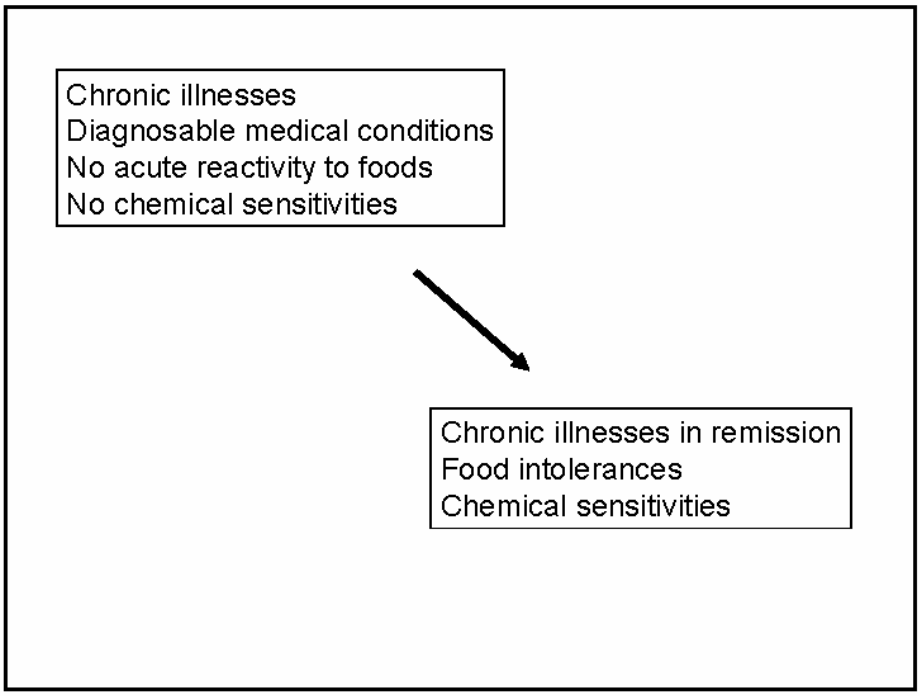
- Social isolation
  - Unable to visit family & friends
  - Unable to attend church
- Unemployed
  - Social security disability
- Spends a great deal of time on health
  - What to eat
  - what to wear
  - where to go, how to travel.

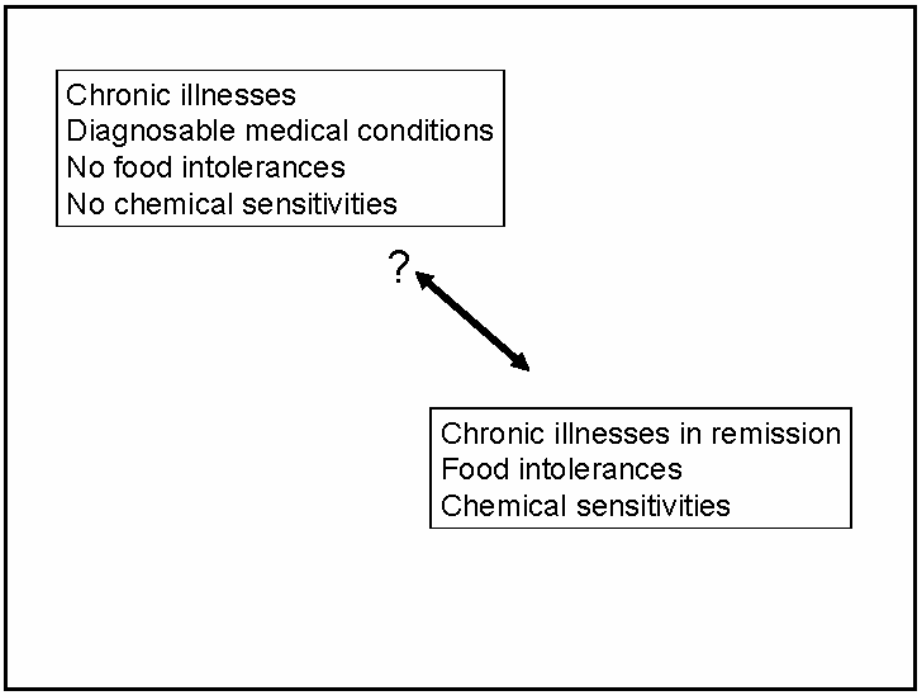
Chemical Avoidance

- Products of combustion
  - Tobacco smoke, diesel and gasoline vehicle exhaust, furnace fumes, gas cook stoves and appliances
- Perfumes and fragrances
- Drinking water contaminants
- Commercial foods, used organic foods only
- Products for Cleaning
- Pesticides
- Paints and other solvents
  - Outgassing of VOCs from fabrics, carpets, etc.

Food Avoidance

- Rotation diet
  - One food per meal
  - Pure foods, no mixtures
  - Only eats a food once each 5 to 7 days
- Monitors reactivity to each food
  - Eliminates any non-tolerated food from rotation
- Organic foods
- Bottled spring water


Chronic illnesses
Diagnosable medical conditions
No acute reactivity to foods
No chemical sensitivities
Chronic illnesses in remission
Food intolerances
Chemical sensitivities


Chronic illnesses
Diagnosable medical conditions
No food intolerances
No chemical sensitivities
?
Chronic illnesses in remission
Food intolerances
Chemical sensitivities

Historical Roots of Environmental Medicine

- Allergists
- American mid-west
- 1930's and 1940's

Early Beginnings

- Food intolerance
- *Masked* food allergy
  - Tolerance of food if ingested daily
  - Period of abstinence followed by re-exposure results in acute reaction
- Cyclical vs. Fixed food allergy
  - REF: *Food Allergy* by Rinkel HJ, Randolph TG, Zeller M. CC Thomas, Springfield IL, 1951. [out of print].

Diagnostic Approach

- Period of avoidance
- Re-exposure
- Monitor for symptoms
- Non-reaginic [not IgE mediated]

Case Report: Dr. HJ Rinkel

- Son of egg farmer
- Impecunious medical student with family
- Father sent gross of eggs each week
- Profuse rhinorrhea
  - Multiple physician visits without help
- Egg was suspected
- Egg avoidance for five days– rhinorrhea resolved
- Ate birthday cake containing egg and had severe reaction

Systemic Manifestations of 'Food Allergy'

- Fatigue
- Headache
- Brain-fag
  - Difficulty with cognition, memory, concentration
- depression, psychosis
- Myalgias
- Arthralgias, arthritis
- Cardiovascular manifestations
  - Fluid retention
  - Tachycardia

Methodology

- Setting: private practice
- Detailed history
- Trial & error
- Abstinence followed by re-exposure
- Carefully record signs & symptoms of illness
- Generalizations from individual cases

Fasting

- Introduced by Dr. Donald Mitchell, Montreal dermatologist & environmental physician
- Hospital practice
- Fast on spring water with sodium and potassium bicarbonate [2:1] until symptoms clear
- Re-expose to foods one by one

