Indoor air pollution hits EPA too close to home

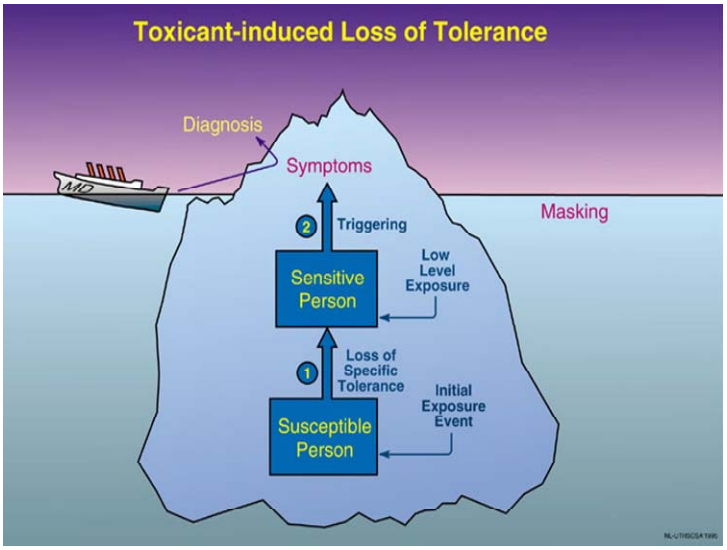
By Aaron Epstein
Knight-Ridder News Service

Washington – The pollution experts at the Environmental Protection Agency should know a sick building when they see it. They work in one.

Yet, despite all their expertise and expenditures, they have not yet found a cure.

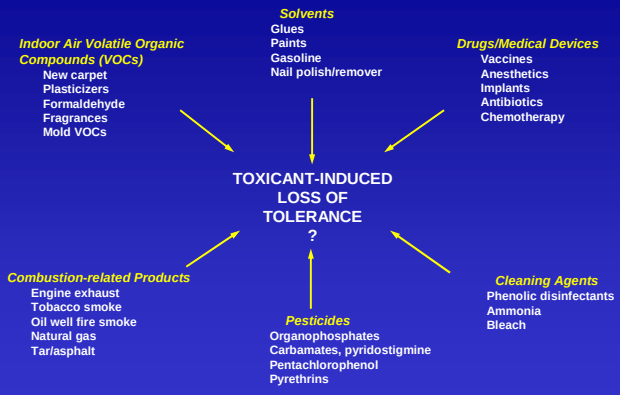
tified. "The EPA won't publicly say so, but we definitely have Sick Building Syndrome right here."

Sick Building Syndrome, or SBS, is an unscientific term used to describe a pattern of health symptoms linked to poor indoor air quality in workplaces, schools, homes and other buildings – but difficult to trace to any particular source. It is believed to be the cause

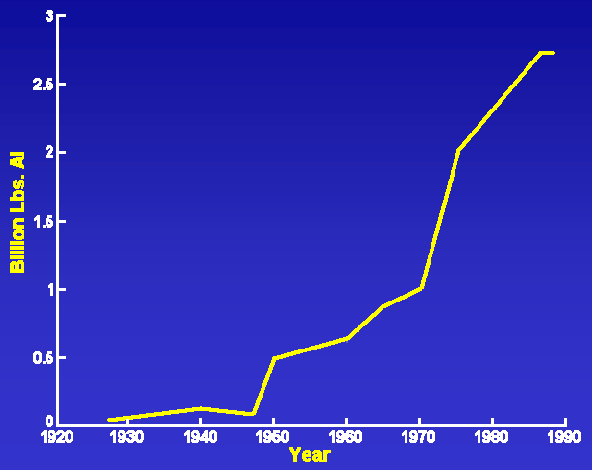


Evidence for Toxicant-induced Loss of Tolerance

- **Similar reports in different regions/countries**
- **Complaints of new intolerances for foods, alcoholic drinks, caffeine, and medications, *not only* chemicals**
- **Resemblance to addiction**
- **Plausible anatomic locus**
- **Recent animal models**

