Are we too clean? Evidence from NHANES

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University of Michigan
Department of Epidemiology and
Center for Social Epidemiology and Population Health

The Impact of Bisphenol A and Triclosan on Immune Parameters in the U.S. Population, NHANES 2003–2006

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Presentation Outline

- The development of sanitation and hygiene
- Today's use (and misuse?) of antibacterial products
- The antibacterial agent triclosan and its impact on immune function
- Practical implications for public health professionals

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The "Good" Old Days?

c. 1900

http://www.skyscrapercity.com/showthread.php?t=34300&page=57

The "Good" Old Days?

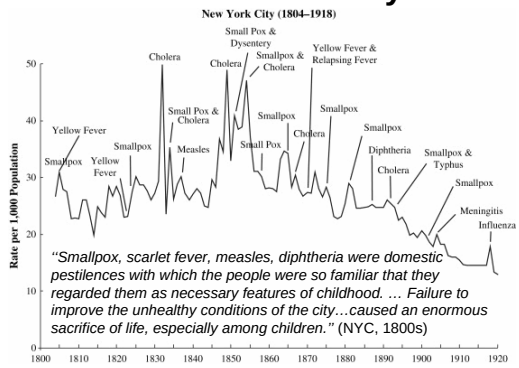
"Domestic garbage and filth of every kind is thrown into the streets… sending forth perennial emanations which must generate pestiferous disease."
(NYC, 1865)

http://theboweryboys.blogspot.com/2008/08/podcast-five-points-wicked-slum.html

The "Good" Old Days?

Aiello AE, Larson EL, Sedlak R. (2008) *Am J Infect Control* 36(10 Suppl):S111-5

The "Good" Old Days?

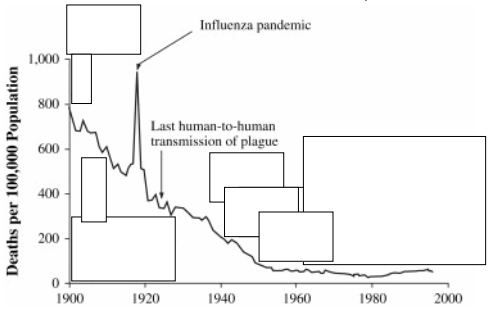


"Smallpox, scarlet fever, measles, diphtheria were domestic pestilences with which the people were so familiar that they regarded them as necessary features of childhood. … Failure to improve the unhealthy conditions of the city…caused an enormous sacrifice of life, especially among children." (NYC, 1800s)

Aiello AE, Larson EL, Sedlak R. (2008) *Am J Infect Control* 36(10 Suppl):S111-5

Enter: The "Health Revolution"

Crude death rate for infectious diseases, U.S.



Aiello AE, Larson EL, Sedlak R. (2008) *Am J Infect Control* 36(10 Suppl):S116-27

Enter: The “Health Revolution”

The health revolution…

- Changed the average age of death
- Increased life expectancy at every age
- Significantly reduced the probability of a given person dying in a given year from a given cause

Aiello AE, Larson EL, Sedlak R. (2008) *Am J Infect Control* 36(10 Suppl):S116-27

Enter: The “Health Revolution”

Contributors to the control of infectious disease

Medical Innovations
Vaccines
Antibiotics
Diagnostic tests
Medical instrumentation
Discovery of specific microbial pathogens
Advances in molecular biology and genetics

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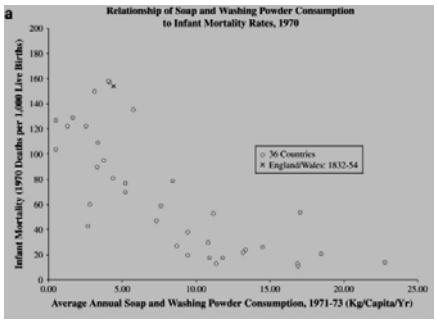
Enter: The "Health Revolution"

Contributors to the control of infectious disease

Medical Innovations	Environmental Sanitation	Social and Technological
Vaccines	Personal hygiene	Education
Antibiotics	Disinfection antiseptics and sanitary chemicals	Agricultural and food technology
Diagnostic tests	Pasteurization	Transportation
Medical instrumentation	Insect and rodent control	Housing improvements
Discovery of specific microbial pathogens	Sewage treatment and disposal	Health services organization and financing
Advances in molecular biology and genetics	Water purification technology	Communication innovations