Rotation Diet

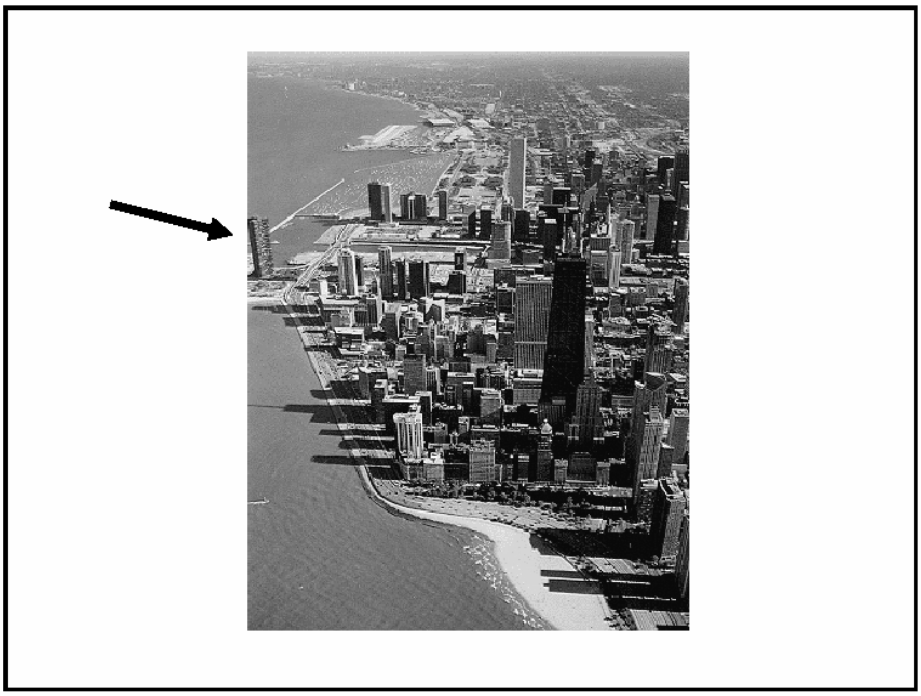
- One food per meal
- Repeat each food every 5 to 7 days
- Monitor for reactions
- Use organically grown, untreated, pure foods
- Eliminate any foods with untoward reactions

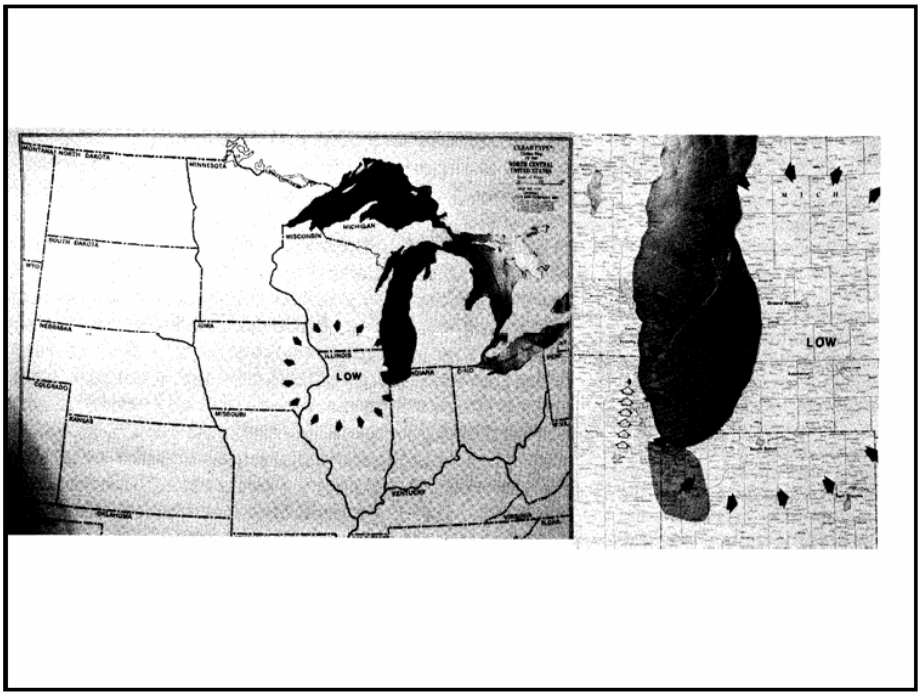
Pesticide Sensitivity

- Patient tested and found allergy to peaches
- Patient reported peaches from abandoned orchard gave no reaction
- Patient found to be intolerant of grocery store peaches but tolerant of peaches from abandoned orchard
- Sulfites, fungicides, insecticides

Sensitivity to 'Air Pollution'

- Allergy to the South Wind
- Industrial area
- Symptoms flare in some individuals when the winds are from the south




LOW
LOW

Gas Appliances

- Burn unvented natural gas in cook stoves, water heaters
- Patients turn off their gas for 5 to 7 days, use a hot plate, toaster oven, electric frying pan, etc., then turn it back on.
- "Shock Reactions" can occur, considered diagnostic
- Homes with gas cook stoves have levels of sulfur dioxide and oxides of nitrogen above levels allowed in factories

Chemical Sensitivity

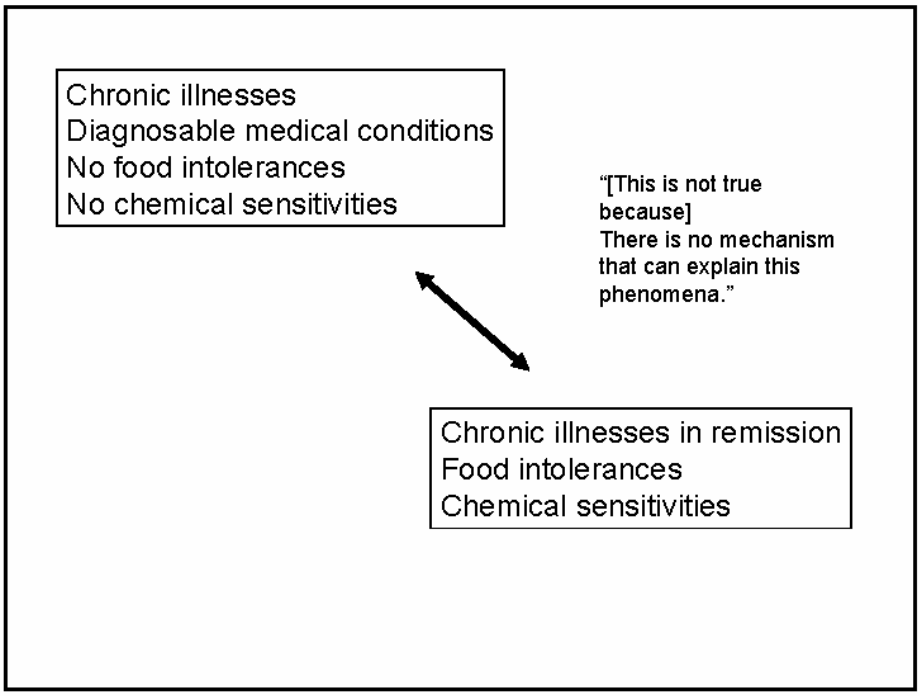
- Individual susceptibility
- Products of combustion
  - Tobacco smoke, vehicle exhaust, furnance fumes, gas appliances
- Perfumes and fragrances
- Products for Cleaning
- Pesticides
- Paints and other solvents
  - Outgassing of VOCs

Exposures said to drive …

- Spreading
  - Sensitivity to increasing numbers of substances
- Progression
  - To include more and more symptoms, more and more organ systems

Induction

- Onset of chemical sensitivity often associated with a single high dose exposure.