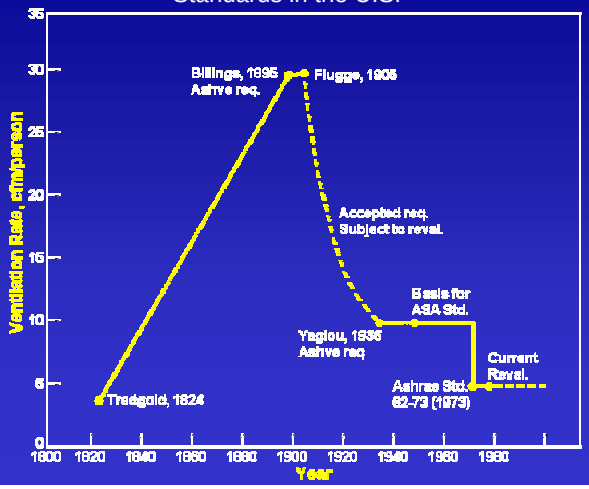


U.S. Pesticide Production, All types, 1927-1988

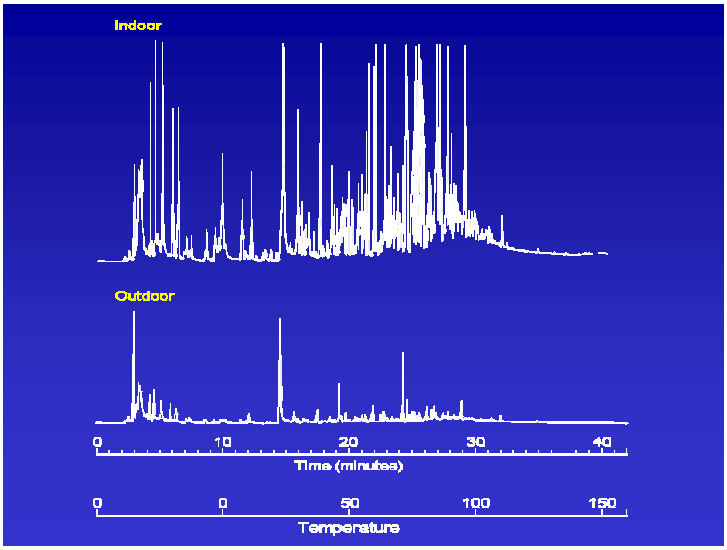


Source: EPA Market Estimates, 1986, 1988; Pimentel & Andow, 1984; Metcalf, 1980.

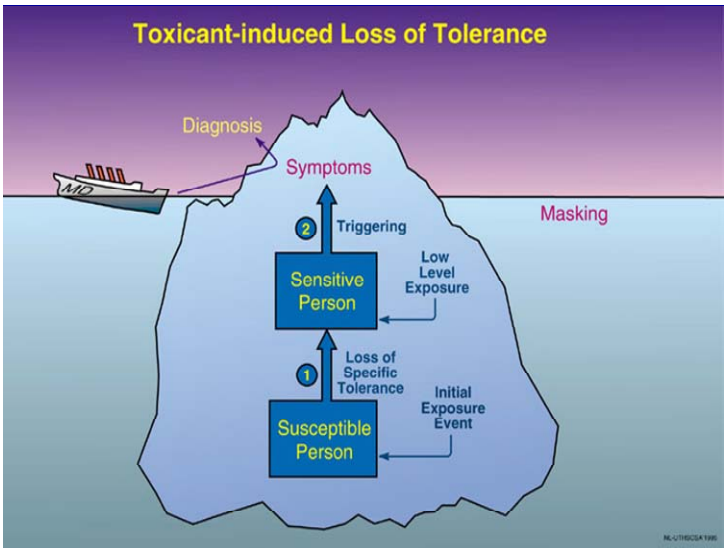
Historical Development of Ventilation Standards in the U.S.