Aiello AE, Larson EL, Sedlak R. (2008) *Am J Infect Control* 36(10 Suppl):S116-27

Hidden heroes: Sanitation and Hygiene



Aiello AE, Larson EL, Sedlak R. (2008) *Am J Infect Control* 36(10 Suppl):S128-51

Soaps and detergents: 1900s to now

Advertisements for Soap and Bathroom Fixtures in Sears 1902 Catalogue

Aiello AE, Larson EL, Sedlak R. (2008) *Am J Infect Control* 36(10 Suppl):S128-51

Soaps and detergents: 1900s to now

1950s
Automatic dishwasher powders
Liquid laundry, hand dishwashing and all-purpose cleaning products
Fabric softeners (rinse-cycle added)
Detergent with oxygen bleach

1960s
Prewash soil and stain removers
Laundry powders with enzymes
Enzyme presoaks

1970s
Liquid hand soaps
Fabric softeners (sheets and wash-cycle added)
Multifunctional products (e.g., detergent with fabric softener)

1980s
Detergents for cooler water washing
Automatic dishwasher liquids
Concentrated laundry powders

1990s
Ultra (superconcentrated) powder and liquid detergents
Ultra fabric softeners
Automatic dishwasher gels
Laundry and cleaning product refills

2000s
Disposable cleaning wipes
Pre-measured dissolvable packets
Spa scents and natural options

http://www.cleaninginstitute.org/clean_living/soaps__detergent_history_3.aspx

The health revolution continues…

- Good hygiene continues to be a primary (yet often "silent") disease-prevention strategy
- Infectious diseases are still a part of everyday life
- New and emerging infections have been identified over the past few decades
- "Superbugs" and "germs" are buzzwords for dangers we want to – and *need* to – eliminate

Aiello AE, Larson EL, Sedlak R. (2008) *Am J Infect Control* 36(10 Suppl):S152-65

…with the rise of antibacterial agents

- Initially developed to prevent disease transmission in hospitals
- Have been effectively used in hospitals for decades, under stringent guidelines
- Now, over 700 antibacterial products are available to US consumers (including antibacterial mattresses and chopsticks!)

Levy SB. (2001) *Emerg Infect Dis* 7(3 Suppl):512-5

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Prevalence of antibacterial soaps

- Physician-performed survey
- 23 stores in 10 states
- December 1999 through April 2000
- Determined # of national brand liquid and bar soaps
- Determined # of these soaps containing an antibacterial agent

Perencevich EN, Wong MT, Harris AD. (2001) *Am J Infect Control* 29(5):281-3

Prevalence of antibacterial soaps

Proportion of liquid or bar soaps available for sale at national, regional, and Internet stores that contain antibacterial compounds.

Store type	Liquid soaps (%)	Bar soaps (%)	All soaps (%)
National	134/177 (75.7)	88/333 (26.4)	222/510 (43.5)
Regional	136/178 (76.4)	110/338 (32.5)	246/516 (47.7)
Internet	30/40 (75.0)	15/62 (24.2)	45/102 (44.1)
All stores	300/395 (75.9)	213/733 (29.1)	513/1128(45.5)

Perencevich EN, Wong MT, Harris AD. (2001) *Am J Infect Control* 29(5):281-3

Is there a benefit to antimicrobial soap use in the community?

- Systematic literature review conducted in 2007
- Reviewed 27 studies published from 1980 – 2006
- Antibacterial soaps no more effective than plain soaps at preventing infectious illness symptoms or reducing bacteria on hands

Aiello AE, Larson EL, Levy SB. (2007) *CID* 45:S137-47

Benefit to use of other antimicrobial products?

- Do products labeled as “antibacterial” provide a false sense of security?
- Are marketing and labeling strategies sometimes misleading consumers?
  - -“Kills germs”? “Stops disease transmission”?
  - -Examples:
    - -Antibacterial sponge
    - -Protection of materials from odors and deterioration

Favero MS. (2002) *J Appl Microbiol* 92 Suppl:72S-7S

Cause for concern?

