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The Impact of Early-Life Exposure to Antimicrobials on Asthma and Eczema Risk in Children

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Abstract

Purpose of Review—We examined recent research on associations of prenatal and early-childhood exposure to the antimicrobial compounds, triclosan, and parabens, with the risk of asthma and eczema in children. We will discuss potential biological mechanisms of this association and highlight strengths and limitations of the study design and exposure assessment of current findings.

Recent Findings—Results of available toxicological and epidemiologic studies indicate a potential link of triclosan and paraben exposures with asthma and eczema in children, as well as changes in microbiome diversity and immune dysfunction, which could possibly mediate an association with the health outcomes.

Summary—A small number of studies suggest that triclosan and paraben exposures could be related to the risk of asthma and eczema in children. Although current findings are far from conclusive, there is emerging evidence that changes in microbiome diversity and immune function from antimicrobial exposure may mediate these relations.

Keywords

Triclosan; Parabens; Children's health; Eczema; Asthma; Immune system

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Introduction

Environmental exposures during the prenatal period and early-childhood may lead to alterations in the maturation of the immune system, impacting its development in the growing fetus, infant, and child. A number of early-life environmental exposures have been identified as risk factors for the development of asthma and eczema in children, including environmental tobacco smoke, aeroallergens, air pollution, microbial diversity, and environmental compounds [1–3, 4•, 5, 6•, 7•]. Among environmental compounds, triclosan and parabens are of concern in the development of asthma and eczema given their ubiquitous nature, known antimicrobial activity, and potential immunotoxic properties.

Childhood asthma and other allergic diseases pose significant burdens on children's health [8–12]. In 2015, the prevalence of asthma among children aged 5–14 years in the USA was 9.7%. Moreover, the total medical costs associated with asthma increased from \$39.3 billion to \$67.5 billion between 2008 and 2012 [13, 14]. Thus, identifying modifiable risk factors for asthma and allergic disease has tremendous potential to reduce the burden of these diseases and improve the quality of life for children.

Little is known regarding which life stages are most susceptible to these exposures. Some children who develop allergic diseases follow the “atopic march,” a pathway in which genetically predisposed children develop immune dysregulation leading to allergic sensitization (the production of immunoglobulin E (IgE) antibodies), which may lead to increased risk of allergic diseases including asthma and eczema during early-childhood [4•, 5, 6•, 7•]. Although asthma and eczema affect different organs, most patients have elevated concentrations of inflammatory cells including antigen presenting cells, eosinophils, and elevated immune response markers including cytokines (interleukins (IL)) and IgE levels in the blood [15]. Thus, exposure to environmental factors known to elicit these types of immune responses may also increase the risk for asthma and eczema in children.

There are two compelling reasons suggesting that early-life antimicrobial exposure could adversely affect immune development to increase the risk of asthma and eczema in children. First, decreased exposure to microbes, due to antimicrobial use, during pregnancy and in early-childhood may alter the priming of the immune system, increasing the risk of allergic disease development. This priming effect is related to the “hygiene hypothesis” which posits that early-life exposure to microbes decreases the risk of developing allergic diseases by stimulating the immune system contributing to its development [16, 17•]. Second, direct exposure of antimicrobial compounds through oral and dermal routes may alter the microflora on the skin or in the gut inducing a hypersensitive reactive state of immune system receptors in these organs, thereby increasing the risk for hypersensitivity diseases such as asthma and eczema [18•]. This seems especially plausible given the important role of the skin microbiota in the development of allergic sensitization and the potential for dermal antimicrobial exposure to affect skin and gut microbial communities [19•].

To better understand the potential role antimicrobial exposure plays in asthma and eczema risk in children, we will examine recently published studies assessing prenatal and early-

childhood triclosan and paraben exposures in relation to microbiome diversity, immune function, and the risk of asthma and eczema in children.