Generalized Adapatation Syndrome

- Discovered by Hans Selye, MD
- Injecting impure extracts of ovary and placenta into rats [? new hormone]
- Resulting definitive syndrome
  - Adrenal enlargement
  - Atrophy of lymphatic structures: thymus, spleen, lymph nodes
  - Hemorrhagic ulcers of stomach and duodenum

Puzzling Observation

- No matter what extracts he injected into the rats, he got the same syndrome
  - Liver, kidney, spleen
- He injected rats with formalin and got the same syndrome
- Non-specific toxic reactivity

Selye H. A syndrome produced by diverse noxious agents. 1936.J Neuropsychiatry Clin Neurosci. 1998 Spring;10(2):230-1.
Selye H. *The Stress of Life*. McGraw-Hill. New York 1956

3 stages

- Alarm reaction
- Stage of resistance
- Stage of exhaustion

Generalized Reaction to Stress

- Non-specific
- Diverse noxious agents
- Psychological stress cross reacts with physical stress

Generalized Adaptation Syndrome

Stage I. Preadaptation (Nonadapted)	Shock Reaction (Acute reactivity to chemicals)
Stage II. Addicted (Adapted) IIa. Adapted IIb Maladapted	 Tolerance Chronic Illness
Stage III. Postadapted (Nonadapted)	Exhaustion

Chemical Stress Syndrome.

Stage 0. Normalcy	Tolerance of chemical exposures, wellness without symptoms
Stage 1. –algia	Sensory Hyper-reactivity. Subjective symptoms associated with chemical exposures. (arthralgias, myalgias, etc.)
Stage 2. –itis	Inflammatory reactions to chemicals (arthritis, myositis, etc.)
Stage 3. –osis	Fibrosis. Necrosis. Tissue destruction (arthritic deformities, muscle atrophy and necrosis,etc.)

Organ system involvement in chemical sensitivity

Respiratory	Asthma, Rhinitis, Sinusitis, Pneumonitis
Musculoskeletal	Myositis, Arthritis, Collagen Vascular diseases
Gastrointestinal	Irritable Bowel Syndrome, Inflammatory Bowel Disease
Dermatological	Dermatitis, Rosacea, Cutaneous Vasculitis

Organ system involvement in chemical sensitivity

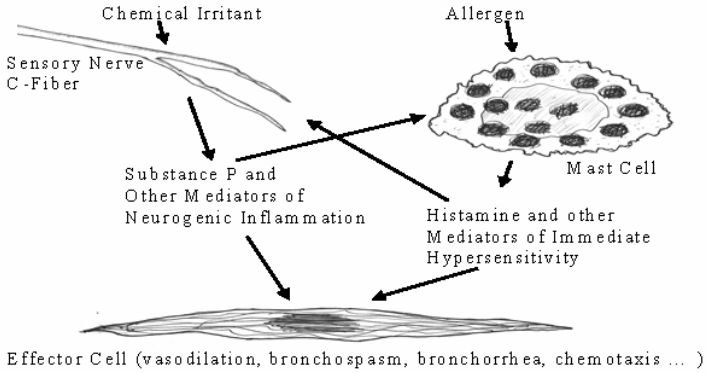
Cardiovascular	Hypertension, Arrhythmias, Vasculitis, Recurrent Anaphylaxis
Neurological	Migraine, Fatigue, Cognitive dysfunction, Seizures, Coma
Psychiatric	Bipolar disorder, Depression, Psychosis

Mechanism of Chemical Sensitivity

- Best studied in the airway
- Airway remodeling
- Pathology of airway is changed in a way that makes one more sensitivity to irritants

Crossover Network

- Nerve fibers have histamine receptors
- (some) Mast cells have substance P receptors

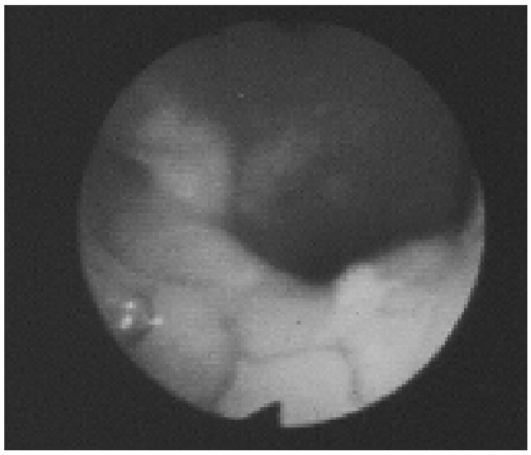


Irritant Rhinosinusitis

- Acquired disorder with onset related to irritant exposures.
- Persistent airway inflammation.
- Exacerbations by irritant exposures that were previously tolerated.
- Burning rather than itching sensation with irritant exposures

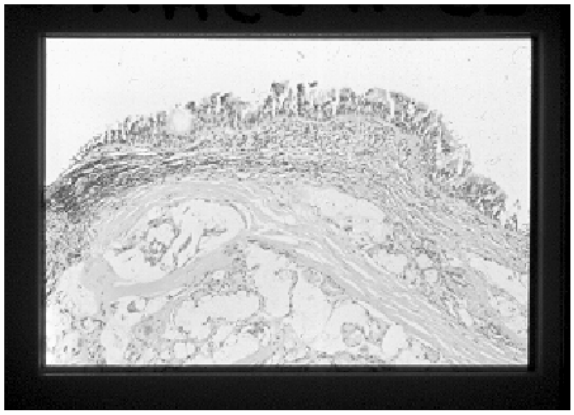
Irritant Rhinosinusitis: Physical Findings

- Edema and hypertrophy of the airways
- Abnormal mucous
  - Thick, white to yellow, crusty exudates
- Nodular hyperplasia
- Hemorrhage
- Injection
  - Posterior pharynx, uvula, soft pallet
- Discoloration
  - Pale yellow to white patches of mucosa with prominent blood vessels



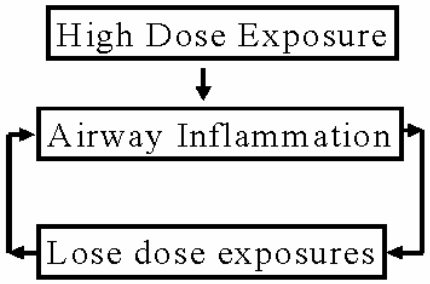
Irritant Rhinosinusitis: Pathological Features

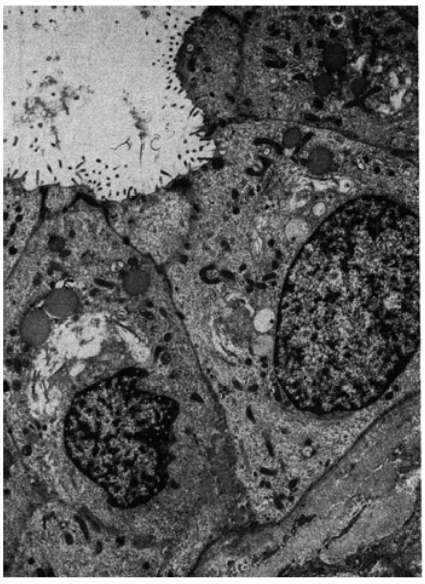
- Chronic inflammation with lymphocytic infiltrates
- Glandular hyperplasia
- Basement membrane thickening
- Nerve fiber proliferation
- Desquamation of the respiratory epithelium
- Defects in tight junctions