- Ineffective use in households and community settings
- May leave residues on surfaces where they are diluted down to less-than-effective concentrations
- Although not the cause of antimicrobial resistance, may maintain and propagate resistant strains
  - - mechanisms of action same as for antibiotics: cross-resistance

Levy SB. (2002) *Arch Dermatol* 138:1087-8

Antibiotics vs. antimicrobials

- Antibiotics kill bacteria by targeting specific cellular components
- These cellular targets regularly undergo mutations, causing antibiotics to become ineffective
- Antimicrobials not intended to target specific cellular constituents in bacteria
- At lower levels, some antimicrobials found to have a specific enzyme target in bacteria – therefore, concern about cross-resistance

Dann AB, Hontela A. (2011) *J Appl Toxicol* [Epub ahead of print]

A second potential concern

- Antibacterial products can change the microbial ecology of our homes and daily environment
- Immune systems may need exposure to microbes in order to develop properly
- Excessive cleanliness (i.e., lack of exposure to any microorganisms) may contribute to increases in allergies, asthma, and eczema in recent decades

Levy SB. (2001) *Emerg Infect Dis* 7(3 Suppl):512-5

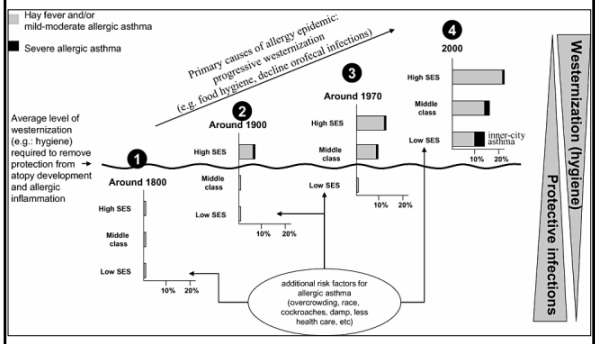
The hygiene hypothesis

"Over the past century …higher standards of personal cleanliness have reduced the opportunity for cross infection in young families. This may have resulted in more widespread clinical expression of atopic [allergic 'hyper-sensitivity'] disease…"

- DP Strachan, 1989

Strachan DP. (1989) *BMJ* 299(6710):1259-60

Hypothetical hygiene hypothesis model



Matricardi PM. (2010) *Clin Exp Immunol* 160:98-105

Recent support for the hygiene hypothesis

- Children living on farms less likely to have asthma

  Ege MJ et al. *New Engl J Med.* 2011; 364[8]: 701-709

- Greater exposure to variety of microbes lowers risk of asthma

  Ege MJ et al. *New Engl J Med.* 2011; 364[8]: 701-709

- Women have higher rates of asthma, allergies, and autoimmune disorders and there is a greater focus on cleanliness for girls than for boys

  Clough S. *Soc Sci Med.* 2011; 72[4]: 486-493

Hampton T. (2011) *JAMA* 305(14):1400-1

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Prevalence of antibacterial soaps

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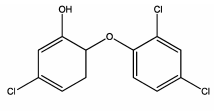
Store type	Liquid soaps (%)
National	134/177 (75.7)
Regional	136/178 (76.4)
Internet	30/40 (75.0)
All stores	300/395 (75.9)

100% of liquid antibacterial soaps contained the antibacterial agent triclosan

Perencevich EN, Wong MT, Harris AD. (2001) *Am J Infect Control* 29(5):281-3

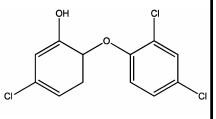
Triclosan



- Synthetic, broad-spectrum antimicrobial
- First used in personal care products in 1960s
- Found in hand soaps, laundry detergents, toothpastes, deodorants, facial tissues, medical devices, and toys… just to name a few

Triclosan

- Structurally similar to polychlorinated biphenyls (PCBs), bisphenol A (BPA), and dioxins



- At high concentrations, targets multiple non-specific bacterial targets
- At lower concentrations, acts on specific bacterial enzyme (a well-conserved antibiotic target!)

Dann AB, Hontela A. (2011) *J Appl Toxicol* [Epub ahead of print]
Coulborn RM, Rees Clayton E, Aiello AE. (2010) *ACS Symposium Series* pp 367-82

Triclosan in the environment

- Two main sources of triclosan release into the environment:

  (1) discharge of wastewater treatment plant effluent into receiving waters

  (2) land application of biosolids containing triclosan residues

Dann AB, Hontela A. (2011) *J Appl Toxicol* [Epub ahead of print]

Triclosan in the environment

- U.S. Geological Survey sampled 139 streams across 30 states in 1999-2000
- Measured concentrations of 95 organic wastewater contaminants (OWCs)
- 80% of streams contained at least 1 OWC
- Triclosan was one of the most frequently detected OWCs