Triclosan and Paraben Background

Triclosan is a man-made antimicrobial compound used in consumer products. Triclosan has bactericidal or bacteriostatic activity, which act through inhibition of enoyl reductases that are essential to synthesize fatty acids and disrupts cell membrane integrity [20, 21]. Triclosan exposure is prevalent among persons in the USA, including pregnant women, infants, and children [22•, 23–31]. Exposure occurs primarily through oral intake (e.g., toothpaste and mouthwash) and dermal absorption (e.g., soaps and cosmetics) [32]. After ingestion or absorption, triclosan is glucuronidated and primarily excreted in urine [33]. Triclosan does not persist in the body and has an estimated biological half-life of approximately 21 h [33]. Geometric mean urinary triclosan concentrations in the US (NHANES 2003–2004) were 13 µg/L and there were significant differences in children and adolescents compared with older adults with concentrations generally decreasing with age [22•]. Triclosan has also been detected in the plasma and breast milk of lactating women [34, 35•]. However, triclosan levels were much lower or below the limit of detection in plasma and breast milk compared with urine concentrations [34, 35•]. Because of concerns about antimicrobial resistance and developmental toxicity, the FDA issued rulings in 2016 and 2017 that triclosan could no longer be used in over-the-counter (OTC) consumer and healthcare antiseptic products [36].

Parabens are a group of phenols used primarily as preservatives in pharmaceuticals, foods, cosmetics, and personal care products to prevent the growth of microorganisms [37]. While the mechanism by which parabens destroy microbes is not clear, parabens may disrupt bacterial membrane integrity and there is also evidence of parabens stimulating the release of histamine [38]. Paraben exposure typically occurs through dermal and oral absorption from using cosmetic products and consuming foods, respectively, that contain parabens [39, 40]. Similar to triclosan, parabens have a relatively short half-life (~ 2–3 h) [41], and are primarily excreted in urine as both glucuronide conjugates and para-hydroxybenzoic acid [42•]. Methyl, propyl, ethyl, and butyl parabens have been detected in urine samples of US children and adults; however, ethyl and butyl paraben detection rates were lower (42–47%) compared with methyl and propyl paraben (92–99%) and median ethyl and butyl paraben urine concentrations were at least one order of magnitude lower than methyl and propyl paraben levels [42•]. Methyl and propyl paraben exposure is also ubiquitous among pregnant women [43]. Biomonitoring studies using NHANES 2005–2006 found differences in median concentrations of methyl and propyl parabens by both sex and race/ethnicity, with significantly higher concentrations in females compared with males. Moreover, non-Hispanic blacks had higher odds of having concentrations greater than the 95th percentile compared with non-Hispanic whites. The FDA has determined that parabens are safe to use in cosmetics and food products [37].

Summary of Findings

We identified toxicological and epidemiologic studies assessing the association between triclosan and paraben exposure and asthma and eczema in children published over the last 5 years (2014–2019). We used Google scholar to search for manuscripts examining associations between triclosan and parabens with allergic disease outcomes between 2014 and July 2019. We only included methyl and propyl paraben exposures for this review due to low detection rates of other paraben esters [42•]. Our search included the following terms: triclosan, paraben, methyl paraben, propyl paraben, antimicrobial compound, asthma, respiratory function, lung function, forced expiratory volume, vital capacity, pulmonary function, eczema, atopic dermatitis, allergy, rhinitis, atopy, sensitization, allergic sensitization, immunoglobulin E, IgE, skin prick test, immune function, cytokine, inflammation, microbiome diversity, gut microbiome, and skin microbiome in various combinations. In addition, we reviewed the references from relevant original research and review articles using both Google scholar and PubMed. After screening titles, abstracts, and/or full manuscripts, we identified 2 animal and 12 epidemiology studies that we summarize below. A summary of all 12 epidemiology studies can be found in Table 1. We have organized the outcomes of the toxicological and epidemiological studies into three broad categories: immune system biomarkers, asthma or eczema, and microbiome diversity.

