Case Studies in Environmentally-Induced Illnesses

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Learning Objectives
At the end of this presentation the participant will be able to:
1. Define Toxicant-induced Loss of Tolerance (TILT)
2. Recognize TILT symptoms that may be overlooked in the pediatric patient
3. Understand how exposures affect the pediatric population

(e.g., discuss, define, list, characterize, relate, compare, distinguish, demonstrate, diagnose, treat, manage, develop, educate, improve, refer, etc., etc.)

TILT Objectives
› Explore case studies of environmentally induced illnesses
› Define Toxicant-induced Loss of Tolerance (TILT)
› Recognize TILT symptoms that may be overlooked in the pediatric patient
› Understand how exposures affect the pediatric population
› Recognize contributing factors

School Exposure
› Teacher acutely exposed to organophosphorus (OP) pesticide during 13th week of pregnancy
› Initial Sx: Bloody nose, dizziness, diarrhea, headaches, memory, and confusion; initially lost her sense of smell
› Others complained of headaches and odor; two IT technicians experienced GI and respiratory symptoms

Case Study 1

Newborn Outcome
› Exposed teacher's newborn had colic 24/7, digestive and respiratory issues, and “shook all the time” with seizure-like activity not evident on EEG
› 10 months—delays on Rt side of his body affecting ability to crawl
› Age 4: Dx with Asperger Syndrome, ADHD and severe anxiety
› Cannot function in normal classroom setting

Case Study 1 (cont’d)
Case Study I (cont’d)

**Mother’s Outcome**
- Constellation of symptoms Dx as Lupus and severe anxiety
- Developed severe intolerances to cleaning chemicals, fragrances, and wheat; can no longer use her art supplies

“**My chest fills up with fluid when I’m exposed to strong odors.**”

**Home Exposure**
- Mother and 2 children exposed to Dursban from home extermination
- Sx: extreme fatigue, severe diarrhea, nausea, sweating, memory loss, and confusion
- Children exhibited asthma-like symptoms & rhinorrhea—no GI symptoms
- Did not relate symptoms to exposure; didn’t seek medical attention for >2wks

“I thought I had a bad stomach flu and my boys had colds”

Case Study II (cont’d)

**Treatment History**
- Poison control staff dismissed children’s symptoms on two occasions/acknowledged mother’s symptoms
- Urgent care physician referred children to ER for evaluation
- ER pediatrician advised family to move out and seek environmental cleanup

Case Study II

**Mother’s Outcome**
- Mother continued w/ cognitive issues and diarrhea x6 months (BMI ↓ to 18.2)
  - “I had to drop calculus and be driven to med school interview because I couldn’t add 2+2 and was too tired to drive myself.”
- Developed severe intolerances to medications, fragrances, cleaning products, laundry detergent, car exhaust, gas fumes, and medications, etc.
- Developed dairy and wheat intolerances; mild asthma, hypothyroidism; chronic B-12 & Vit D deficiencies, dry eyes & mouth; painful joints/muscles; occasional prolonged low-grade fevers

Case study II (cont’d)

**Children’s Outcome**
Mother recalled having same Sx with 1st pregnancy
- 1st born: colic, explosive bowel movements, PDD/NOS, ADHD, fine/gross motor delays, auditory processing disorder and severe anxiety
- 2nd child Dx: ADHD, dyslexia, auditory processing disorder and anxiety
- Father (ENT surgery resident): Dx new onset anxiety/mood disorder

Case study II (cont’d)

**PON 1 Test Results**
- Mother (teacher) and 2 children extremely sensitive to neurotoxic effects of Dursban

Case Study I
**PON 1 Test Results**

![Graph showing PON 1 test results with points scattered across the graph.]  

- Mother and 2 children extremely sensitive to neurotoxic effects of Dursban

**Case study II (cont’d)**

**OP Toxidrome (acute symptoms)**

<table>
<thead>
<tr>
<th>CNS</th>
<th>Muscarinic</th>
<th>Nicotinic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ataxia</td>
<td>Bradycardia</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Tremors</td>
<td>Rhinorrhea</td>
<td>Bronchorrhea/cough</td>
</tr>
<tr>
<td>Seizures</td>
<td>Bronchorrhea</td>
<td>Pallor</td>
</tr>
<tr>
<td>Confusion</td>
<td>Increased lacrimation</td>
<td>Increased saliva</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Increased salivation</td>
<td>Diaphoresis</td>
</tr>
<tr>
<td>Restlessness</td>
<td>Incontinence</td>
<td>Muscle fasciculations</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Headache</td>
<td>Myotonic jerks</td>
</tr>
<tr>
<td>Emotional</td>
<td>Blurred vision</td>
<td>Muscle cramping/weakness</td>
</tr>
<tr>
<td>lability/</td>
<td>Miosis</td>
<td></td>
</tr>
<tr>
<td>agitation</td>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paralysis</td>
<td>Diaphragmatic failure</td>
</tr>
</tbody>
</table>