Kolpin DW, et al. (2002) *Environ Sci Technol* 36(6):1202-11

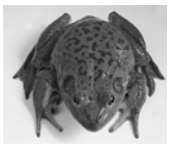
Triclosan in the body

- Detected in human fat tissue, blood, urine, and breastmilk
- CDC study in 2003-2004 detected triclosan in urine of 75% of study population (n= 2,517) ages 6+
  - Unadjusted concentrations: 2.4 – 3,790 ug/L
- Significance of these findings currently unknown

Calafat AM, Ye X, Wong LY, Reidy JA, Needham LL. (2008) *Environ Health Perspect* 116(3):303-7

Triclosan as an EDC

- EDC = Endocrine-disrupting compound
- First labeled as an EDC in 2006, when shown to affect hormone-mediated development of bullfrogs



- Effect observed with triclosan concentrations as low as 0.15 ug/L

  (recall: urinary concentrations in humans 2.4 – 3,790 ug/L)

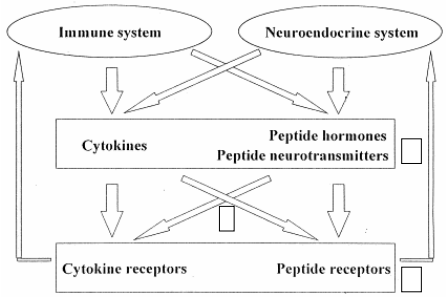
Veldhoen N, et al. (2006) *Aquat Toxicol* 80(3):217-27

EDCs: A public health concern

- In 1996, U.S. Congress mandated that the EPA identify and monitor EDCs in the environment
- EDCs mimic, or affect activity of, hormones
  - Exact mechanisms of action often unknown
- Controversy surrounding what concentrations – if any – are safe for human use

Clayton EM, Todd M, Dowd JB, Aiello AE. (2011) *Environ Health Perspect* 119(3):390-6

Endocrine and immune systems share a chemical language



Jiang CL, Lu CL, Liu XY. (1998) *Domest Anim Endocrinol* 15(5):363-9

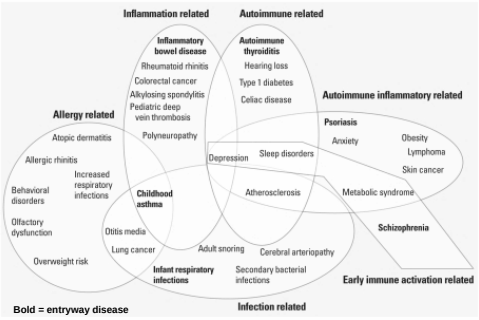
Do prevalent EDCs, such as triclosan, negatively affect human immune function?

Why study immune function?

- Mounting epidemiological evidence suggests immune homeostasis important for health across the life course
- Many prevalent diseases are part of emerging complex “patterns” of disease
- Immune dysfunction is often an underlying mechanism of disease patterns

Dietert RR et al. (2010) *Environ Health Perspect* 118(8):1091-9

Example: Six patterns of immune-related diseases



Dietert RR et al. (2010) *Environ Health Perspect* 118(8):1091-9

Why triclosan and immune function?

- Many research studies show association between exposure to EDCs and different disease outcomes
- Immune dysfunction often involved in disease development
- Lack of epidemiological data examining whether exposure to prevalent EDCs such as triclosan affects immune function

Hypothesis

Exposure to triclosan leads to impaired immune function

Source of data

- National Health And Nutrition Examination Survey (NHANES)
- CDC program of studies designed to assess the health and nutritional status of adults and children in the United States
- Combines interviews and physical examinations/lab data
- Since the early 1960s, examines a nationally representative sample of about 5,000 persons each year

http://www.cdc.gov/nchs/nhanes/about_nhanes.htm#intro

Source of data

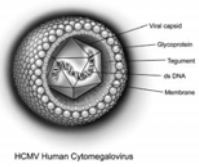
- We used NHANES data from the years 2003-2006
- Exposure: urinary levels of triclosan
- Immune function outcomes
  - -two measurements:
    (1) reported diagnosis of allergies/hay fever
    (2) serum cytomegalovirus (CMV) antibodies

Why allergies and CMV antibodies as measures of immune function?

- Because these data exist in NHANES!
- Allergies result from improper response of the immune system to normally harmless substances
- Therefore, we can use diagnosis of allergies as an indication of immune dysfunction or dysregulation
- Additionally, high and increasing prevalence of allergies in children (up to 1/3 of general population!)