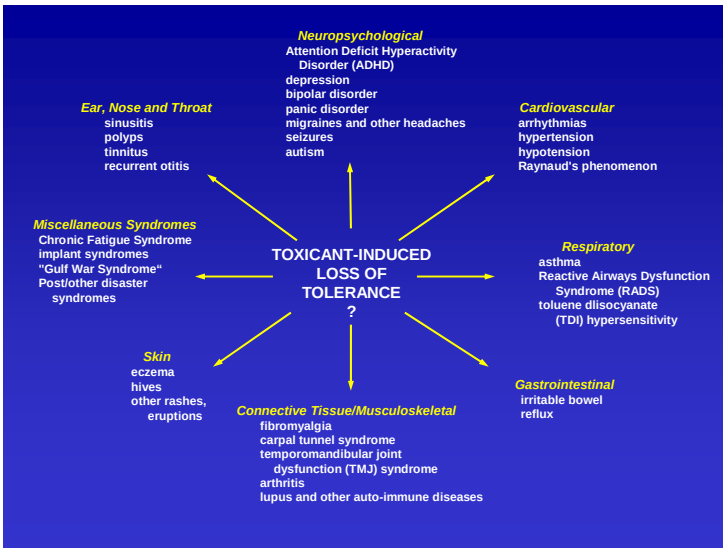


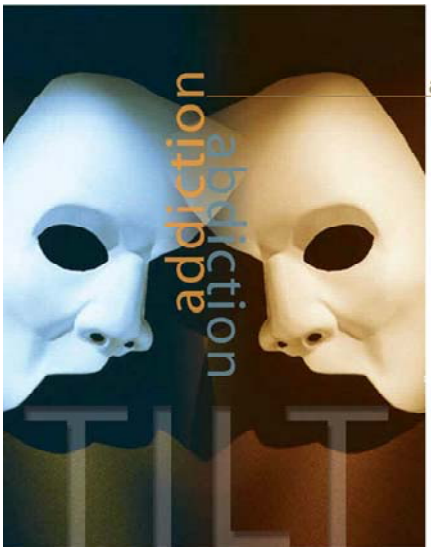
Mage and Gammage 1985, Evaluation of Changes in Outdoor Air Quality Occurring over the Past Several Decades, in Indoor Air and Human Health. Gammage and Kaye Eds., Chelsea, MI, Lewis Publishers, p. 13)



Nail polish remover	Perfumes
New carpeting	Cigarette smoke
Detergent aisle in grocery store	Diesel exhaust
Insecticides	Asphalt or tar
Fresh newspaper/newsprint	Restroom deodorizers
Felt-tip dry marking pen	Particle board
Poorly ventilated meeting room	Traffic exhaust
New automobile interior	Cigar smoke
Fabric stores	Hairspray
Hotel rooms	Fresh paint

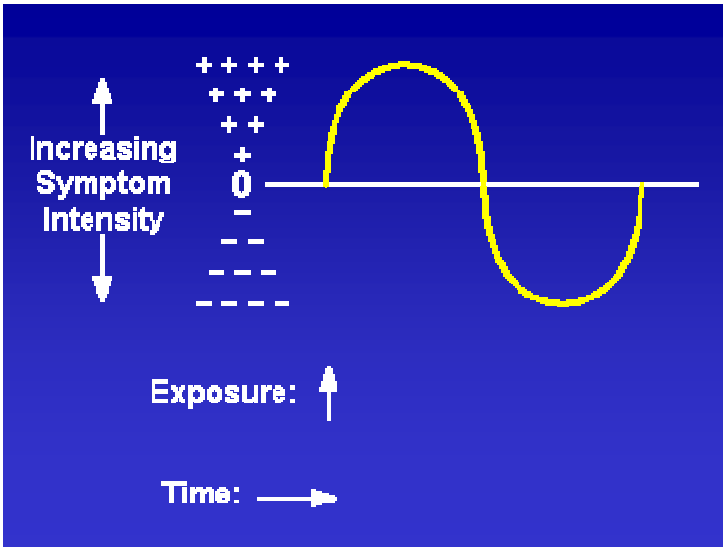




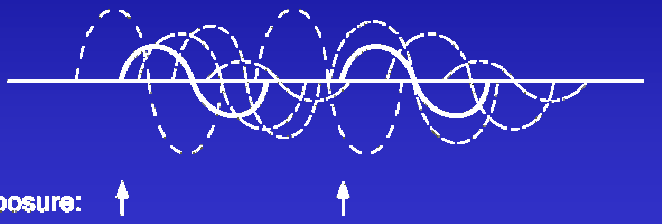


Addiction and Chemical Intolerance: A Shared Etiology?