Antimicrobial Compounds and Immune System Biomarkers

Antimicrobial chemical exposures may induce immune system imbalances by enhancing Type 2 helper T cell (Th2) dominance consistent with immune response patterns found in Type 1 hypersensitivity disorders such as asthma and eczema [53•, 55]. There have been 2 animal and 6 epidemiologic studies examining associations between triclosan/parabens and immune system biomarkers.

Triclosan and Immune System Biomarkers

An experimental study in mice found that dermal exposure to triclosan caused increased frequency of immune system biomarkers including, B cells, T cells, and natural killer (NK) cells in skin lymph nodes [56]. Another animal study also found positive associations between triclosan and Th2 cytokines (IL-4 and IL-13) and dust mite-specific IgE concentrations in sensitized mice [57•]. There is also evidence of triclosan promoting skin sensitization to peanut. In a study of mice, researchers administered a 50 µg epicutaneous dose of peanut extract and found that increased triclosan exposure caused higher peanut-specific IgE and IgG compared with naïve mice; when subsequently peanut challenged, triclosan-exposed mice developed anaphylaxis [58].

Several epidemiological studies report that urinary triclosan levels during pregnancy and in early-childhood were associated with biomarkers of altered immune function including increased levels of IgE, cytokines, and other inflammatory markers (Fig. 1a). Using data from children aged 6–18 years ($n = 837$) in the National Health and Nutrition Examination Survey (NHANES) conducted from 2005 to 2006, researchers observed an increased odds of elevated IgE concentrations (OR 1.91, 95% CI 1.02, 3.57) with increasing urinary triclosan

concentrations [44••]. In the Maternal-Infant Research on Environmental Chemicals (MIREC) cohort of mother-baby dyads in Canada ($n = 1219$), prenatal urinary triclosan concentrations (4th quartile compared with 1st) were associated with increased odds of elevated IL-33 in cord blood (OR 1.32, 95% CI 0.85, 2.05), but no association was observed with total IgE (OR 1.03, 95% CI 0.63, 1.68) in cord blood [50]. Data from a randomized, double-blind, placebo trial of vitamin D supplementation during pregnancy, the Vitamin D Antenatal Asthma Reduction Trial (VDAART, $n = 386$ – 389), was used to investigate the relation of prenatal and childhood urinary triclosan concentrations with food and environmental sensitization at age 3, measured by serum specific IgE [52••]. Overall, the study found no association between both prenatal and childhood urinary triclosan and these immune system biomarkers [52••]. In a nested case-control study of preterm birth (LIFECODES, $n = 482$), repeated urinary triclosan concentrations were associated with the pro-inflammatory cytokines IL-1 β , IL-6, tumor necrosis factor α (TNF α) and C-reactive protein (CRP), and the anti-inflammation marker IL-10 in maternal plasma during pregnancy. Each interquartile range increase in urinary triclosan concentrations was associated with a 12.5% (95% CI 3.67, 22.0) increase in CRP, a 7.95% (95% CI 1.95, 14.3) increase in IL-10, and a 7.93% (95% CI 3.82, 12.2) increase in TNF α in maternal plasma [49••]. Using data from the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS, $n = 301$ – 306) Study [53••], a US longitudinal cohort study in an agricultural community in Salinas Valley, California investigated associations between prenatal urinary triclosan concentrations and atopy measured by T-helper cells at ages two, five, and 7 years. Geometric mean urinary triclosan concentrations were modestly higher in this cohort (22.4 $\mu\text{g/L}$) compared with NHANES (13 $\mu\text{g/L}$) [22•]. The authors reported a 2.33% (95% CI -0.56 , 5.3) increase in Th1/Th2 cell ratio in children at ages 2–7 years with a 2-fold increase in prenatal urinary triclosan concentrations [53••].

