Impacts of Psychosocial Environment

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Primary Prevention of Asthma: A Symposium on Current Evidence, Research Needs and Opportunities for Action

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Mental suffering impairs physical well-being and adversely affects the respiratory organs.

Universally understood in the 12th century...

..’ the success of relieving the patient depends largely on an intimate knowledge of the total patient.”

*Treatise on Asthma*

**Maimonides**
Rabenu Moshe Ben Maimon
(1135 - 1204)
Figure 2. Meta-analysis about the effect of stress on atopic disorders.

The stress reaction is neither good nor bad in itself

Depends on circumstances

Stress is useful when it protects us in times of danger or helps us to adapt in times of change.

OPTIMAL BALANCE = HEALTH
Overview Model

External event/Stressor

- Appraisal of demands and coping capabilities

Benign appraisal

Perceived stress

Physical toxins
- Tobacco smoke
- Ambient AP
- Allergens

Negative emotional responses

Appraisal of demands and coping capabilities

Atopic Disease
Airway responses
Lung growth
Social & Physical Toxins Impact Fetal Programming

Measures of Stress & Stress Correlates

► Acute life events:
  – Recent life experiences (job loss, housing problems)
  – Remote life experiences (trauma)

► Chronic strains:
  – Persistent life difficulties (poverty)
  – Role strains (e.g., balancing work & home responsibilities)
  – Racism / Discrimination
  – Community-wide strain / Ecologic level strain
    • community violence
    • collective efficacy/disorder

► Stress Correlates:
  – Pregnancy Anxiety
  – Perceived Stress
  – Depression/Anxiety/PTSD
## Individual-level Stress/Stress Correlates

<table>
<thead>
<tr>
<th>LITERATURE</th>
<th>STUDY TYPE</th>
<th>SUBJECTS</th>
<th>EXPOSURE/OUTCOME</th>
<th>RESULT [+/-; OR/RR/HR (95% CI)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cookson et al., JACI 2009</td>
<td>Unselected Pregnancy Cohort (N=5,810)</td>
<td>Child (7.5 yrs)</td>
<td>Maternal anxiety (32 wks gestation and 1st yr postpartum) MD Dx Asthma w/symptoms and/or meds in past 12 mos</td>
<td>OR 1.64 (1.3, 2.2) Exposure response, p&lt;0.001</td>
</tr>
<tr>
<td>Reyes et al., Ann All Asthma Immunol 2011</td>
<td>Unselected Pregnancy Cohort (N=279)</td>
<td>Child (birth – 5 yrs)</td>
<td>Maternal demoralization (3rd trimester and postpartum) Wheeze phenotypes, total/specific IgE</td>
<td>OR 1.7 (1.3, 2.1) Ever Wheeze OR 2.3 (1.3, 3.8) Transient whz OR 2.7 (1.5, 4.8) Persistent whz No association with IgE</td>
</tr>
<tr>
<td>Kozyrskyj et al., AJRCCM 2008</td>
<td>Canadian Healthcare/Rx Database (N=13,907)</td>
<td>Child (7 yrs)</td>
<td>Maternal distress (Rx depression/anxiety in yr 1 and age 7 yrs) Asthma (healthcare/Rx records)</td>
<td>OR 1.6 (1.3, 2.0) longterm distress</td>
</tr>
<tr>
<td>Fang et al., PLoS ONE 2011</td>
<td>Swedish Birth/Patient/Drug Registries N=426,334</td>
<td>Child (1-4 yrs)</td>
<td>Maternal bereavement (2nd trimester)</td>
<td>HR 1.55 (1.2, 2.0) (boys)</td>
</tr>
<tr>
<td>Fang et al., PLoS ONE 2011</td>
<td>Swedish Birth/Patient/Drug Registries N=493,813</td>
<td>Child (7-12 yrs)</td>
<td>Maternal bereavement (2nd trimester)</td>
<td>HR 1.58 (1.1, 2.3) (boys)</td>
</tr>
<tr>
<td>Khashan et al., Psychosom Med 2012</td>
<td>Swedish Birth/Patient/Drug Registries N~3.2 million births 1973-Dec 2006</td>
<td>Children/Adults</td>
<td>Maternal bereavement 6 mos before – during pregnancy</td>
<td>RR 1.27 (1.2, 1.4) Any period RR 1.40 (1.1,1.7) Pregnancy only</td>
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<td>Wood RA et al., JACI 2011</td>
<td>Urban Environment and Childhood Asthma (URECA)</td>
<td>Child (1 yr)</td>
<td>Perceived Stress (late pregnancy)</td>
<td>See figure</td>
</tr>
<tr>
<td></td>
<td>Selected Pregnancy Cohort (N=515)</td>
<td></td>
<td>Depression (yr 1)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Repeated wheeze ($\geq 2$)</td>
<td></td>
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Each model adjusted for site, child gender, season of birth