Cytomegalovirus

- Member of the herpes virus family
- Useful as marker of immune function because:
  - -primary infection usually occurs at a young age
  - -the virus persists in the infected host for life
  - -containment of the virus becomes a top priority for the immune system



HCMV Human Cytomegalovirus

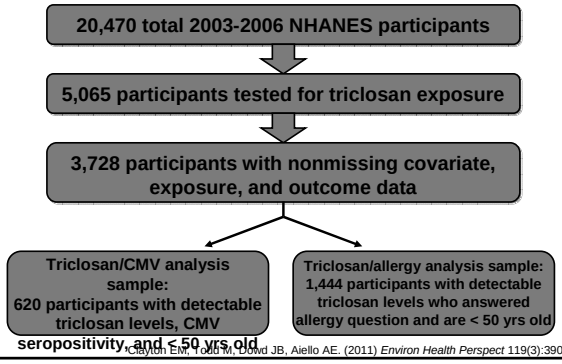
- High antibody levels indicate that the cellular arm of the immune response is less effective in keeping the virus in a persistent latent state

Hypothesis

Exposure to triclosan leads to impaired immune function

urinary triclosan → allergy/hay fever or CMV antibodies

Analytic sample scheme



Clayton EM, Todd M, Dowd JB, Aiello AE. (2011) *Environ Health Perspect* 119(3):390-6

Statistical methods

- All models used sampling weights and adjusted for NHANES complex survey design
- Ordinary least squares regression models for continuous CMV antibody level outcome
- Logistic regression models for dichotomous allergy/hay fever outcome
- Models stratified by age (< 18 yrs vs. ≥ 18 yrs)
- Two models for each outcome:
  - -Model 1: controlled for age, sex, race, and creatinine
  - -Model 2: model 1 + BMI, family income, and education

Clayton EM, Todd M, Dowd JB, Aiello AE. (2011) *Environ Health Perspect* 119(3):390-6

Description of study population, NHANES 2003-2006

- Mean age: 35 years – 50.5% male
- Mean urinary triclosan concentration: 116.3 ng/mL
- 46.7% CMV seropositive
- 33.8% with allergies or hay fever
- Race/ethnicity, income, and education representative of US population

Clayton EM, Todd M, Dowd JB, Aiello AE. (2011) *Environ Health Perspect* 119(3):390-6

Estimated triclosan levels by sociodemographic characteristics, NHANES 2003-2006

Characteristic	Mean (ng/mL)	*p*-value
Sex		**0.008**
Male	**136.76**	
Female	**95.38**	
Race		**0.095**
White	**110.56**	
Black	**110.74**	
Mexican American	**160.59**	
Other groups	**119.56**	
Family income quartile		**0.119**
1 (lowest)	**94.80**	
2	**103.94**	
3	**113.41**	
4 (highest)	**138.06**	

No statistically significant differences in [triclosan] by education, CMV seropositivity, or allergy/hay fever diagnosis

Clayton EM, Todd M, Dowd JB, Aiello AE. (2011) *Environ Health Perspect* 119(3):390-6

Association between triclosan levels and immune function measured by CMV antibody levels, NHANES 2003-2004

	Model 1	
Independent variable	**< 18 years of age (n = 252)**	**≥18 years of age (n = 368)**
Ln(triclosan) (ng/mL)	0.003	-0.024
Age (years)	-0.026	**0.020 (p<0.001)**
Male	-0.093	**-0.316 (p<0.001)**
Creatinine (mg/dL)	0.001	0.001
Race (ref: white)		
Non-Hispanic Black	0.039	0.123
Mexican American	0.028	0.093
Other race/ethnic groups	-0.092	-0.081

Clayton EM, Todd M, Dowd JB, Aiello AE. (2011) *Environ Health Perspect* 119(3):390-6

Association between triclosan levels and immune function measured by CMV antibody levels, NHANES 2003-2004

	Model 1		Model 2	
Independent variable	**< 18 years of age (n = 252)**	**≥18 years of age (n = 368)**	**< 18 years of age (n = 252)**	**≥18 years of age (n = 368)**
Ln(triclosan) (ng/mL)	0.003	-0.024	0.012	-0.022
Age (years)	-0.026	**0.020 (p<0.001)**	-0.025	**0.021 (p<0.001)**
Male	-0.093	**-0.316 (p<0.001)**	-0.130	**-0.311 (p<0.01)**
Creatinine (mg/dL)	0.001	0.001	0.001	0.000
Race (ref: white)				
Non-Hispanic Black	0.039	0.123	0.077	0.046
Mexican American	0.028	0.093	0.109	-0.045
Other race/ethnic groups	-0.092	-0.081	-0.003	-0.136
BMI (kg/m²)			0.005	-0.003
Family income quartiles (ref: low)				
Quartile 2			-0.176	-0.109
Quartile 3			-0.276	-0.122
Quartile 4			-0.063	-0.353
Head of household education (ref: <HS)				
Completed high school			0.193	-0.095
> High school			0.121	-0.096