**Evidence for OP-related pediatric illnesses**

<table>
<thead>
<tr>
<th>Evidence</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased IQ &amp; head circumference, abnormal reflexes</td>
<td>Eskanazi et al. 2008 (Minireview: Ag/Res)</td>
</tr>
<tr>
<td>Increased insulin levels</td>
<td>Debost-Legrand et al. 2016 PELAGIE cohort (Res)</td>
</tr>
<tr>
<td>Recurrent otitis media</td>
<td>Buscaï et al. 2015 PELAGIE cohort (Res)</td>
</tr>
<tr>
<td>Decreased lung function</td>
<td>Ranaan et al. 2016 CHAMACOS cohort (Ag)</td>
</tr>
<tr>
<td>DNA damage (bronchial cells and hepatocytes, buccal mucosa cells)</td>
<td>Arteaga-Gómez E et al. 2016; Benitez-Trinidad et al. 2015; Sutriss et al. 2016 (Res)</td>
</tr>
</tbody>
</table>

**Residential Pesticide Studies**

- Motor/mental developmental delays at age 3, IQ deficits at age 7
- ADHD and PDD (Autism)  
  (Pediatrics, Raul et al. 2006)
- For every 10-fold increase in urinary OP exposure, 55%-72% increase in odds of children having ADHD  
  (NHANES, Bouchard et al. 2010)

**The 7 A’s are Epidemic!**

<table>
<thead>
<tr>
<th>A</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autism</td>
<td>2%</td>
</tr>
<tr>
<td>AD/HD</td>
<td>11%</td>
</tr>
<tr>
<td>Autoimmune Disease</td>
<td>Tripled last few decades, 50 million affected, AARDA.org</td>
</tr>
<tr>
<td>Asthma</td>
<td>8%</td>
</tr>
<tr>
<td>Allergy</td>
<td>40%</td>
</tr>
<tr>
<td>Affective (Mood) Disorders</td>
<td>14%</td>
</tr>
<tr>
<td>Addiction</td>
<td>47%</td>
</tr>
</tbody>
</table>

**References**

- Eskanazi et al. 2008 (Minireview: Ag/Res)
- Debost-Legrand et al. 2016 PELAGIE cohort (Res)
- Buscaï et al. 2015 PELAGIE cohort (Res)
- Ranaan et al. 2016 CHAMACOS cohort (Ag)
- Arteaga-Gómez E et al. 2016; Benitez-Trinidad et al. 2015; Sutriss et al. 2016 (Res)
**Predicament:**
The Diagnosis Varies With Which Specialist a Patient Sees

- Neurologist– migraine
- Gastroenterologist– irritable bowel
- Rheumatologist– fibromyalgia
- Psychiatrist– depression
- Allergist– rhinitis
- Gulf War Syndrome, Chronic Fatigue Syndrome, etc.

All are right... and all are wrong!

**Toxicant-induced Loss of Tolerance (TILT) involves:**

- Initiating toxic exposure(s)
- Breakdown in innate tolerance
- Adverse and amplified responses to previously tolerated exposures including common chemicals, foods, drugs, alcoholic beverages, caffeine, and tobacco smoke
- Problems with multiple organ systems (multimorbidity); some are completely debilitated

**TILT Prevalence**

Do you consider yourself sensitive to everyday chemicals like those in household cleaning supplies, paints, perfumes, soaps, garden sprays, or things like that?

