Human Variability in Chemical Susceptibility (Intolerance/Sensitivity), Research Findings to Date and Their Implications for Future Study Design

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National Academy of Sciences
Biological Factors that Underlie Individual Susceptibility to Environmental Stressors, and Their Implications for Decision-Making
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What can we learn about individual susceptibility by studying **humans**?

Two research tools:
The QEESI and the EMU
20 years ago…

1991 National Research Council

Consensus recommendations:

- Case definition for chemical susceptibility
- Animal models
- Epidemiological studies
- Environmental control unit
…environmental control unit, a clinical research unit in which subjects are housed for the control of exposures to foods and chemicals…. uses of units would include control of exposures and challenging subjects in a well-defined environment.
Synthetic Organic Chemical Production
United States, 1945 - 1985

Source: U.S. Intern. Trade Commission
U.S. Pesticide Production, All types, 1927-1988

Historical Development of Ventilation Standards in the U.S.

Why Is Indoor Air Important?

90% of Americans spend 90% of the day indoors (office, home, school, vehicles)

- Increased chemical exposures indoors
- Decreased fresh air
- Evolutionarily novel xenobiotics
EPA’s “Sick Building”

Air Pollution Claims Victims Inside Headquarters of EPA

‘Sick Building Syndrome’ a Growing Problem

By Michael Weisskopf
Washington Post Staff Writer

Since 1985, Bobbie Lively-Diebold has worked at the Environmental Protection Agency mapping a strategy to clean up the nation’s most polluted industrial dump sites.

Now the pollution has hit closer to home. When she enters her office, the slightest contamination sets in.

Despite its implications for the millions of U.S. office workers, indoor air pollution is one of the most elusive varieties of environmental contamination and one of the last to remain unregulated. Emitted at low levels, the pollutants are difficult to trace to a specific source, and the symptoms they cause are not always easily linked.

Surveys show the public and the workplace that governs the self-scheduling industry...
Chemical Intolerance Appears in Different Demographic Groups

- Industrial workers
- Sick building occupants
- Exposed communities
  - Near toxic waste sites, aerial pesticide spraying, contaminated water sources
- Individuals exposed at home
  - Indoor air, consumer products, pesticides, drugs
Chemical Intolerance

Indoor Air Volatile Organic Compounds (VOCs)
- New carpet
- Plasticizers
- Formaldehyde
- Fragrances
- Mold VOCs

Solvents
- Glues
- Paints
- Gasoline
- Nail polish/remover

Drugs/Medical Devices
- Vaccines
- Anesthetics
- Implants
- Antibiotics
- Chemotherapy

Combustion-related Products
- Engine exhaust
- Tobacco smoke
- Oil well fire smoke
- Natural gas
- Tar/asphalt

Pesticides
- Organophosphates
- Carbamates, pyridostigmine
- Pentachlorophenol
- Pyrethrins

Cleaning Agents
- Phenolic disinfectants
- Ammonia
- Bleach
Compelling Anomaly

• Similar reports in different regions/countries from demographically diverse groups
  • Well-documented initiating exposure event
  • Subsequent adverse and amplified responses to previously tolerated and structurally diverse exposures including common chemicals, foods, drugs, alcoholic beverages, caffeine
  • **Not** explained by allergy or classical toxicity

Could we be dealing with a new theory of disease?
Evidence for Toxicant-Induced Loss of Tolerance (TILT)

- Similar reports in different regions/countries
- Complaints of new intolerances for foods, alcoholic drinks, caffeine, and medications, *not only* chemicals = Kuhn’s “compelling anomaly”
- Resemblance to addiction
- Plausible anatomic locus
- Recent animal models
The challenge:

- Different symptoms in different people
- Different initiating exposure events
- Different symptom triggers

Research requires a way to differentiate cases and controls
The QEESI enables researchers to differentiate between cases and controls.
The QEESI

- Validated, published questionnaire, screening tool
- 4 scales + masking index
- 50 questions, self-administered (12-15 min)
- Sensitivity 92%
- Specificity 95%
- Good validity and reliability
## Symptoms

The following questions ask about symptoms you may have experienced commonly. Rate the severity of your symptoms on a 0-10 scale. Do not leave any items blank.

**For each item, circle one number only:**
- **0 = not at all a problem**
- **5 = moderate symptoms**
- **10 = disabling symptoms**

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
<th>Rating 0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Problems with your muscles or joints, such as pain, aching, cramping, stiffness or weakness?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
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<td>2.</td>
<td>Problems with burning or irritation of your eyes, or problems with your airway or breathing, such as feeling short of breath, coughing, or having a lot of mucus, post-nasal drainage, or respiratory infections?</td>
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<td>3.</td>
<td>Problems with your heart or chest, such as a fast or irregular heart rate, skipped beats, your heart pounding, or chest discomfort?</td>
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<td>4.</td>
<td>Problems with your stomach or digestive tract, such as abdominal pain or cramping, abdominal swelling or bloating, nausea, diarrhea, or constipation?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
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<td>5.</td>
<td>Problems with your ability to think, such as difficulty concentrating or remembering things, feeling spacey, or having trouble making decisions?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
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<td>6.</td>
<td>Problems with your mood, such as feeling tense or nervous, irritable, depressed, having spells of crying or rage, or loss of motivation to do things that used to interest you?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
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<td>7.</td>
<td>Problems with balance or coordination, with numbness or tingling in your extremities, or with focusing your eyes?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
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<td>8.</td>
<td>Problems with your head, such as headaches or a feeling of pressure or fullness in your face or head?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
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<td>9.</td>
<td>Problems with your skin, such as a rash, hives or dry skin?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
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<td>10.</td>
<td>Problems with your urinary tract or genitals, such as pelvic pain or frequent or urgent urination! (For women: or discomfort or other problems with your menstrual period!)</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
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</table>

**Total Symptom Score (0-100):**
QEESI Symptom Star

Before exposure event

Since exposure event
Chemical Exposures

The following items ask about your responses to various odors or chemical exposures. Please indicate whether or not these odors or exposures would make you feel sick, for example, you would get a headache, have difficulty thinking, feel weak, have trouble breathing, get an upset stomach, feel dizzy, or something like that. For any exposure that makes you feel sick, on a 0-10 scale rate the severity of your symptoms with that exposure. For exposures that do not bother you, answer “0.” Do not leave any blank spaces.