Clayton EM, Todd M, Dowd JB, Aiello AE. (2011) *Environ Health Perspect* 119(3):390-6

Association between triclosan levels and immune function measured by allergies or hay fever diagnosis, NHANES 2003-2006

	Model 1	
Independent variable	**< 18 years of age (n = 252)**	**≥18 years of age (n = 368)**
Ln(triclosan) (ng/mL)	**1.245 (p<0.05)**	1.004
Age (years)	1.043	1.015
Male	1.396	0.624
Creatinine (mg/dL)	0.999	0.999
Race (ref: white)		
Non-Hispanic Black	1.199	0.781
Mexican American	**0.439 (p<0.05)**	**0.578 (p<0.05)**
Other race/ethnic groups	1.202	0.807

Clayton EM, Todd M, Dowd JB, Aiello AE. (2011) *Environ Health Perspect* 119(3):390-6

Association between triclosan levels and immune function measured by allergies or hay fever diagnosis, NHANES 2003-2006

	Model 1		Model 2	
Independent variable	**< 18 years of age (n = 252)**	**≥18 years of age (n = 368)**	**< 18 years of age (n = 252)**	**≥18 years of age (n = 368)**
Ln(triclosan) (ng/mL)	**1.245 (p<0.05)**	1.004	**1.257 (p<0.01)**	0.996
Age (years)	1.043	1.015	1.023	1.014
Male	1.396	0.624	1.379	0.631
Creatinine (mg/dL)	0.999	0.999	0.999	0.999
Race (ref: white)				
Non-Hispanic Black	1.199	0.781	1.303	0.803
Mexican American	**0.439 (p<0.05)**	**0.578 (p<0.05)**	0.588	0.755
Other race/ethnic groups	1.202	0.807	1.226	0.880
BMI (kg/m²)			1.024	1.004
Family income quartiles (ref: low)				
Quartile 2			0.691	1.216
Quartile 3			**0.498 (p<0.05)**	0.801
Quartile 4			0.760	1.099
Head of household education (ref: <HS)				
Completed high school			**2.488 (p<0.05)**	1.638
> High school			**3.107 (p<0.05)**	**2.198 (p<0.05)**

Clayton EM, Todd M, Dowd JB, Aiello AE. (2011) *Environ Health Perspect* 119(3):390-6

Results

Outcome 1: CMV antibody levels

-Increasing levels of urinary triclosan show no statistical association with levels of CMV antibodies in children or adults

Outcome 2: Allergy/hay fever diagnosis

-Increasing levels of urinary triclosan are statistically associated with diagnosis of allergies/hay fever in children (<18 yrs) but not adults

Clayton EM, Todd M, Dowd JB, Aiello AE. (2011) *Environ Health Perspect* 119(3):390-6

How can we explain these results?

Triclosan and allergies in children:

-May support the “hygiene hypothesis,” which argues that we may be “too clean”

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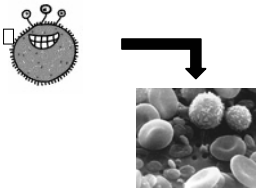

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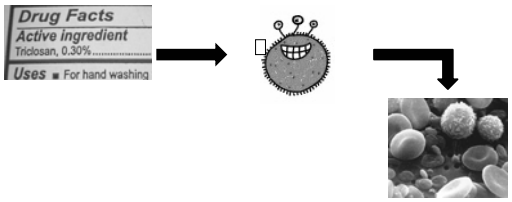
Triclosan and allergies in children:

-May support the “hygiene hypothesis,” which argues that we may be “too clean”



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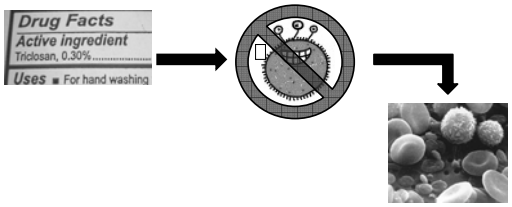