- ~ 15% of people report chemical intolerances (CI)
- Frequently, intolerances also include food, caffeine, medications, and alcoholic beverages
- Mothers who report chemical intolerances 3X more likely to have a child with autism and 2.3X more likely to have a child with ADHD
- Mothers w/CI also report that their children have intolerances (Heilbrun et al. J. Am. Fam. Med. 2015)

**TILT is Pandemic**

Available for download at: https://redcap.uthscsa.edu/REDCap/surveys/?s=LJNLAN8XTP
Chemical Intolerance/TILT

20% of patients seen in a US family practice clinic have been shown to have CI (Katerndahl et al., Annals of Family Medicine 2012)

“Physicians are seeing more patients with multimorbidities of unknown etiology and pathophysiology.”
(Genuis, Canadian Family Physician, 2014)

TILT is a *new disease paradigm* often referred to as:
- Multiple Chemical Sensitivity (MCS)
- Chemical Intolerance (CI)
- Idiopathic Environmental Illness (IEI)
- Gulf War Illness (GWI)

TILT = chemical intolerances initiated by chemical exposures (gene-environment interactions)

What factors are contributing to TILT?

Synthetic organic chemical production, United States, 1945 - 1985

Annual U.S. pesticide production
All types, 1927 - 1988

Top five US states for toxic chemical releases (EPA 2002)

- Texas: 245,761,545 pounds
- Pennsylvania: 139,337,978 pounds
- Ohio: 137,075,843 pounds
- Louisiana: 135,215,670 pounds
- Indiana 134,272,453 pounds
Probable Carcinogen (WHO)
Endocrine disruptor at [100X] lower than agricultural use; toxic to placental cells (Richard et al. 2005)
Inhibitor of P450s (Richard et al. 2005; Cassault-Meyer et al. 2014)

90% of Americans spend 90% of the day indoors
- Increased indoor air pollution sources
- Decreased fresh air intake (none with residential HVAC)
- Chemicals humans never previously encountered

Indoor vs. Outdoor Air VOC levels
Dust and air pesticide levels highly correlated in homes
Half-life of Chlorpyrifos: 4.5 – 6 years

Persistence of Pesticides in Homes

<table>
<thead>
<tr>
<th>Year</th>
<th>Indoor Air ng/m³</th>
<th>Chair Cushion (μg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Outer Inner</td>
<td>2004 2010</td>
</tr>
<tr>
<td>2004</td>
<td>6.8 2.78</td>
<td>0.20 &lt;0.002</td>
</tr>
<tr>
<td>2010</td>
<td>2.78 0.20</td>
<td>&lt;0.002 0.05</td>
</tr>
</tbody>
</table>

Persistence of Pesticides in Residential Indoor Air and Chair Seat Foam · Camann DE, You A, Redburn LR, Walker T, Miller CS (Indoor Air 2011 Conference)
Chemical Intolerance and Autism Study

Are mothers of children with autism and/or AD/HD more chemically intolerant than mothers of neurotypical children?

- National online survey >600 mothers
- AD/HD: professional diagnosis, DSM criteria
- Autism: parental report of professional diagnosis

Mothers of children with Autism (n=282), AD/HD (n=258) and Controls (n=154)

Children’s Intolerances

<table>
<thead>
<tr>
<th></th>
<th>Autism</th>
<th>ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>3.5</td>
<td>2.00</td>
</tr>
<tr>
<td>95% CI</td>
<td>1.9–6.8</td>
<td>1.1–4.0</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;.001</td>
<td>.041</td>
</tr>
</tbody>
</table>

Paul

- 10 year old boy w/ autism
- Extreme case of hyperactivity
- Couldn’t complete exam
- Racing around exam room, overturning chairs, tearing papers
- Temper tantrums began at 13 mo
  - Learning well until 17 months old
  - Transferred from one school to another
  - Placed in school for problem children and tranquilized
  - Occasionally in straightjacket

Case Study III
Theron Randolf, MD

Treatment History

- Doctors suggest medications, vitamins and institutionalization
- Feingold diet removes most (but not all) processed foods
- History of food addictions (sugar, milk, corn and oranges) led to flare-ups of behavioral issues
- Susceptible to everyday environmental chemicals
- Would scream, kick and bite when exposed to nail polish, perfume, or similar odors

Case Study III
Theron Randolf, MD

Intervention with Environmental Medical Unit

- Aggressive and hyperactive symptoms significantly improved after five days in an environmental medical unit
- Abstention from offending foods and chemicals
- Organic foods did not trigger symptoms, but when given as conventional foods (pesticides and food additives) did result in hyperactivity, irritability, and an increase in autistic behavior

Case Study III
Theron Randolf, MD
Intervention with Environmental Medical Unit

Paul truly needed organic foods to stay well, otherwise parents unable to cope with him

Randolph: With appropriate diet, "despite the supposedly 'incurable' nature of his problems, specifically with autism, he is able to lead a relatively normal life."

Case Study III
Theron Randolf, MD

Hoffman TILT Research and Education Project