Masking



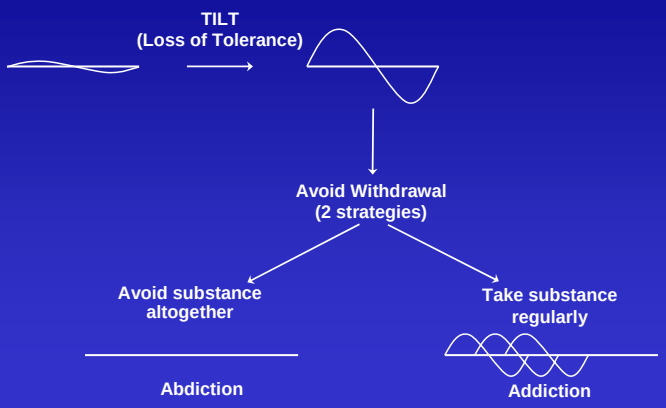
Masking: Apposition



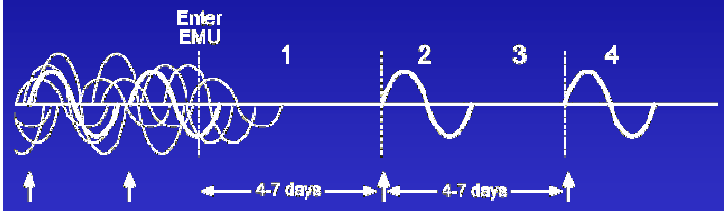
Exposure: ↑ ↑

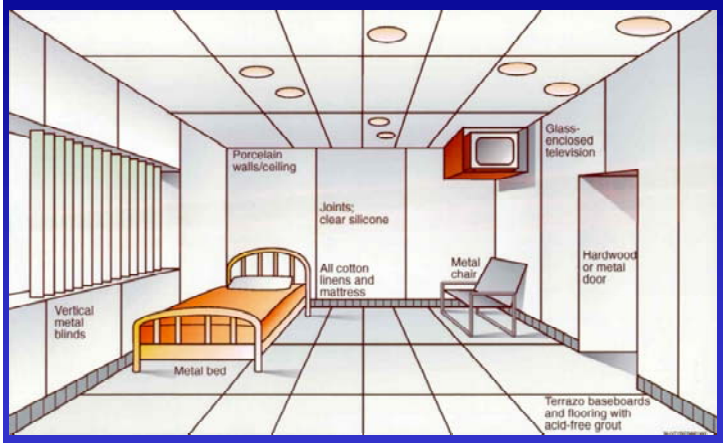
Time →

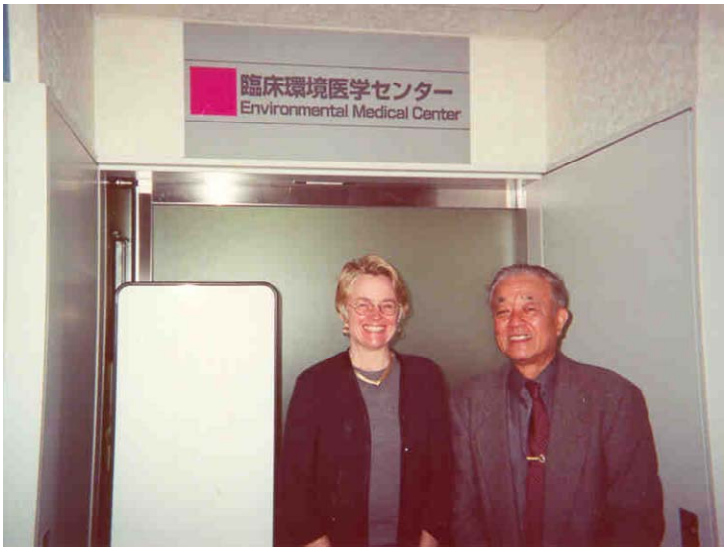
Relationship between TILT, Addiction and Abdiction



Chemical Intolerance: Postulates



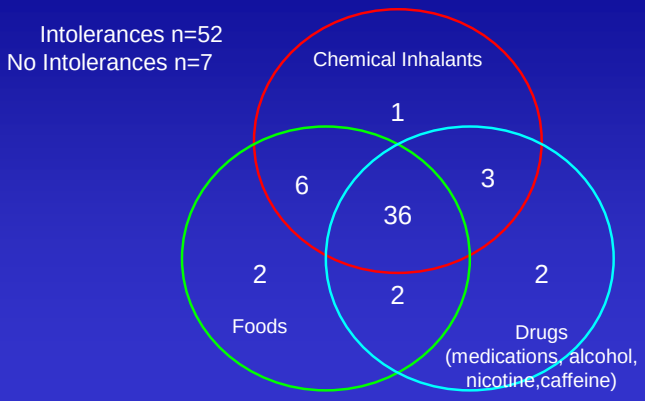




Frequency of New-onset Intolerances Reported by the First 59 Consecutive Gulf War Veterans Seen at the Houston VA Regional Referral Center

