Toxic Threats:  
Preconception to Young Adults

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Environmental exposures at critical developmental periods may permanently alter structure of airways.

A portion of adult lung function (≈14%) is predicted by function at 2 months.

Adapted from The Lancet 370: Stern et al. Poor airway function in early infancy and lung function by 22 years: a non-selective longitudinal cohort study. Pg 761, copyright 2007.
Knowledge Gap

• 89% report getting questions from families

• ~ ½ uncomfortable discussing environmental exposures

• 92% would find it helpful to have information about environmental exposures

A Story of Health

Story of Health with permission
The ecological framework can include multiple levels from sub-cellular to societal. It is not hierarchical in the sense that one level is more important than another, but rather in the sense that individual biology is progressively nested within the person, family, community, society and ecosystem. The interactions and feedback loops within, across, and among these levels are complex and variable. They exert their influences on health across time.
Some early life environmental risk factors have been identified.
For example, prenatal and early life exposure to social stressors, such as violence, can increase the risk of asthma as well as increase the impacts on respiratory health from allergens, air pollution, and tobacco smoke.
Secondhand smoke alone is a risk factor for new cases of asthma in preschool-aged children.
Karen was surprised to learn that some doctors are even concerned about acetaminophen and its relationship to asthma.
Brett has experienced many of these risk factors in his short life. More details about these can be found as you read his story.

Stress affects our health. Watch this video by Dr. Rosalind Wright to see how social stressors, along with environmental factors, can be linked to asthma. (5 min.)

Rosalind J. Wright, MD MPH, Horace W. Goldsmith Professor of Pediatrics, Vice-chair, Clinical and Translational Research, Department of Pediatrics, Icahn School of Medicine at Mount Sinai
INFERTILITY  Reiko & Toshio’s Story

They discuss a range of other possible environmental exposures including endocrine disruptors. Dr. Patel says she will have the test results in about a week, so they set up another appointment.

Watch: Little Things Matter: The Impact of Toxins on the Developing Brain
Dr. Bruce P. Lanphear, MD MPH
Professor, Simon Fraser University

Endocrine disruptors and infertility/reproductive health

Endocrine disruptors are chemicals that impact endocrine functions by interfering with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for development, behavior, fertility, and maintenance of homeostasis (normal cell metabolism).

These disruptions can cause cancerous tumors, birth defects, and other developmental disorders. As the cells begin to grow and differentiate, there are critical balances of hormones and protein changes that must occur. The Endocrine Society released a statement on Endocrine-Disrupting Chemicals (EDCs) specifically listing obesity, diabetes, male reproduction, female reproduction, hormone-sensitive cancers in females, prostate cancer in males, thyroid, and neurodevelopment and neuroendocrine systems as possible effects of being exposed to EDCs.
Dr. Lopez mentioned other environmental exposures that might affect fertility, such as air pollution, and says there are some good resources that she can also send to Reiko.

Reiko thinks about her training runs around some of the major roads, and remembers the emissions from the trucks and cars. She wonders how that might have affected her.

Dr. Lopez suggests that a fertility specialist may be able to provide even more information.

**Vulnerable populations and environmental disparities**

**Air pollution and fertility, reproductive health**

**Link:** ACOG Evaluating Infertility

**Links:**
- ACOG American Congress of Ob/Gyn: Vulnerable populations and environmental disparities
- FIGO Opinion: International Federal of Gyn/Ob: Reproductive health impacts of exposure to toxic environmental chemicals
Dibromochloropropane DBCP

- Soil fumigant - Introduced 1950s
- Toxic to sperm and testis
- Caused male infertility in 1500 pesticide plant workers in U.S.
- Continued export after US ban
- Over 30 years later there are still wells in California near production plant requiring special filtration
Females – Born with Finite Number Oocytes in Primordial Follicles

- Called Ovarian Reserve
- Toxicants that decrease follicle pool can result in ovarian senescence and menopause
- Examples include:
  - PAHs
  - 2- bromopropane
  - Ionizing radiation
  - Chemotherapeutic agents

Age-Related Decline in Human Follicles

Adapted from Faddy and Gosden, 1992
After talking with Tricia and examining Stephen, Dr. Jones was also concerned. She confirmed that Stephen appeared ill and that the cause could be a number of things. She said she needed laboratory tests to make an accurate diagnosis.