Parabens and Immune System Biomarkers

Several epidemiological studies found evidence of parabens perturbing the immune system. In the CHAMACOS study, prenatal urinary methyl paraben concentrations were associated with fewer Th1 cells, suggesting an immune-mediated response to paraben exposure [53••]. Specifically, researchers found a 3.54% (95% CI -6.78 , -0.18) decrease in Th1 cells for every 2-fold increase in prenatal urinary methyl paraben [53••]. Results from the NHANES (2005–2006) indicate an increased odds of aeroallergen sensitization (serum IgE 0.35 kU/L) with increasing methyl (OR 1.15, 95% CI 1.06, 1.26) and propyl (OR 1.18, 95% CI 1.08, 1.29) paraben urine concentrations in children age 6–18 years old [44••]. The previously mentioned VDAART study also assessed the associations of methyl and propyl paraben urine concentrations and allergic outcomes. Similar to triclosan, no association was observed of both prenatal and childhood paraben urine concentrations with food and environmental sensitization [52••]. However, there was an increased odds of sensitization (serum IgE 0.35 kU/L) in boys at age 3 (OR 2.47, 95% CI 1.16, 5.37) comparing the third with first tertile of childhood propyl paraben urine concentrations. In the LIFECODES study, increasing methyl paraben urine concentrations were associated with a 6.7% increase in IL-6 (95% CI 0.02, 13.8), but not the other inflammatory biomarkers [49••].

Antimicrobial Compounds and Asthma and Eczema in Children

There have been an additional 12 studies, examining associations between triclosan/parabens and asthma/eczema in children (Fig. 1b).

Triclosan and Asthma and Eczema Studies

A prospective pregnancy and birth cohort study from France (EDEN), found no associations between increasing prenatal urinary triclosan concentrations and asthma risk (HR 0.99, 95% CI 0.92, 1.07) in boys; girls were not included in this study [51••]. A recent small nested case-control study, the Melbourne Atopy Cohort ($n = 60$), observed no association between triclosan concentrations in breast milk collected at 3 months and eczema at 1 year of age (HR 0.83, 95% CI 0.27, 2.55) [35•]. Data from VDAART was used to examine the relation of prenatal and childhood urinary triclosan exposure with child asthma at age 3 years. No association was observed between asthma and prenatal (OR 0.86, 95% CI 0.5, 1.46) or childhood (OR 0.72, 95% CI 0.42, 1.23) urinary triclosan [52••]. However, prenatal urinary triclosan was associated with and increased odds of asthma in boys (OR 1.25, 95% CI 0.61, 2.57) and a decreased odds in girls (OR 0.42, 95% CI 0.16, 1.01) [52••]. Using a cohort study of mother-child pairs (The Mount Sinai Children's Environmental Health Study, $n = 159$), Buckley et al. found no association of prenatal urinary triclosan with asthma (OR 0.88, 95% CI 0.57, 1.37) or eczema (OR 1.03, 95% CI 0.75, 1.42) in children at ages 6–7 years [54••]. Finally, in the CHAMACOS study, Berger et al. reported that prenatal urinary triclosan concentrations were associated with asthma at age 7 years (OR 1.13, 95% CI 0.99, 1.29) [53••]. A study using NHANES (2005–2006, $n = 837$) data found that urinary triclosan concentrations in children at age 6–18 years were associated with the prevalence of atopic asthma and eczema [44••]. A monotonic dose-response association between increasing urinary triclosan concentrations and atopic asthma was also observed, but there were no associations with eczema (OR 0.68, 95% CI 0.29, 1.57) [44••]. Another study utilizing NHANES (2005–2010, $n = 639$) data found positive associations between urinary triclosan and asthma symptom exacerbation (OR 1.79, 95% CI 1.01, 3.15) [45••]. Finally, investigators using the National Center for Child Health and Development study ($n = 117$) in Japan, reported no association between triclosan product use in children less than 15 years old and current asthma and/or eczema (urinary triclosan concentrations were under the limit of detection) [47••].