Chemical Inhalants	78%
Medications	40% of those who took drugs
Alcoholic beverages	66% of alcohol users
Caffeine	25% of caffeine users
Foods	78%
Specific foods	64%
Illness after meals	49%
Tobacco use	74% of tobacco users

New-Onset Intolerances Reported by 59 Consecutive Gulf Veterans



Frequency of "Severe" Symptoms Among Three Exposure Groups versus Controls (%)

Symptom	Gulf War Veterans n=59	Pesticide-Exposed n=37	Remodeling-Exposed n=75	Controls N=112
Fatigue	78	68	52	3
Depression	29	49	33	6
Headaches	53	38	31	5
Shortness of breath	38	43	31	2
Asthma or wheezing	12	27	15	0

Chemical Intolerance – Genotypes

- Canadian case control study to determine whether chemically intolerant individuals differ from controls for genetic polymorphisms in drug-metabolizing enzymes
- Caucasian female cases (203) and controls (162)
- CYP2D6, NAT1, NAT2, PON1, PON2, MTHFR were genotyped
- Significant difference found in cases vs. controls for CYP2D6 (p=0.02)
- OR CYP2D6 homozygous active=3.36 (p=0.01)
- OR NAT2 rapid metabolizer=4.14 (p=0.01)

Source: McKeown-Essen et al, Int J Epidemiol 2004; 33:1-8

Chemical Intolerance – Genotypes

- CPY2D6 metabolizes centrally acting drugs and toxins such as tricyclic antidepressants, selective serotonin re-uptake inhibitors, monoamine oxidase inhibitors, amphetamines, codeine, neuroleptics, neurotoxins, and endogenous neurotransmitters
- Latter finding may be relevant to observations that poor metabolizers score higher on anxiety scales and lower on socialization scales
- NAT2 expresses arylamine transferase which determines susceptibility to aromatic amines

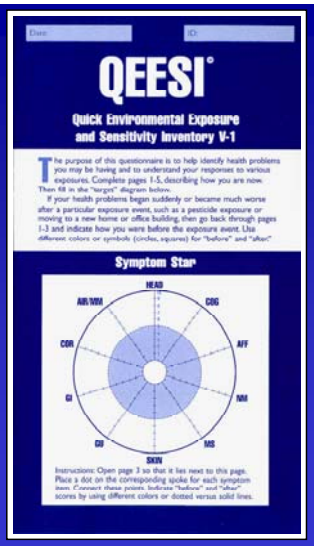
Source: McKeown-Essen et al, Int J Epidemiol 2004; 33:1-8

Chemical Intolerance – Genotypes

- Cases were more likely to be heterozygous for PON1-55 (OR=2.05, p=0.04) and PON1-192 (OR=1.57, p=0.04)
- PON genes have been linked to Gulf War veterans' illnesses (Haley et al., 1999)
- *Post hoc* analysis showed significant effect of being a rapid metabolizer for both NAT2 and CYP2D6:

  OR for rapid/rapid vs. slow/slow combination of CYP2D6 and NAT2 was 18.7
- Conclusion: chemically intolerant individuals differ from controls for genetic polymorphisms in enzymes that metabolize drugs/toxins/endogenous neurotransmitters

Source: McKeown-Essen et al, Int J Epidemiol 2004; 33:1-8



High validity, reliability

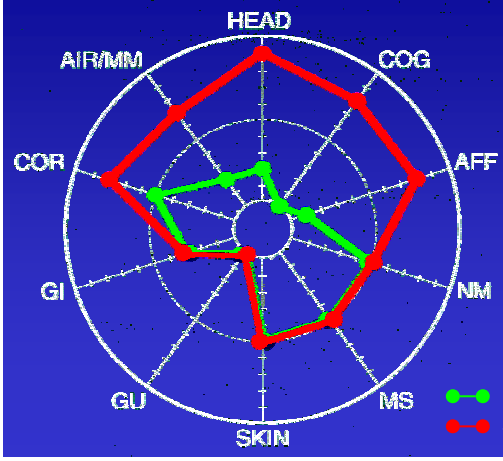
Sensitivity 92%, specificity 95%

Symptom scale derived by factor analysis

"Symptom star"

(Miller and Prihoda, Tox Industr Health 15:370-385, 1999)