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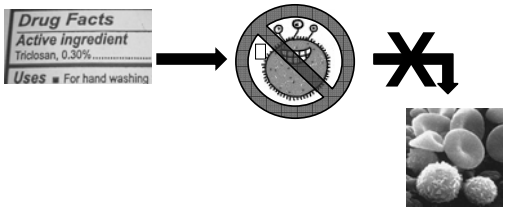

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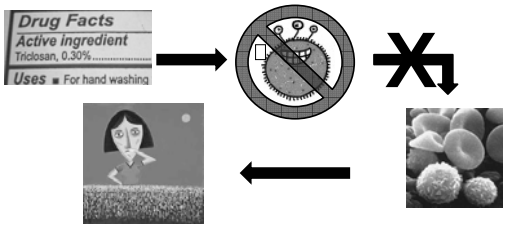

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Limitations

- Cross sectional study
- No consideration of mixture effects
- No consideration of psychosocial stress or genetics
- Allergy/hay fever outcome was self-report of doctor diagnosis
- Small sample sizes for age-stratified analyses

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Strengths

- Nationally representative sample
- Looks at two distinct markers of immune function
- Examines children and adults separately
- Addresses literature gap on effect of EDCs (triclosan) on immune function

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Remaining questions

- Does triclosan exposure *cause* adverse health outcomes in humans?
- How does the timing and quantity of triclosan exposure over the life course influence disease susceptibility and severity?
- How does triclosan-related resistance develop and spread?
- What is the effect of triclosan on bacterial biofilms and commensal bacteria?
- What are the risks associated with interaction of multiple antimicrobial chemicals?

Presentation Outline

- The development of sanitation and hygiene
- Today's use (and misuse?) of antibacterial products
- The antibacterial agent triclosan and its impact on immune function
- Practical implications for public health professionals

Regulatory agencies in the U.S.

- Environmental Protection Agency (EPA) – regulates triclosan in pesticides and surface disinfectants
- Food and Drug Administration (FDA) – regulates triclosan in personal care products and topical antiseptics

Coulborn RM, Rees Clayton E, Aiello AE. (2010) *ACS Symposium Series* pp 367-82

Triclosan regulation by FDA

- FDA advisory panel, 1974: insufficient evidence to support the safety and effectiveness of triclosan
- Debate over safety of triclosan such that final monograph with regulatory standards still not issued
- FDA announced in 2010 that it would review existing data on triclosan, with findings announced to the public in spring 2011 (still waiting…)

Coulborn R, Rees Clayton E, Aiello AE. (2010) *ACS Symposium Series* pp 367-82
http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM206222.pdf

Regulations in other countries

- German, Finnish, Danish governments discourage regular use of antibacterial products
- Four major UK grocery chains have banned triclosan-containing products
- Europe has banned use of triclosan in textiles
- March 2010: EU removed triclosan from list of additives in plastic food-contact materials

Kepner J. (2004) *Pesticides and You* pp 9-11
Dann AB, Hontela A. (2011) *J Appl Toxicol* [Epub ahead of print]

Recommendations?

- Great need for additional studies on human health impacts of triclosan exposure
- Stay tuned for FDA conclusions
- Read labels when purchasing products
- Encourage and practice good hygiene habits
- Wash hands, but with plain soap; use alcohol-based hand sanitizer if soap and water unavailable

http://www.thisispublichealth.org/CampaignIdeas.html

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UM CIAHD (ERC)
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Thank you for your attention!

Bisphenol A (BPA)

- Industrial chemical commonly found in polycarbonate plastics, epoxy resins, dental sealants
- Animal and human data suggest BPA is an EDC
- Recent animal studies show very low doses (>200 times below the current EPA recommended dose) of BPA are associated with adverse health outcomes

BPA results

Estimated population mean BPA concentration (NHANES 2003-2006):

4.4 ng/mL

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Estimated mean BPA levels by sociodemographic characteristics, NHANES 2003-2006

Characteristic	Mean BPA (ng/mL)	*p*-value
Race		< 0.001
Non-Hispanic White	4.04	
Non-Hispanic Black	5.38	
Mexican American	5.32	
Other race/ethnicity	5.21	
Family income quartile		0.001
1 (lowest)	5.73	
2	4.61	
3	4.37	
4 (highest)	3.75	

No statistically significant differences in [BPA] by sex, education, CMV seropositivity, or allergy/hay fever diagnosis

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Association between BPA levels and allergy/ hay fever diagnosis, NHANES 2003-2006