Paraben and Asthma and Eczema Studies

The VDAART study did not observe an association between urinary paraben concentrations and asthma in children. However, there was evidence of sex modifying the association between childhood methyl paraben urine concentrations and odds of asthma (males OR 0.57, 95% CI 0.28, 1.13 and females OR 1.81, 0.62, 5.46) [52••]. Neither the CHAMACOS nor EDEN cohorts reported associations between methyl and propyl paraben and asthma risk [51••, 53••]. The Melbourne Atopy cohort, a nested case-control study of children with a family history of asthma or atopic disease, found a positive association of methyl (OR 3.69, 95% CI 0.97, 14.0) and propyl (OR 1.94, 95% CI 0.67, 5.65) paraben measured from breastmilk collected at age 3 months with eczema at age 1 year [35•]. Results from an

analyses of the 2005–2006 NHANES analyses, indicated an increased odds of atopic asthma with increasing methyl (OR 1.11, 95% CI 0.84, 1.47) and propyl (OR 1.05, 95% CI 0.91, 1.21) paraben urine concentrations [44••]. A more recent NHANES analyses, using data from 2005 to 2014, observed an increased prevalence odds of reporting emergency department visits with increasing methyl (OR 2.61, 95% CI 1.40, 4.85) and propyl (OR 2.18, 95% CI 1.22, 3.89) paraben urine concentrations among boys with asthma [48••]. The NCCHD cross-sectional study of children with eczema also found higher methyl paraben urine concentrations in children less than 15 years old with current eczema. Researchers also reported a positive association between paraben use in the previous 3 days and parent-reported eczema (OR 4.61, 95% CI 1.23, 17.3) [47••]. In the mother-child Danish study ($n = 845$), investigators examined associations between parent-reported application of moisturizer on children (ages 4–9 years) and urinary paraben concentrations [46••]. Methyl and propyl paraben urine concentrations in children with eczema were significantly higher (237%, 95% CI 191, 291; and 165%, 95% CI 129, 206, respectively) compared with children without eczema. [46••].

Antimicrobial Exposure and Microbiome Diversity

There is increasing evidence that the microbiome plays a role in allergic disease development. Recent studies have identified differences in skin, oral, and gut microbiome diversity, which may influence immune function; this has been referred to as the “microflora hypothesis” [16, 18•, 19•, 59, 60•, 61•, 62••]. The microflora hypothesis, an extension of the hygiene hypothesis [17•], suggests that altered microbiome diversity may promote immune dysfunction leading to allergic disease development [16, 17•, 18•]. Microbiome diversity can be defined by the abundance, types, and distribution of microorganisms inhabiting the body. The gut microbiome is typically dominated by bacteria of two phyla, Bacteroidetes and Firmicutes [63, 64]. In humans, differences in the abundance distribution and ratio of these bacteria, low diversity, have been linked to several adverse health outcomes [64–67].

Results from birth cohort and mice studies suggests that a deficiency or skewed microbial colonization of the lung and/or gut may result in altered immune function increasing the risk for atopy and viral respiratory infections [68•, 69••]. A recent study of asthma and the microbiome found evidence of microbes in the gut influencing immune function in the lung via a hypothesized “gut-lung axis” [70]. Thus, early-life exposure to antimicrobial compounds such as triclosan and parabens may affect gastrointestinal or respiratory tract microbiome diversity to increase the risk of developing asthma and eczema in children.

Triclosan and Microbiome Diversity

Triclosan is effective against many strains of bacteria and may alter the bacterial flora of the skin, oral mucosa, and intestinal track [32, 71]. Because triclosan has bactericidal activity and exposure is predominately through oral routes [32, 72, 73], it may destroy bacteria in the gut and potentially disrupt the gut microbiome. Relatively few studies have examined triclosan exposure and its impact on the gut microbiome. Three experimental studies, one in fish and two in rats, found that triclosan exposure caused altered gut microbiome diversity, increased abundance of Bacteroidetes, and decreased abundance of Firmicutes [74, 75]. A

recent study evaluated triclosan-induced gut microbiome changes and airway hyperresponsiveness in aeroallergen sensitized mice reporting changes of the gut microbiome in response to triclosan [57•].

