Topical Toxicity in Tots

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Topical Toxicity in Tots

Endocrine Disrupting Chemicals (EDC’s)

• Who is worried and why?
  – Sources of societal concern
  – Endocrine disruption & low level exposures
• Should we worry?
  1. Oxybenzone
  2. Phthalates
  3. Parabens
  4. Triclosan
• Should our patients/parents worry?

Activist Network

• Breast Cancer Activists
  – Zero Breast Cancer
    • Advocates collaborating with Breast Cancer and the Environment Research Program (BCERP)
  – Breast Cancer Fund
• Environmental Groups
  – Environmental Working Group (EWG)
    • Campaign for Safe Cosmetics/Skin deep
  – Teens Turning Green

Disclosures

Endocrine Disrupting Chemicals (EDC’s)

in Skin Care Products

• Ubiquitous
• Can potentiate or inhibit hormone effect or both
  – Nonlinear dose response curve so low doses relevant
  – “The dose makes the poison”?

Toxicologists vs. Endocrinologists (linear vs. non-monotonic)


Endocrine Disrupting Chemicals

- Animal, cell culture studies
- Human studies difficult
  - National Health and Nutrition Education Study (NHANES)
- Long lag time to see effects
- Critical periods of exposure?

www.cdc.gov/nchs/nhanes.htm

Breast Cancer Fund “State of the Evidence 2010”

Smensier, LUCAL, et al. “Endocrine Disrupting Chemicals in the Environment” (Stockholm, 2001). The results for EDCs have been replicated in another laboratories (Stock, 2001). A recent laboratory rat study has demonstrated that application of OMC on the skin of the animals enhances the penetration of the endocrine-disrupting herbicide 2,4-D (Brand, 2007).


EDC Health Concerns

- Breast & other cancer
- Early puberty
- Obesity
- Infertility
- Immune dysfunction
  - Savage 2012
- Developmental Problems
  - Meeker 2012

"Poisoned by everyday life. Gender bending chemicals...found in every home may cause breast cancer, asthma, infertility, and birth defects..."

Zerobreastcancer.org

www.breastcancerfund.org/about/victories/46378109400
PARANOIAGENS

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Zerobreastcancer.org

Early Puberty

- Increasing numbers of young acne patients
- Hysteria around early puberty studies 1997, 2010

Goldberg 2011, Herman-Giddens 1997, Biro 2010

“Typical acne patient”

13 year old boy 15 year old girl

Initiation vs. Completion of Puberty

Age 3.5 Age 8

Menarche age 13
Why is Puberty Taking Longer?

- Worry about peripheral, exogenous triggers of development – environmental toxins (EDC’s)
  - “I think we need to think about the stuff we’re exposing our bodies to and the bodies of our kids…This is a wake-up call, and I think we need to pay attention to it.”
  - Frank Biro*

BCERP.org: Early Puberty

- “environmental exposures, including chemicals in personal and household products that may be hormonally active; lifestyle factors, such as food intake and physical activity; body size and development; and psychosocial factors”

Topical Toxicity in Tots:
Endocrine Disrupting Chemicals

- Who is worried and why?
  - Sources of societal concern
  - Endocrine disruption: low level exposure

- Should we worry?
  1. Oxybenzone
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- Should our patients/parents worry?

EDC’s in Skin Care Products

- Oxybenzone
- Parabens
- Phthalate esters
- Triclosan

*Grady New York Times 2010
Oxybenzone (benzophenone-3= BP3)

- Organic UVA filter widely used in sunscreen
- FDA-approved in early 1980's
- Present in urine of 96% of Americans in 2003-4 NHANES, breast milk of 13% Swiss mothers (BP-3)

Calafat 2008, Schlumpf 2010

Oxybenzone as EDC in Humans

- Estrogenic, anti-androgenic in vivo and in vitro
- Adult male & female volunteers
  - Well absorbed, rapidly excreted in urine
  - Affected reproductive hormone levels at 24 hours but not after
- Authors concluded hormone changes unrelated
  - Janjua 2004
- NHANES 12-16 yo females
  - Benzophenone-3 not associated with menarche
  - Buttke 2012

Lesson from Oxybenzone

- Absorption ≠ toxicity
- May be absorbed and excreted without significant biological effect so probably safe

Zinc and Titanium nano

- Penetrate only into the stratum corneum in healthy, undamaged skin
- Aggregate in sunscreen so not so nano
- Concern is that the rapid integration into many skin care products outpaced research into safety
- National Institute of Environmental Health Sciences “ONE-Nano”

Sunscreen in infants < 6 months

- AAP guidelines now state can be used on small areas of skin not covered by clothing
- Concern about greater absorption
- Unscented, zinc-based creamy sunscreens best
- Emphasize protective clothing

Phthlate esters

- Many different compounds
- Thickener, softener, scent
- Percutaneous absorption
- Metabolism depends on route of entry, type
- Extensive exposure
  - Soap, shampoo, perfume, nail polish

Janjua 2008, BCERP 2007
“Personal Care Products”
1. Soap
2. Shampoo
3. Conditioner
4. Hair spray
5. Sunscreen
6. Makeup
7. Lipstick
8. Antiperspirant
9. Moisturizer

Phthalate Threat Outside Skin Care
- Soft toys
  - Rattles, pacifiers, teethers
- Baby care
  - Bottle nipples
- Medical equipment
  - IV tubing, blood bags, catheters
- Other
  - Raincoats, shower curtains, vinyl flooring, dust(!)