![Graph showing odds ratios with 95% CI for various exposures and outcomes.](image-url)
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<td>Wright RJ et al., AJRCCM 2002</td>
<td>Home Allergen &amp; Asthma Study (HAA)</td>
<td>Child (14 mos)</td>
<td>Perceived Stress (repeated q 2 mos from birth)</td>
<td>OR 2.1 (1.3, 3.4)</td>
</tr>
<tr>
<td></td>
<td>Selected Pregnancy Cohort (N=496)</td>
<td></td>
<td>Repeated wheeze (≥ 2)</td>
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Adjusted for maternal race, education, smoking, breastfeeding, child gender, season of birth, BW, LRIs, household allergens
## Individual-level Stress/Stress Correlates

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<td>Chiu Y-HM et al., AJRCCM 2011</td>
<td>Asthma Coalition on Community, Environment &amp; Social Stress (ACCESS)</td>
<td>Child (2 yrs)</td>
<td>Maternal NLEs (mid-pregnancy and 12-18 mos postpartum)</td>
<td>Exposure Response</td>
</tr>
<tr>
<td></td>
<td>Prospective</td>
<td></td>
<td>Repeated wheeze (≥ 2)</td>
<td>OR 3.0 (1.7, 5.5) high-high vs. low-low NLEs</td>
</tr>
<tr>
<td></td>
<td>Unselected Pregnancy Cohort (N=653)</td>
<td></td>
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### Graphs

**Pre- and Postnatal Maternal NLEs and Repeated Childhood Wheeze**

Adjusted for maternal atopy, race, education, smoking, child gender, season of birth, BW z-score, household cockroach allergen, traffic-related BC, ND index
Stress x Environment Interactions

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<tr>
<td>Peters JL et al., Allergy</td>
<td>Pregnancy Cohort (N=403)</td>
<td>Child (birth)</td>
<td>Prenatal maternal NLEs x Dust mite mother’s bedroom x Maternal Atopy</td>
<td>P for 3-way interaction =0.005</td>
</tr>
<tr>
<td>2012</td>
<td></td>
<td></td>
<td>Cord Blood Total IgE</td>
<td></td>
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Prenatal stress (NLEs) x DM allergen x maternal atopy

![Graph showing the interaction between prenatal stress, dust mite allergen, and maternal atopy on cord blood total IgE levels.](image)
## Stress x Environment Interactions

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<tr>
<td>Shankardass K et al., PNAS 2009</td>
<td>Children’s Health Study</td>
<td>Child (5-9 yrs followed for 3 years)</td>
<td>Prenatal maternal NLEs Dust mite mother’s bedroom Maternal Atopy Cord Blood Total IgE</td>
<td>See figure</td>
</tr>
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### Effect of TRAP on incident asthma across parental stress quartiles

![Graph showing effect of TRAP on incident asthma across parental stress quartiles](image_url)

Adjusted for child age, gender, race/ethnicity and community random effects
# Place-Based Stress – Community Violence