A small crossover study of 16 healthy adults did not observe associations between the use of triclosan containing products and gut microbiome diversity; however, they did observe statistically significant differences in the relative abundance of several Bacteroidetes and Firmicutes taxa when comparing the high and low triclosan exposure groups before correcting for multiple comparisons [76]. Another study examined the association between triclosan concentrations in breastmilk and infant fecal microbiome diversity. Differences in the diversity of fecal microbiome were observed in infants whose mothers had detectable levels of triclosan in their breast milk ($n = 12$) compared with those with non-detectable concentrations ($n = 33$) [77•]. A recent review described preliminary analyses examining environmental exposures on the diversity of the gut microbiome of farm children; however, they did not find evidence that gut microbiome diversity mediates the relationship between environmental exposures and asthma in these children [17•].

Parabens and Microbiome Diversity

We were unable to identify any studies examining the relations between paraben exposure and microbiome diversity.

Conclusions

The available animal and epidemiological literature suggest that early-life exposure to triclosan and parabens has the potential to alter immune function and microbiome diversity to increase the risk of allergic diseases in childhood. While the results to date are far from conclusive, additional studies are warranted given the ubiquitous nature of triclosan and paraben exposures among pregnant women and children and available evidence suggesting a potential effect of these chemicals on childhood asthma and allergy risk.

There were several notable limitations of the available epidemiological studies. Many were cross-sectional, limiting the interpretation of the results since we cannot discern whether exposure to triclosan and parabens occurred before or after the outcome was assessed. Additionally, triclosan and parabens have a relatively short half-life and most studies only collected a single spot urine sample to determine exposure levels [44•, 45•, 46•, 47•, 48•, 49•, 52•]. The within-person variation of urinary triclosan concentrations during pregnancy and childhood could have introduced exposure misclassification in these studies. While there were five prospective studies with more than one exposure measurement, [35•, 50, 51•, 53•, 54•] additional samples may be necessary to accurately assess exposure. Relatedly, there was variation in how (urine vs. serum vs. breastmilk) and when (prenatal vs. childhood) triclosan and paraben exposure was assessed across studies which contributed to variation in urinary triclosan and paraben concentrations across studies as well. Moreover, many studies relied on parent- or self-reported questionnaires to identify asthma or eczema outcomes, which may increase misclassification of the outcome being assessed. Since triclosan and parabens are suspected endocrine disruptors [78–82], there may be differential

susceptibility by sex. Among investigators examining modification by sex, the results were inconsistent [44•, 48•, 49•, 50, 52•, 53•, 54•]. However, some studies were not designed to assess sex modification [51•] and others did not present these results [35•, 45•, 46•, 47•, 59, 60•, 61•, 62•].

This review highlights the potential role that antimicrobial chemical exposure in early life may play in immune function, microbiome diversity, and the risk for asthma and eczema in children. To better identify potential periods of heightened susceptibility to the immunotoxic effects of these compounds, future studies should utilize longitudinal pregnancy and birth cohorts in order to examine links between antimicrobial exposures across the lifespan, immune biomarkers, the microbiome, and asthma/allergy/eczema risk. This would enhance our knowledge of the potential underlying biological mechanism and identify potentially modifiable risk factors for asthma and eczema development in children.