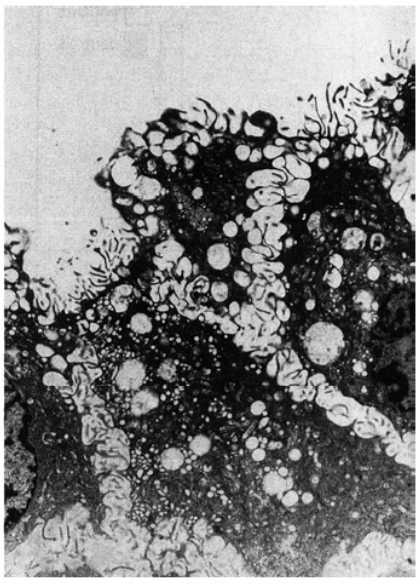


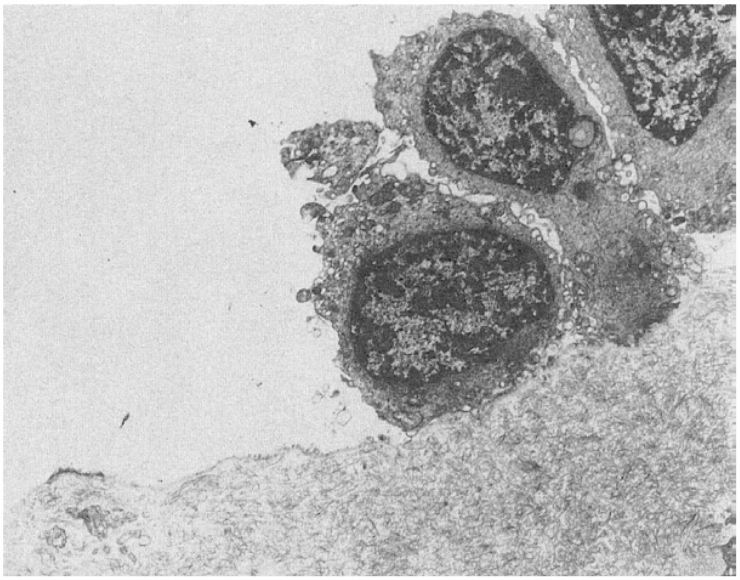
Induction Mechanism

- Positive feed back loop
- Induction exposure produces neurogenic inflammation
- Inflammation produces remodeling
- Remodeled airway more sensitivity to irritants

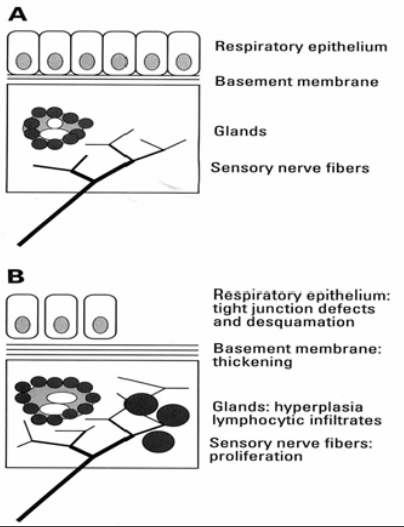


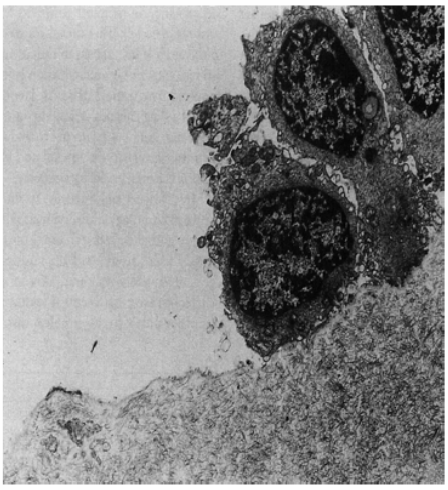




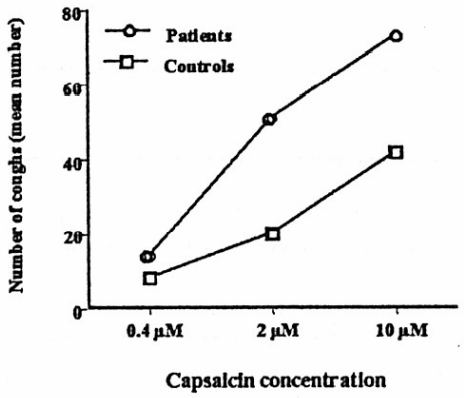


End Organ Sensitization





Millqvist Capsaicin inhalation cough test in patients with "Sensory Hyperreactivity"



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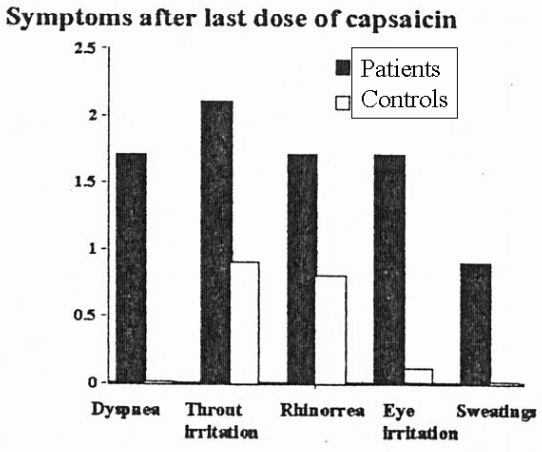
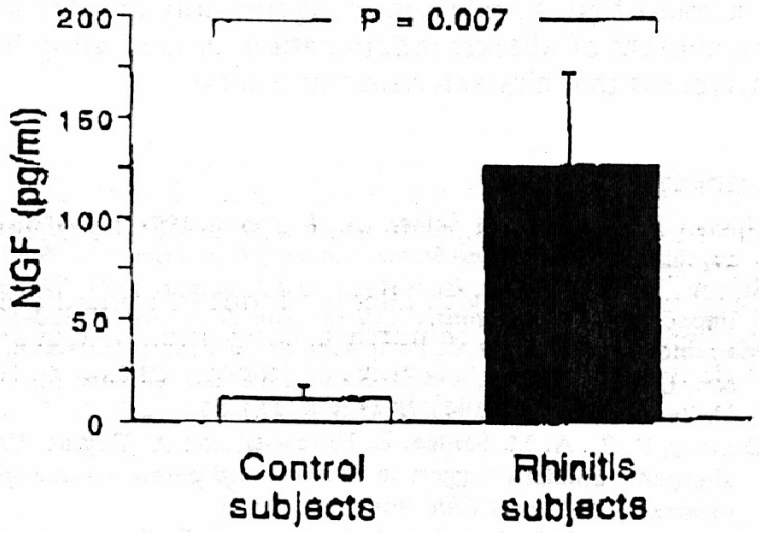




Sanico et al.
Am J Respir Crit Care Med. 2000 May;161(5):1631-5.

Millqvist E et al.

- Changes in levels of nerve growth factor in nasal secretions after capsaicin inhalation in patients with airway symptoms from scents and chemicals.
- Environ Health Perspect. 2005 Jul;113(7):849-5

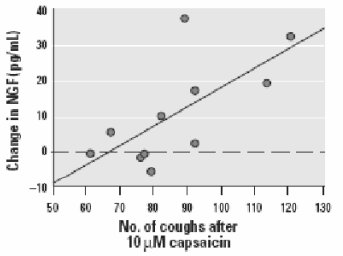


Figure 2. Correlation between change in NGF after provocation with three concentrations of capsaicin and number of coughs after inhalation of the highest dose of capsaicin (10 µM). $r = 0.7$.

Methods

- 13 patients with Sensory Hyper-reactivity and 14 control subjects
- provoked with capsaicin inhalation at three different doses
- Nerve Growth Factor measured in Nasal Lavage Fluid before and after provocation
- cough and capsaicin-induced symptoms recorded

Results

- All subjects demonstrated a dose-dependent cough response to capsaicin inhalation
- more pronounced in patients than in controls.
- Basal levels of NGF were significantly lower in the patient group than in the control subjects ($p < 0.01$).
- After capsaicin provocation, the patients showed a significant increase in NGF ($p < 0.01$)
  - related to capsaicin cough sensitivity

Conclusion

- In patients with airway symptoms induced by scents and chemicals, sensory hyperreactivity is real and measurable, demonstrating a pathophysiology in the airways of these patients compared to healthy subjects.