QEESI Symptom Star
Pre- and Post-Exposure

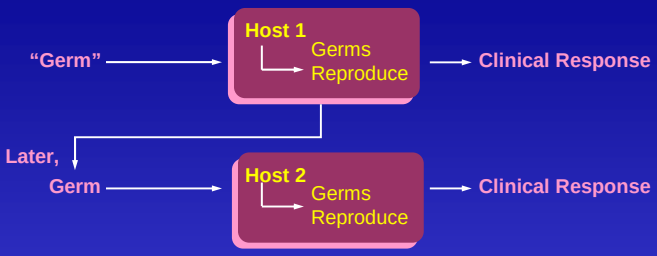


Theories of Disease

Theories of disease are our attempt to explain what is going on inside a "host" by postulating a general mechanism

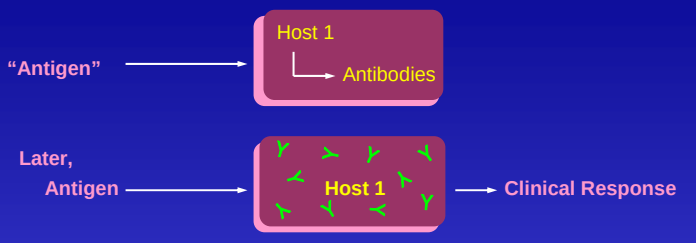
A "theory of disease" is a yet-to-be proven general mechanism for a class of disease

Germ Theory of Disease



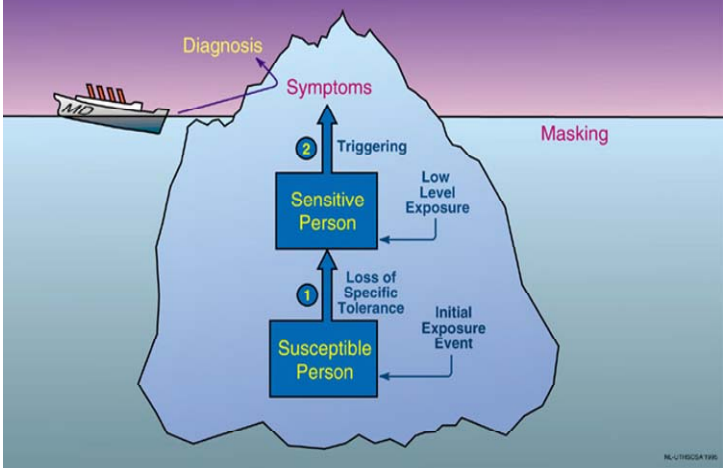
1. Many different kinds of germs cause response
2. Many different responses involving any and every organ system
3. Specific mechanisms may vary greatly (cholera vs. AIDS vs. shingles)
4. No single biomarker. Identification of specific germs took years
5. Prevention—avoidance, antiseptics, sanitation, use of gloves—preceded our knowledge of specific mechanisms

Immune Theory of Disease

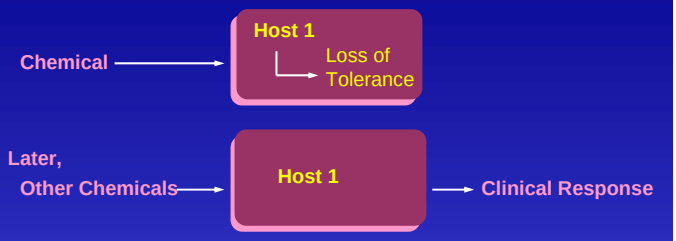


1. Many different kinds of antigens cause response
2. Many different responses involving any and every organ system
3. Specific mechanisms vary greatly (poison ivy vs. allergic rhinitis vs. serum sickness)
4. No single biomarker, identification of specific antibodies took years
5. Prevention—avoidance, allergy shots—preceded our knowledge of specific mechanisms

Toxicant-induced Loss of Tolerance



TILT Theory of Disease



1. Many different kinds of chemicals cause response
2. Many different responses involving any and every organ system
3. Specific mechanisms may vary greatly
4. Currently no biomarker
5. Prevention—avoidance—may precede our knowledge of specific mechanisms

The 7 A's

- Asthma
- Autoimmune diseases
- Affective disorder
- Attention deficit/hyperactivity disorders
- Autism spectrum disorders
- Allergies
- Addiction (masking)

What is plausible depends upon the biological knowledge of the time.