For each exposure listed below, circle the number that best describes your reaction:

[0 = not at all]

1. Diesel or gas exhaust
2. Tobacco smoke
3. Insecticide
4. Gasoline
5. Paint or paint thinner
6. Cleaning products (disinfectants, bleach)
7. Certain perfumes, aftershave, or fragrances
8. Fresh tar or asphalt
9. Nail polish or hairspray
10. New furnishings (carpet, shower curtain)

Total Chemical Exposures

Name any additional exposures and rate them from 0 to 10.
• Chlorinated tap water
• Foods or food additives
• Food cravings for feeling ill if meal is missed
• Feeling ill after meals
• Caffeine
• Feeling ill if stop or decrease caffeine
• Alcohol in small amounts
• Fabrics, jewelry, creams and cosmetics that touch skin
• Adverse reactions to drugs or medications
• Classical allergic reactions (pollen, dust, mold, dander, insect stings)
### Masking Index

The following items refer to ongoing exposures you may be having. Circle “0” if the answer is “NO” or if you don’t know whether you have the exposure. Circle “1” if the answer is “YES,” you do have the exposure. Do not leave any items blank.

**Circle “0” or “1” only:**

1. **Do you smoke or dip tobacco once a week or more?**
2. **Do you drink alcohol, beer, or wine once a week or more?**
3. **Do you consume any other beverages once a week or more?**
4. **Do you routinely use perfume, body spray, or scented personal care products?**
5. **Has either you or a household member been sprayed with insecticides in the past year?**
6. **In your current employment, do you routinely (once a week or more) use any chemicals?**
7. **Other than your work, do you routinely smoke cigarettes?**
8. **Is either a gas or a propane stove cooking in your home?**
9. **Is a scented fabric softener (or dryer sheet) used on your clothes or bedding?**
10. **Do you routinely take any of the following medications: prednisone, pain relievers, anxiety, or mood (tranquilizers, sleep, or recreational drugs)?**

- Tobacco
- Alcohol
- Caffeine
- Scented personal care products
- Insecticides
- Chemical or smoke exposure at work
- Second-hand smoke
- Gas or propane stove
- Scented fabric softener
- Drugs (steroids, pain relievers, recreational)
Impact of Sensitivities

If you are sensitive to certain chemicals or foods, on a scale of 0-10 rate the degree to which your sensitivities have affected various aspects of your life. If you are not sensitive or if your sensitivities do not affect these aspects of your life, answer "0." Do not leave any items blank.

How much have your sensitivities affected:

<table>
<thead>
<tr>
<th>Item</th>
<th>Rating (0-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Your diet?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>2. Your ability to work or go to school?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>3. How you furnish your home?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>4. Your choice of clothing?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>5. Your ability to travel to other cities or drive a car?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>6. Your choice of personal care products, such as deodorants or makeup?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>7. Your ability to be around others and enjoy social activities, for example, going to meetings, church, restaurants, etc.?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>8. Your choice of hobbies or recreation?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>9. Your relationship with your spouse or family?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>10. Your ability to clean your home, iron, mow the lawn, or perform other routine chores?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
</tbody>
</table>

Total Life Impact Score (0-100): [ ]

For copies of the QEEIS call 210-567-7407 or email milsce@stcroix.edu.

REFERENCES:
Background information:

Sensitivity, specificity, reliability and validity of the QEEIS:


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Interpreting the QEESI

To assess chemical intolerance, use these 3 scores:

- Symptom Severity
- Chemical Intolerance
- Masking

What is Masking?

Masking results from background exposures which can hide the cause-effect relationship between specific symptoms and their triggers.
## Interpreting the QEESI

<table>
<thead>
<tr>
<th>Chemically Intolerant?</th>
<th>Symptom Severity Score</th>
<th>Chemical Intolerance Score</th>
<th>Masking Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Suggestive</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Very Suggestive</td>
<td>High</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Suggestive</td>
<td>High</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Not Suggestive</td>
<td>High</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Problematic</td>
<td>Low</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Problematic</td>
<td>Low</td>
<td>High</td>
<td>Low</td>
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<tr>
<td>Not Suggestive</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
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<tr>
<td>Not Suggestive</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
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</tbody>
</table>
Chemical Intolerance Research Tools

**QEESI**
Screening tool—differentiates cases and controls

**Environmental Medical Unit (EMU)**
Eliminates background exposure “noise” so that responses to low-level exposures can be observed, permitting
- Blinded exposure challenges
- Opportunities for “-omic” studies pre- and post-challenge
- Objective measures (e.g., pulmonary function, brain imaging) pre- and post-challenge
The Environmental Medical Unit

- Porcelain walls/ceiling
- Joints; clear silicone
- All cotton linens and mattress
- Metal bed
- Vertical metal blinds
- Glass-enclosed television
- Metal chair
- Hardwood or metal door
- Terrazo baseboards and flooring with acid-free grout
Need for an Environmental Medical Unit
20 years from now…
where will we be?

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