"Subtle" Neurotoxicity

- Bedside neurological examination is often normal.
- CNS imagining often normal.
- Abnormal results of tests such as heart rate variability & pupillography correlate with other neurological deficits.

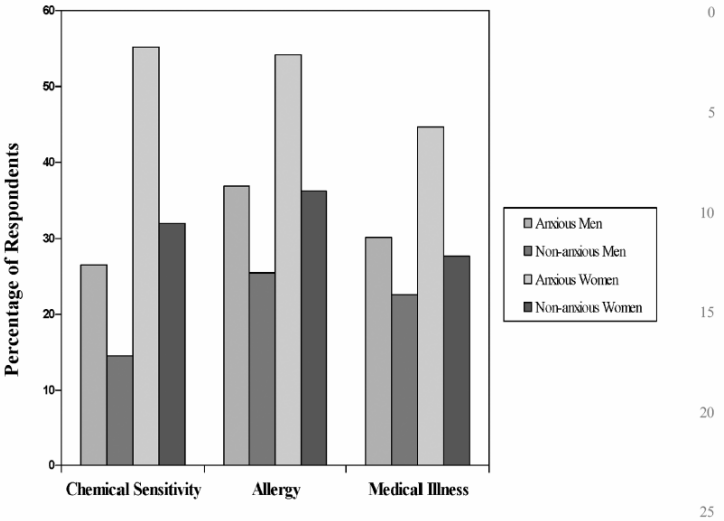
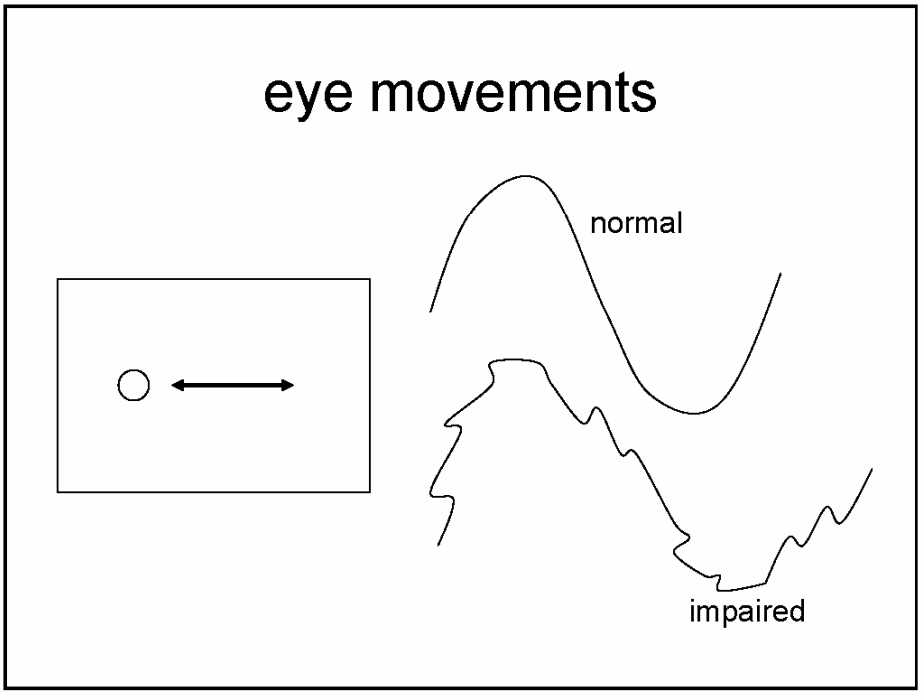


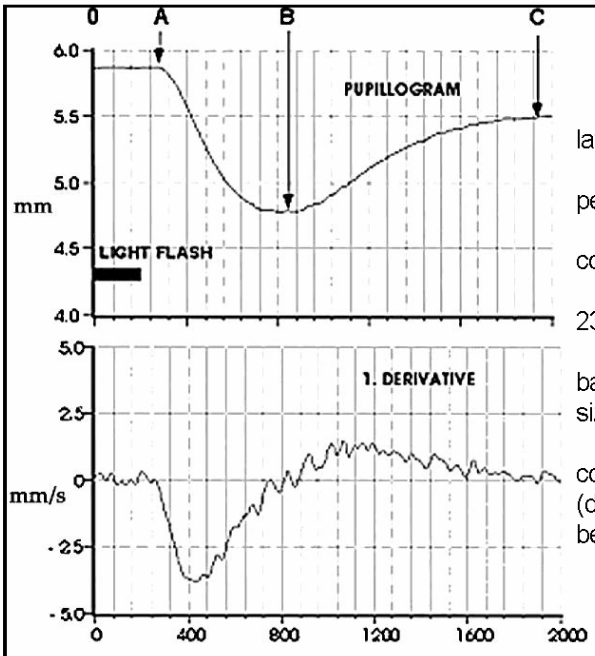
Figure 1. Comparison of gender differences in anxiety relationships with chemical sensitivity, allergy, and mixed medical illnesses.

Comorbidity Patterns of Self-Reported Chemical Sensitivity, Allergy, and Other Medical Illnesses with Anxiety and Depression



Professor S. Ishikawa

- [Former Chair] Department of Ophthalmology, [Former Dean] School of Medicine, Kitasato University, Tokyo, Japan.
- 20+ year study of *subtle* neuro-opthamalogical abnormalities in poisoned individuals [organophosphate pesticides]
- Pupillography – autonomic dysfunction
- Defects in extra-ocular movements



latency time (0 to A)

peak time (0 to B),

constriction time (A to B)

23 redilation time (B to C)

baseline diameter (pupil size between 0 and A)

constriction amplitude (difference in size between A and B).

Classic Study

- 1st study to assess effects of OPs on autonomic nervous system
- Pupillography
- Controlled study
- 20 patients, 18 controls
- Autonomic dysfunction is 18/20 patients (90%)

Shirakawa S. Ishikawa S. Miyata M. Rea WJ. Johnson AR. [A pupillographical study on the presence of organochlorine pesticides in autonomic nerve disturbance]. [Japanese] Nippon Ganka Gakkai Zasshi - Acta Societatis Ophthalmologicae Japonicae. 94(4):418-23, 1990 Apr.

Defects in Pupil Response

- pupil area (p less than .006), velocity of both constriction and dilatation (p less than .001), and dilatation time (p less than .02)
- Sympathetic nerve inhibition i.e. sympatholytic pattern in 10/18 (55%)
- toxicity of the pesticide on the autonomic nerve appear as an inhibitory effect on pupil light reflex.

Shirakawa S. Ishikawa S. Miyata M. Rea WJ. Johnson AR. [A pupillographical study on the presence of organochlorine pesticides in autonomic nerve disturbance]. [Japanese] Nippon Ganka Gakkai Zasshi - Acta Societatis Ophthalmologicae Japonicae. 94(4):418-23, 1990 Apr.

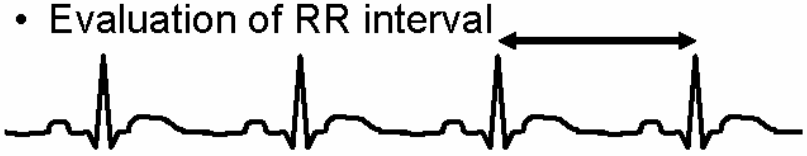
Occupational organophosphate insecticide Exposure

- Abnormal pupillographty in workers with occupational exposure to organophosphate insecticides
- Recommend use of pupillography in detecting poisoning in workers

Filippov VL. Shumakova KM. Tsimbal FA. [Use of pupillometry in the diagnosis of neurologic disorders caused by organophosphorus compound poisoning]. [Russian] Meditsina Truda i Promyshlennaia Ekologiia. (6):11-6, 1997.