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Fig. 1.
a Associations of triclosan and paraben exposure with immune biomarkers. **b** Associations of triclosan and paraben exposure with child asthma and eczema outcomes. Abbreviations: TCS (triclosan), MP (methyl paraben), PP (propyl paraben), IgE (immunoglobulin E), IL (interleukin), CRP (C-reactive protein), TNF (tumor necrosis factor), and TH (T-helper cell).
 *Note that the timeline is not drawn to scale

Table 1

Triclosan and paraben exposure and allergic outcome epidemiology studies

Study	N	Matrix (units)	Phenol	Concentration (range)	Outcome assessment	Age (years)
Cross-sectional studies						
NHANES 2005–2006 [44••]	837	Urine (ng/mL)		GM (95% CI)	Serum IgE	6–18
		TCS		16 (13, 19)	Self/parent report asthma and eczema	
		MP		42 (35, 50)		
		PP		5.3 (4.0, 7.0)		
NHANES 2005–2010 [45••]	639	Urine (log ng/mL)		GM (95% CI)	Self/parent report asthma	6+
		TCS		1.2 (1.1, 1.2)		
		Asthmatics		1.2 (1.1, 1.3)		
		Urine (ng/mL)		Median (min-max)		
Danish cohort [46••]	845	MP		8.4 (0.5–2870)	Self/parent report eczema	4–9
		With eczema		12 (0.5–1652)		
		PP		0.7 (0.3–2201)		
		With eczema		1.4 (0.3–1878)		
NCCHD [47••]	223	Urine (pmol/Cr)		Mean (min-max)	Self/parent report asthma and eczema	15
		TCS		< LOD		
		MP		8.3 (0–41,151)		
		PP		< LOD		
NHANES 2005–2014 [48••]	4023	Urine (ng/mL)		Median (p25–p75)	Self/parent report asthma	6–19
		MP		31 (10–136)		
		PP		3.7 (0.9–21)		
Prospective studies						
LIFECODES [49••]	482	Urine (ng/mL)		GM (SD)	Serum CRP	1st trimester through 38 weeks.
		TCS		16.0 (6.66)	Serum IL-1β	
		MP		161 (4.28)	Serum IL-6	
		PP		36.1 (5.74)	Serum TNF α	
MIREC [50]	1219	Urine (μg/L)		Median (IQR)	Serum IgE	Birth (cord blood)
		TCS		9.5 (10.2)	Serum IL-33	
EDEN [51••]	587	Urine (μg/L)		Median (p5, p95)	Self/parent report asthma	5 (boys only)

Study	N	Matrix (units)	Phenol	Concentration (range)	Outcome assessment	Age (years)
VDAART [52••]	467	TCS		29 (0.1, 744)		
		MP		118 (7.8, 1730)		
		PP		16 (0.5, 289)		
	467	Urine (ng/mL)		Median (p25–p75)	Serum IgE	3
		TCS		5.5 (2.1, 17)	Self/parent report asthma	
		MP		63 (22, 304)		
CHAMACOS [53••]	297–329	PP		6.8 (2.1, 24)		
		Urine (µg/L)		GM (p25, p75)	Whole blood Th1 cells	7
		TCS		22 (6.0, 112)	Whole blood Th2 cells	
		MP		153 (76, 365)	Self/parent report asthma	
		PP		40 (12, 166)		
		Urine (µg/L)		Median (p25–p75)	Self/parent report asthma	6–7
The Mount Sinai Study [54••]	164	TCS		11 (2.9, 62)	and eczema	
Melbourne Atopy Cohort [35•]	60	Breast milk (ng/mL)		(min–max)	Self/parent report eczema	1
		TCS		0.08–23		
		MP		0.06–18		
		PP		0.04–0.5		

NHANES National Health and Nutrition Examination Study, *GM* geometric mean, *CI* confidence interval, *TCS* triclosan, *MP* methyl paraben, *PP* propyl paraben, *IgE* immunoglobulin E, *NCCHD* National Center for Child Health and Development, *IQR* interquartile range, *IL* interleukin, *CRPC*-reactive protein, and *TNF* tumor necrosis factor, *MIREC* Maternal-Infant Research on Environmental Chemicals, *EDEN* Etudes des Déterminants pré et postnatals du développement et de la santé de l'Enfant, *VDAART* Vitamin D Antenatal Asthma Reduction Trial, *CHAMACOS* Center for the Health Assessment of Mothers and Children of Salinas