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</table>
TC High v. Low  
VC High v. Low  
Race Adjusted VC High v. Low  
MD Dx Asthma | OR 1.5 (1.3, 1.8) OR 1.8 (1.5, 2.2) OR 1.3 (1.04, 1.6) |
| Cagney KA et al., J Gen Intern Med 2004 | Cross-sectional  
N=3,268 individual  
N=338 neighborhoods | Adults (43 ± 16 yrs) | Collective Efficacy  
Neighborhood Disorder  
MD Dx asthma/emphysema/chronic bronchitis or other breathing problems | 18% residual neighborhood variance for respiratory outcome |
| Sternthal MJ et al., ERJ 2010 | Project on Human Development in Chicago Neighborhoods (PHDCN) Prospective Unselected Accelerated Prospective Cohort N=2,071 individuals  
N=338 neighborhoods | Child (0-9 yrs two waves of follow up) | Community Violence  
Low Medium High  
Asthma MD Dx or Rx Meds | --- OR 1.6 (1.2, 2.2) OR 1.6 (1.1, 2.2) |
**Place-Based Stress – Community Violence**

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<td>Chiu Y-HM et al., submitted manuscript</td>
<td>ACCESS Study Prospective unselected pregnancy cohort</td>
<td>Child (2 yrs)</td>
<td>Prenatal ECV Prenatal TRAP • Black Carbon • PM2.5</td>
<td>See figure</td>
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**ECV, Black Carbon, and PM2.,5**

![Graphs showing the relationship between ECV, Black Carbon, and PM2.,5 with various outcomes](image-url)
Prenatal ECV, BC and Early Asthma Phenotypes

* Adjusted for child’s gender, season of birth, maternal race, education level, atopy, and prenatal cockroach allergen.
Interactions of ECV & TRAP

Prenatal ETV and Repeated Wheeze, stratified by BC level

- Medium ETV vs. Low ETV
  - Low BC: p for interaction = 0.94
  - High BC: p for interaction = 0.40

- High ETV vs. Low ETV
  - Low BC: p for interaction = 0.40
  - High BC: p for interaction = 0.94

Prenatal ETV and Repeated Wheeze, stratified by PM$_{2.5}$ level

- Medium ETV vs. Low ETV
  - Low PM$_{2.5}$: p for interaction = 0.21
  - High PM$_{2.5}$: p for interaction = 0.24

- High ETV vs. Low ETV
  - Low PM$_{2.5}$: p for interaction = 0.24
  - High PM$_{2.5}$: p for interaction = 0.21
Cortisol in Health and Disease
Maternal prenatal cortisol trajectory associated with early asthma risk in children

Immune Function in Health and Disease

- Decreased
- Increased
Higher prenatal maternal stress alters child’s immune response at birth

Wright RJ et al., AJRCCM 2010; 182:25-33.
Causal Inference from Observational Data on Psychosocial Stress and Early Asthma Phenotypes

- Biological plausibility
- Temporal sequence – prospective prenatal & early childhood cohorts a particular strength
- Exposure-response relationship
- Robust to adjustment for a number of important confounders and pathway variables
- Robust to sensitivity analyses – alternate approaches to characterizing stress; alternate analytical approaches
  - Known to be associated with early asthma phenotypes
Summary

- Socially toxic environments are **NOT** simply a marker of a more toxic physical environment.
- Social contexts and consequent stress may be as detrimental to children’s health as chemical toxins.
  - Social pollutants/toxins
- Psychological stress disrupts biological systems overlapping with those altered by physical pollutants/toxins.
  - Independent effects
  - Interactive (joint) effects
- Individual- and place-based psychosocial stress may impact host resistance such that physical toxins (e.g., indoor allergens, traffic-related air pollution) may have adverse effects, even at relatively lower doses.
- Epidemiological studies and interventions need to address physical toxins and social stress jointly to impact public health most effectively.
Looking ahead.....