Heart Rate Variability

- Measure of integrity of autonomic nervous system
- autonomic nervous system related to cardiovascular disease, cardiac sudden death [30% of population]
- Commercial devices
- Evaluation of RR interval

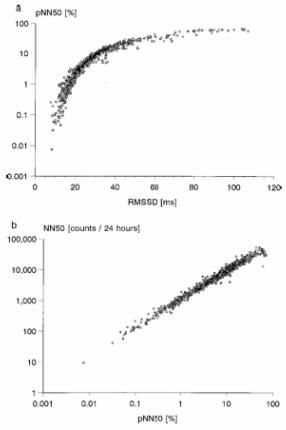


Simple Time Domain Variables

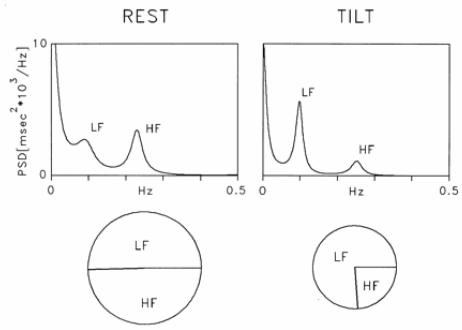
- mean RR interval
- mean heart rate
- difference between the longest and shortest RR interval
- difference between night and day heart rate
- variations in instantaneous heart rate
  - respiration, tilt, Valsalva, phenylephrine, etc.

complex statistical time domain measures

- RR [NN] interval measurements
  - Standard deviation of RR interval = variance
  - Varies with recording period
- Differences in RR intervals



RMSSD = square root of the mean squared differences of successive NN intervals
NN50 = number of interval differences of successive NN intervals > 50 ms
pNN50 = proportion derived by NN50 / total number of NN intervals



Spectral Analysis

Ref: *Circulation*. 1996;93:1043-1065 http://circ.ahajournals.org/cgi/content/full/93/5/1043

LF = low freq component
HF = high freq component
Ratio LF/HF represents balance of parasympathetic/sympathetic

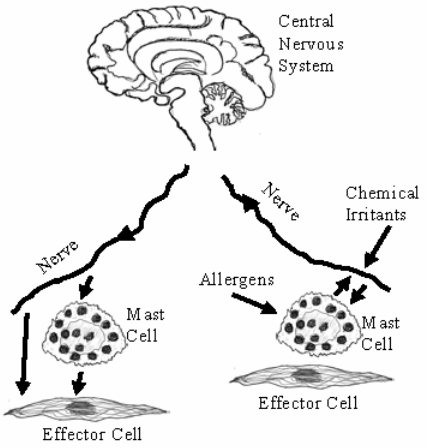
Spectral analysis (autoregressive model, order 12) of RR interval variability in a healthy subject at rest and during 90° head-up tilt. At rest, two major components of similar power are detectable at low and high frequencies. During tilt, the LF component becomes dominant, but as total variance is reduced, the absolute power of LF appears unchanged compared with rest.

Syndromes with Neurotoxicity and Autonomic Dysfunction

- Gulf War Syndrome
- World Trade Center Syndrome
- Solvent neurotoxicity
- Organophosphate toxicity [OPIDN]
- Chronic fatigue syndrome
- Sick building syndrome & so-called 'MCS'

Neurogenic Switching

- The site of inflammation can be switched from the site of stimulation
- Occurs in both allergic and irritant airway inflammation
- May play a role in many disease processes



Gulf War Syndrome

What is Gulf War Illness?

- Significant % of the ~700,000 Gulf War Veterans affected
- Not a symptom based syndrome
- Chronic, multi-system disease
  - Neurological
    - ALS
  - Constitutional
  - Respiratory
  - Gastrointestinal
  - Dermatological
- Correlates with chemical exposures in epidemiological studies
- Prevalence varies with geographic assignments

Chemical Exposures in the Gulf War:

- Nerve gas: Khamasia and other demolitions
- Kuwaiti oil fires
- Organophosphate pesticides
- DEET and pyrethroids
- Diesel fuel, kerosene
- Pyridostigmine bromide
- Anthrax and other vaccines
- Depleted uranium

Treatment

Table 2. Perceived efficacy of 101 treatments tried by 917 persons with MCS.

	Number tried	Very harmful (%)	Somewhat harmful (%)	No noticeable effect (%)	Somewhat helpful (%)	Very helpful (%)	Help:harm ratio[a]
Environmental medicine and oasis techniques							
Chemical avoidance	875	0.5	0.3	4.7	38.0	56.5	110.6
Chemical-free living space	820	0.1	0.5	4.5	38.6	56.2	155.2
P-N for chemicals with preservative	159	22.0	18.1	25.4	27.1	7.3	0.9
P-N for chemicals without preservative	218	11.9	12.8	28.3	31.4	15.5	1.9
P-N without glycerin or preservative	178	12.5	8.3	25.0	30.2	24.0	2.6
Sauna at clinic	151	7.1	7.7	20.6	30.3	34.2	4.4
Sauna at home	245	7.1	11.4	19.6	38.8	23.1	3.4
Rotation diet	560	1.6	4.1	22.1	44.0	28.2	12.7
Air filter (to prevent exposure)	786	1.8	4.2	11.8	47.5	34.6	13.7
Charcoal mask	588	4.5	8.3	9.8	55.1	22.3	6.0
Aluminum foil to seal off-gassing	253	5.6	5.3	14.7	35.7	38.7	6.8
Personal oxygen to cope with exposures	326	2.9	4.4	14.2	39.8	38.6	10.6
Individual nutritional supplements							
Intravenous magnesium	175	4.2	6.8	25.5	40.6	22.9	5.8
Buffered vitamin C powder	516	4.0	8.8	29.4	37.3	20.5	4.5
Other vitamin C	663	2.8	6.7	28.8	35.3	16.4	5.5
Vitamin E supplements	708	2.1	5.1	53.1	29.3	10.3	5.4
Coenzyme Q10	517	2.5	5.8	51.4	28.8	11.5	4.9
Magnesium supplements	644	2.3	3.8	41.4	34.4	18.0	8.6
Calcium supplements	663	2.6	5.2	56.8	25.0	10.6	4.6
Chromium supplements	399	3.8	4.5	57.8	22.2	11.8	4.1
Other mineral supplements	666	2.0	5.7	43.4	35.0	13.8	6.4
Grapefruit seed extract	325	7.7	11.6	43.3	27.6	9.8	1.9
Echinacea	515	5.6	11.8	48.6	23.0	11.0	2.0
Goldenseal	298	5.8	13.5	49.4	21.5	10.9	1.7
Siberian ginseng	283	5.9	15.0	48.3	26.2	4.5	1.5
Milk thistle seed	458	3.2	6.5	41.6	33.6	15.1	5.0
Garlic	555	5.2	10.2	46.5	25.9	12.2	2.5
Acidophilus	661	0.9	3.2	44.0	32.8	19.2	12.7
DHEA	352	8.2	15.1	49.4	20.7	9.5	1.3
Thyroid supplements	406	3.8	8.4	39.8	28.1	19.9	3.9
Holistic therapies							
Homeopathy with homeopathic doctor	401	4.9	9.1	32.6	33.8	19.5	3.8
Over-the-counter homeopathy	425	4.0	6.8	36.6	40.1	12.6	4.9
Bach flower remedies	236	2.5	6.6	50.2	29.6	11.1	4.5
Acupuncture	422	3.9	6.3	36.0	32.5	21.3	5.3
Herbal medicines	650	4.2	7.6	24.5	41.8	22.0	5.5
Macrobiotic diet	182	13.5	15.1	24.0	33.3	14.1	1.7
Juicing	315	4.4	8.8	42.0	31.7	13.6	3.4
Aromatherapy	127	19.8	20.6	19.1	30.5	9.9	1.0
Chelation	131	11.0	13.2	27.2	31.6	16.9	2.0
Neural therapy	56	10.7	10.7	28.0	36.0	14.7	2.4
Detoxification							
Remove mercury dental fillings	425	3.1	6.1	47.1	27.3	16.5	4.8
Hulda Regehr Clark's parasite program	87	18.7	9.3	36.4	27.1	8.4	1.3
Coffee enemas	146	5.4	14.3	32.0	32.7	15.6	2.5
Colonics	222	4.8	8.4	28.2	38.3	20.3	4.4
Liver flushes	146	9.6	9.6	25.5	35.7	19.7	2.9
Gallbladder flushes	95	3.8	9.5	33.3	36.2	17.1	4.0
UltraClear	232	8.7	27.0	30.3	22.8	11.2	1.0
Hydrogen peroxide therapy	123	17.4	13.7	40.3	15.3	13.9	1.0
Eastern origin techniques							
Meditation	423	0.7	2.1	43.3	41.2	12.6	19.2
Yoga asans (postures)	260	3.0	5.9	41.9	37.4	11.9	5.5
Tai chi	154	3.2	9.0	54.5	21.8	11.5	2.7
Qi gong	109	3.3	6.5	40.7	38.6	13.0	5.1