Endocrine Disrupting Compounds
- Bisphenol A (BPA)
- Persistent organic pollutants
  - Polychlorinated, brominated biphenyls
- Flame retardants
  - TetrabromoBPA
- Oxybenzone
- Parabens
- Phthalate esters
- Triclosan

Phthalate Esters:
- Anti-androgenic in animal studies
- More worrisome than the other 3
- Ingestion/inhalation major route of exposure in kids
- Concern about exposures to multiple types
- Many studies in progress

Parabens
- Preservative, antimicrobial
- In many personal care products, most cosmetics
- In urine of 99.1% (methyl) of adults in US
- 63% in postmenopausal Norwegian women & level correlated with topical moisturizer use
  - Calafat 2010, Sandanger 2011

Parabens
- Uptake from dermis but hydrolyzed & excreted rapidly in urine
- Methyl, ethyl safe
- Butyl, propyl still under review as estrogenic and anti-androgenic EDC’s
Parabens in Alternative Topicals

Methyl paraben

TopicalTemerity

Parents may be reluctant to use skin care products we prescribe or recommend & may seek alternatives

Green Skin Care Industry

- AKA “premium baby skin care category”
- Increased 68% 2005-10
  - total baby care 16%
- Parents spend $150-300/month on their child’s “natural” skin care products

Vorta S. New York Times 2012

“Natural”, “Baby” ≠ “Safe”

- Measurable phthalate level in baby skin care products
  Lampel 2011
- In alternative products
  - Highest level of paraben in an alternative kids’ shampoo but not on label
    Dodson 2012
  - Gynecomastia due to lavender and tea tree oil in prepubertal boys
    Henley 2007
- No standards for testing and labeling

Safe Chemicals Act
(Toxic Substances Control Act 1976)

U.S. Senator Frank Lautenberg D-NJ introduced 2005; 2012 passed Environment and Public Works Committee

Precautionary Principle:
Guilty till proven innocent

"I have no idea what gluten is, either, but I'm avoiding it, just to be safe."
Triclosan
- Antimicrobial first registered as a pesticide in 1969
- Used in personal care, medical products
- Poorly absorbed through dermis
- Bioaccumulates in fat, breast milk, urine

Triclosan
- 74.6% of 2003-2004 NHANES participants had triclosan in urine
- Not removed by wastewater treatment
- Safety currently in review by EPA and FDA
  – Calafat 2008

Triclosan toxicity
- Anti-thyroid hormone, estrogenic, androgenic
  Vandenberg 2012
- Link to allergies and asthma
  Clayton 2010
- In vitro and in vivo in mice, impaired cardiac and skeletal muscle contractility via ryanodine receptors ➔ ABC News 8/14/12: “Soap ingredient Triclosan linked to muscle weakness”
  Cherednichenko PNAS 2012

Lesson from Triclosan
- Some drugs and chemical compounds not removed by waste water cleaning so end up in natural waterways
- Even if minimal impact on human health, some agents can have huge impact “downstream” on aquatic and wildlife ecosystems

Toxic Tips
1. Oxybenzone: even if absorbed may have minimal biological effect...precautionary principle?
2. Phthalates: low level exposure, multiple agents can still cause endocrine disruption
3. Parabens: alternative/baby products aren’t necessarily safer
4. Triclosan: need better testing and more research to better protect both human & “downstream” environmental health

Topical Toxicity in Tots ➔
Endocrine Disrupting Chemicals
- Who is worried and why?
  – Sources of societal concern
  – Endocrine disruption: U-shaped controversy
- Should we worry? 4 potential toxins
  1. Oxybenzone
  2. Phthalates
  3. Parabens
  4. Triclosan
- Should our patients/parents worry?
How can we reassure patients?

- Convey perspective
  - Acknowledge uncertainty
  - Inconclusiveness of studies
  - Risk/benefit
- Research your local retail outlets, internet
  - Pricing, safety
- Don’t fight the fanatic
- Listen to activist groups

What advice should we give?

- Be a minimalist: eliminate unnecessary products
- Don’t be fooled by marketing
- Avoid scented & antimicrobial agents
- Rely on covering up for sun protection, zinc?
- Eat organic if possible

“Johnson & Johnson to remove formaldehyde from products”

“Even though as a scientist I will sit here and tell you these things are perfectly safe,” consumers are worried about reports that call her conclusions into question, Ms. Nettesheim said. “I understand that and we can’t ignore that.”

The End

Selected References

- For complete list of references: renee.howard@ucsf.edu