	Model 1		Model 2	
Independent variable	< 18 years of age (n = 793)	≥ 18 years of age (n = 1,340)	< 18 years of age (n = 793)	≥ 18 years of age (n = 1,340)
Ln(BPA) (ng/mL)	0.910 (0.113)	0.896 (0.098)	0.933 (0.123)	0.903 (0.094)
Age (years)	1.045 (0.032)	1.001 (0.005)	1.029 (0.035)	1.003 (0.005)
Male	1.679 (0.262)**	0.707 (0.124)	1.632 (0.236)**	0.692 (0.123)
BMI (kg/m^2)			1.023 (0.016)	1.006 (0.010)
Creatinine (mg/dL)	1.000 (0.002)	1.000 (0.001)	1.000 (0.002)	1.000 (0.001)
Race				
Non-Hispanic black	1.085 (0.256)	0.718 (0.121)	1.167 (0.292)	0.778 (0.133)
Mexican American	0.415 (0.107)**	0.527 (0.100)**	0.541 (0.155)*	0.724 (0.167)
Other race/ethnic groups	1.247 (0.367)	0.728 (0.218)	1.286 (0.399)	0.815 (0.265)
Family income quartile				
2			0.783 (0.344)	1.063 (0.230)
3			0.646 (0.169)	0.839 (0.248)
4			0.956 (0.331)	1.220 (0.265)
Head of household education				
Completed high school			1.669 (0.689)	1.775 (0.438)*
> High school			2.109 (0.990)	2.312 (0.436)***

Data are ORs (SEs) for allergy or hay fever diagnosis among unit changes (or categories) of the independent variable. Models are logistic regressions with dependent variable over diagnosed with allergies or hay fever. Model is estimated among respondents with detected levels of BPA. Model 1 includes age, gender, creatinine, and race as covariates; model 2 includes all of these plus BMI, family income, and educational attainment.
*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$.

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Association between BPA levels and CMV antibody levels, NHANES 2003-2004

	Model 1		Model 2	
Independent variable	< 18 years of age (n = 335)	≥ 18 years of age (n = 452)	< 18 years of age (n = 335)	≥ 18 years of age (n = 452)
Ln(BPA) (ng/mL)	–0.104 (0.053)	0.186 (0.034)***	–0.113 (0.047)*	0.158 (0.035)***
Age (years)	–0.011 (0.013)	0.017 (0.004)***	–0.012 (0.012)	0.018 (0.004)***
Male	–0.151 (0.117)	–0.250 (0.078)**	–0.154 (0.109)	–0.239 (0.078)**
BMI (kg/m^2)			0.004 (0.008)	0.001 (0.006)
Creatinine (mg/dL)	0.001 (0.001)*	–0.001 (0.001)	0.001 (0.001)*	–0.001 (0.001)
Race				
Non-Hispanic black	0.179 (0.086)	0.158 (0.082)	0.145 (0.103)	0.095 (0.093)
Mexican American	0.105 (0.084)	0.128 (0.108)	0.090 (0.097)	–0.006 (0.115)
Other race/ethnic groups	0.288 (0.150)	–0.111 (0.141)	0.294 (0.154)	–0.211 (0.168)
Family income quartile				
2			–0.275 (0.134)	–0.055 (0.101)
3			–0.275 (0.164)	–0.166 (0.099)
4			–0.107 (0.138)	–0.305 (0.132)*
Head of household education				
Completed high school			0.070 (0.148)	–0.136 (0.108)
> High school			–0.015 (0.105)	–0.136 (0.154)

Data are β-coefficients (SEs) for each independent variable in the regression models. Models are OLS regressions with CMV antibody level as the dependent variable. The model is estimated among respondents with detected levels of BPA. Model 1 includes age, sex, creatinine, and race as covariates; model 2 includes all of these plus BMI, family income, and educational attainment.
*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$.

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BPA conclusions

- Increasing levels of urinary BPA show no statistical association with diagnosis of allergies/hay fever in children or adults

- Increasing levels of urinary BPA are statistically associated with:
  - LOWER levels of CMV antibodies in children
  - HIGHER levels of CMV antibodies in adults

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Potential explanation of BPA results?

- Research using rat cells suggests BPA affects macrophage function
- Impaired macrophage function may allow easier replication of the virus
- The host may then need to increase antibody production to counteract increasing viral load
- Unclear why different relation in children and adults; quantity, duration, timing of exposure important?