Continued, next page

Table 2. Continued.

	Number tried	Very harmful (%)	Somewhat harmful (%)	No noticeable effect (%)	Somewhat helpful (%)	Very helpful (%)	Help:harm ratio[a]
Body therapies							
Traditional chiropractic	486	2.2	6.1	47.4	31.8	12.5	5.3
Chiropractic with applied kinesiology	270	3.2	3.6	41.7	35.6	15.8	7.5
Network chiropractic	63	11.6	15.1	36.0	23.3	14.0	1.4
Chiropractic with contact reflex analysis	57	18.8	5.7	32.9	28.6	14.3	1.8
Bast chiropractic	29	7.1	14.3	38.1	23.8	16.7	1.9
Applied kinesiology without chiropractic	191	7.1	5.6	32.0	34.0	21.3	4.4
Alexander technique	38	4.9	4.9	68.3	12.5	2.4	2.3
Trager	31	7.1	14.3	50.0	23.8	4.8	1.3
Reiki	170	2.7	4.8	44.6	34.4	13.4	6.4
Acupressure	308	1.0	3.5	28.3	46.0	21.2	14.9
Massage	501	0.8	7.9	32.5	39.4	19.4	6.8
Touch for health	75	2.5	1.3	41.8	35.4	19.0	14.3
Polarity balancing	117	3.3	4.9	45.9	29.5	16.4	5.6
Reflexology	204	2.4	2.4	38.5	43.4	13.2	11.6
Rolfing	60	7.8	14.1	35.9	26.6	15.6	1.9
Osteopathic adjustment	171	5.0	5.5	44.2	30.4	14.9	4.3
Craniosacral work	270	4.0	2.6	36.6	36.6	20.1	8.6
Total body modification	42	8.6	6.9	29.3	36.2	18.0	3.6
Newer therapies							
Mycrohydrin	57	10.8	15.4	53.8	10.8	9.2	0.8
Oxygen therapy	182	5.6	5.1	20.3	44.1	24.9	6.4
Eye movement desensitization and reprocessing	64	15.8	7.9	51.3	17.1	7.9	1.1
Neurolinguistic programming	37	8.8	2.9	64.7	17.6	5.9	2.0
Prescription items							
Nizoral	153	16	17.8	25.2	31.3	9.8	1.2
Nystatin	402	7.9	14.5	33.2	31.9	12.5	2.0
Diflucan	249	9.9	14.5	28.9	31.4	15.3	1.9
Prozac	183	37.6	21.5	25.8	9.7	5.4	0.3
Zoloft	148	45.5	22.7	23.4	5.8	2.6	0.1
Elavil	149	33.9	23.6	27.3	9.7	5.5	0.3
Other antidepressants	306	32.4	17.6	27.2	17.6	5.1	0.5
Neurontin	100	19.6	15.7	24.5	24.5	15.7	1.1
Other antiseizure medicine	76	37.6	12.9	24.7	16.5	8.2	0.5
Antibiotic therapy for *Mycoplasma fermentans*	38	17.4	13.0	21.7	21.7	26.1	1.6
Acyclovir (Zovirax)	88	19.8	13.6	40.7	18.5	7.4	0.8
Transfer factor	64	13.2	13.2	26.5	30.9	16.2	1.8
Valium	125	23.1	21.6	34.3	17.2	3.7	0.5
Xanax	134	25.0	20.8	27.8	19.4	6.9	0.6
Glutathione in nasal spray	54	16.2	17.6	35.3	25.0	5.9	0.9
Glutathione in nebulizer	33	18.0	10.0	22.0	26.0	24.0	1.8
Other							
Changed residence	513	2.9	4.5	6.0	42.3	44.3	11.7
Enzyme potentiated desensitization	61	19.1	10.3	17.6	20.6	32.4	1.8
Nambudripad desensitization	207	3.8	3.8	38.6	31.0	22.9	7.1
Magnets	265	11.1	9.0	48.4	20.4	11.1	1.6
Prayer	609	0.7	0.7	34.4	35.6	28.6	48.3
Faith healer	127	3.1	1.6	51.6	25.8	18.0	9.3
Exercise	783	4.3	10.4	23.7	40.3	21.3	4.2
Hypnosis	111	7.1	6.3	60.3	16.7	9.5	1.9
Psychotherapy to cure MCS	200	6.6	8.0	65.3	15.5	4.7	1.4
Psychotherapy to cope with MCS	382	3.8	7.0	24.1	47.7	17.3	6.0
Support group	520	1.5	7.2	15.5	42.3	33.6	8.7

[a]Ratio of number reporting help to persons reporting harm.

Chemical Avoidance

Very harmful	0.5%
Somewhat harmful	0.3%
No effect	4.7%
Somewhat helpful	38%
Very helpful	56.5%

Gibson PR et al. Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity. Environ Health Perspect. 2003 Sep;111(12):1498-504.

Rotation Diet

Very harmful	1.6
Somewhat harmful	4.1%
No effect	22.1%
Somewhat helpful	44%
Very helpful	28.2%

Environmental Control Unit

- Developed in 1950's, USA
- A hospital unit to isolate patients, de-adapt them from their environment, and reintroduce agents one-by-one
- Attention to air, water, food
- All Hospital based Environmental Control Units in this country have been shut down
  - Germany, Japan

Environmental Control Unit Protocol

- Highly Individualized
- Day One
  - Admitted to unit
  - History and physical examination with extensive environmental, dietary, and occupational history.
  - Routine laboratory testing was performed.
  - No inhalants on the unit

Environmental Control Unit Protocol

- Stage 1: Approximately 5 to 7 days
- Fasting stage
  - Patients fasted on distilled spring water
  - Monitored for withdrawal symptoms: headache, nausea, vomiting, myalgias, arthralgias, etc.
  - Alkaline salts: 2:1 NaHCO2:KHCO2
  - Monitored for electrolyte abnormalities, dehydration: Rehydrate with IV, glass bottles
  - Fast terminated when withdrawal symptoms end

Environmental Control Unit Protocol

- Stage 2: Approximately 10 to 20 days
- Food testing to establish a safe diet
- 'Suspected Safe' Foods eaten on rotation
- Each meal consisted of single organically grown pure food
- Monitor for adverse reactions

Environmental Control Unit Protocol

- Stage 3: Approximately 7 days
- Food testing to test highly suspect foods, pesticides, additives
- Patients continue their safe diet on 5 to 7 day rotation
- Highly suspect foods and contaminated foods introduced as single feedings, one by one

Environmental Control Unit Protocol

- Stage 4: Approximately 7 days
- Chemical testing
- Highly individualized
- Challenge testing to natural gas, vehicle exhaust, items from home

Environmental Control Unit Protocol

- Stage 5: Discharge
- Patients have been taught to evaluate reactions and avoid those things that make them sick
- Patients instructed to continue rotation diet of safe foods
- Patients instructed to modify home and work environment, automobile, etc.

Residence Inn Dallas Central Expressway
10333 North Central Expressway
Dallas, Texas 75231 USA
Phone: 1-214-750-8220
Fax: 1-214-750-8244
Sales: 1-214-622-1010
Sales fax: 1-214-750-8244

Sauna

	At clinic	At home
Very harmful	7.1	7.1
Somewhat harmful	7.7	11.4
No effect	20.6	19.6
Somewhat helpful	30.3	38.8
Very helpful	34.2	23.1

pharmaceuticals

	Prozac	Zoloft	Elavil	Valium	Xanax
Very harmful	37.8	45.5	33.9	32.4	19.6
Somewhat harmful	21.5	22.7	23.6	17.9	15.7
No effect	25.9	23.4	27.3	27.2	24.5
Somewhat helpful	9.7	5.8	9.7	17.6	24.5
Very helpful	5.4	2.6	5.5	5.1	15.7

Provocative-neutralization

- Skin testing with allergens and chemicals
- Serial dilutions
- Monitor response
  - Wheal & flare
  - symptoms
- Neutralization dose is one dose before the dose that produces wheal & flare [skin reactivity] or dose that ablates symptoms

Provocative-Neutralization

	With preservatives	Without preservatives	Without glycerine or preservatives
Very harmful	22	11.9	12.5
Somewhat harmful	18.1	12.8	8.3
No effect	25.4	29.3	25
Somewhat helpful	27.1	31.4	30.2
Very helpful	7.3	15.5	24

Provocative-Neutralization: Baylor ENT Study

- 37 patients, 5 foods
- Comparison of IPFT SK and IPFT PR with oral food tests
- Double-blinded, 3 tests 7 days apart
- validity coefficients, 0.78 & 0.61, $p < 0.01$
- Reliability coefficients, 0.68 and 0.40, $p < 0.05$

King WP et al. Provocation-neutralization: a two-part study. Part I. The intracutaneous provocative food test: a multi-center comparison study. Otolaryngol Head Neck Surg. 1988 Sep;99(3):263-71

Provocative-Neutralization: Nova Scotia Study

- 13 foods, 9 chemicals, and 4 placebos
- 132 people, double-blind, randomized study
- Reaction by ***symptoms*** to foods, chemicals, and normal saline solution showed a random pattern, although wheal reactions showed a distinct pattern.

Fox RA et al. Intradermal testing for food and chemical sensitivities: a double-blind controlled study. J Allergy Clin Immunol. 1999 May;103(5 Pt 1):907-11.

Nutrients

- Rational: co-factors for detoxification, nutrient elimination
- Well accepted adjuncts for certain acute poisonings
  - Folate for methanol poisoning
- Extensively used in alternative and Complementary Medicine practice

Nutrients

- Given both IV and PO
- Relatively safe
- Testable by double-blinded, placebo controlled challenge

Insecticides & chemical sensitivities

- Agricultural workers with acute organophosphate insecticide poisoning
- Intolerance of previously tolerated agricultural and other chemicals.

Tabershaw IR, Cooper WC. Sequelae of acute organic phosphate poisoning. J Occup Med. 1966 Jan;8(1):5-20.

Insecticides & chemical sensitivities

- 125 people
- Well-documented exposure to cholinesterase inhibitor or remodeling
- Developed chemical sensitivities
- Sx severity > in insecticide group
- Employment: 81% to 12.5%

Miller CS, Mitzel HC. Chemical sensitivity attributed to pesticide exposure versus remodeling.
Arch Environ Health. 1995 Mar-Apr;50(2):119-29.

Plasma Levels of substance P, VIP, NGF

- Controlled study
- Three groups
  - MCS
  - Atopic eczema/dermatitis
  - Normal control group
- Measurements at baseline and after chemical challenge
  - Oil based paint

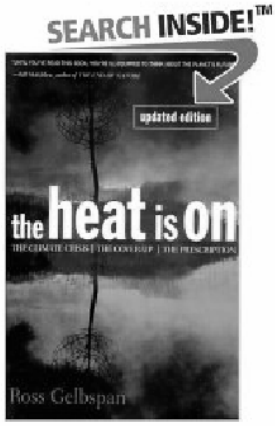
REF: Kimata H. Effect of exposure to VOCs on plastma lefvels of neuropeptides, NGF & histamine in patients with self-reported chemical sensitivity.
Int J Hyg Enviro Health 2004;207:159-163.

Results

- Baseline plasma levels of SP, VIP, NGF, but not histamine were elevated in MCS group but not other groups.
- VOC exposure increased plasma SP, VIP, NGF in MCS pts but not other two groups.
- Exposure to VOCs increased skin wheal response to histamine in MCS but not other two groups.

Suppression of Environmental Medicine in the USA

- Small group of physicians
- Close ties to commercial interests
- Anecdotal, no scientific evidence
  - Absence of evidence is not evidence of absence
  - There is evidence
- Argumentum *ad hominem* – attack the person, not the argument.



Suppression of Environmental Medicine in the USA

- Position statements: pts are crazy & doctors are quacks
  - AMA, AAAAI, California Medical Society
- Industry funded conferences
  - After National Research Council Conference recommended federal funding of ECU
- Lobbied insurance companies to deny payment
- Physicians lost their licenses
- Network TV shows roasting physicians & patients

Recommendations from US Federal Advisory Groups

- NAS sub-committee on Immunotoxicology, Washington, DC, 1991
- NRC Workshop on Multiple Chemical Sensitivity, Irvine, 1991
- Expert Panel on Multiple Chemical Sensitivity, ATSDR, 1993
- Exp Approaches to Chemical Sensitivity, EOSI & NIEHS, Rugers, 1995
- CDC Gulf War Syndrome Meeting, Atlanta, 1999
- ? Research Advisory Committee on Gulf War Illnesses

Environmental Medicine
&
Gulf War Illnesses:
Does the map fit the territory?

Environmental Medicine
&
Gulf War Illnesses:
Does the map fit the territory?

yes

Gulf War Illnesses & Chemical Sensitivities: Similarities

- Onset with exposure to *diverse noxious agents*
- Similar or same Multi-organ system complaints
  - Neurocognitive, Fatigue, etc
- Poor response to pharmaceutical therapies
- Persistence
- Association with organophosphate exposures
- Autonomic dysfunction

Research Suggestions

- Controlled study of plasma levels of Substance P, nerve growth factor, VIP
- Clinical trial of substance P antagonists
  - Aprepitant, Emend®
- Environmental control unit
  - ? Collaboration with EHC-D
- Upper airway evaluations
  - Characteristic findings, nasal washings for NGF, …