Dr. Jones ordered blood tests that could be done at the local hospital and called to make an appointment for Stephen to get his blood drawn that same day.

Tricia was upset and called her husband David with the news. She started to ask a lot of questions. Dr. Jones tried to calm her and said she would call her as soon as she had the results.

Tricia brought Stephen to the hospital laboratory for the tests and went home very worried.
Story of Health: Paintings by Susan Macfarlane used with permission
Special thanks to Dr. Geoffrey Farrer-Brown and Euan MacKay
Meta-analysis ALL and Paternal Smoking around Conception (> 20cpd vs. none)

Milne et al., Am J Epidemiology 2012
## ALL Joint Effect of Pre- and Postnatal Exposure to Tobacco Smoking

<table>
<thead>
<tr>
<th>Exposure to tobacco smoking</th>
<th>Controls N = 975</th>
<th>Cases N = 767</th>
<th>OR&lt;sup&gt;a&lt;/sup&gt; (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No exposure during both periods</td>
<td>670</td>
<td>498</td>
<td>1.00 (—)</td>
</tr>
<tr>
<td>Paternal prenatal smoking only</td>
<td>127</td>
<td>98</td>
<td>0.91 (0.68–1.22)</td>
</tr>
<tr>
<td>Child’s passive smoking only</td>
<td>74</td>
<td>46</td>
<td>0.80 (0.51–1.09)</td>
</tr>
<tr>
<td>Exposure during both periods</td>
<td>88</td>
<td>115</td>
<td>1.50 (1.01–2.23)</td>
</tr>
</tbody>
</table>

<sup>a</sup>OR adjusted for child's age at diagnosis/reference date, sex, and Hispanic status, maternal race, and household annual income.

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Metayer, Cancer Epidemiology, Biomarkers and Prevention, 2013
Preconception/Early Prenatal Exposure and Childhood Leukemia

- Any paint exposure 3 mos < conception (5 studies)  ALL OR 1.54 (1.28-1.85)
- Father – Preconception smoking
  - AML  1.37 (1.07-1.76)
  - ALL  1.44 (1.24-1.68) meta-analysis not CLIC
- Folate supplementation mother (primary education or less)
  - ALL  0.47 (0.33-0.68)

Bailey et al., Cancer, Causes, and Control 2015
Metayer, AJE, 2016;184(4):261–273
Milne et al., Am J Epidemiology 2012
Metayer, Epidemiology, 2014
Figure 1. Incidence of childhood leukemia in California by race-ethnicity, 1988-2012

Childhood leukemia has been trending upward in California in recent decades.

It has risen especially among Latinos, reflecting a national trend and raising concerns about early environmental exposures to harmful chemicals.

Figure adapted from Giddings B, Whitehead TP, Metayer C, Miller MD. Childhood Leukemia Incidence in California: High and Rising in the Hispanic Population. Cancer 2016.
• High and increasing rate of CL in Latino children

• Preconception and prenatal exposures important (as well as early childhood)

• Exposures related to other outcomes
Love in the Time of Toxicants
10 minute video

Outreach
- Community health workers
- Adolescents and young adults
- Pre-marital

http://circle.berkeley.edu/translation-and-outreach/for-parents/
https://wspehsu.ucsf.edu/projects/improving-environmental-health-literacy-young-adults/
Rosa and Carlos get Married

INSIDE:
Recipes
Quick 'n Healthy!

Rosa y Carlos Se Casan

ADENTRO
Recetas
¡Fáciles y saludables!
HOLA AMY! You’re due in a couple of months, si? And you’re taking the FOLATE?

Hola!

MAMI!!

...So has Rosa been complaining about my ANTI-TOXICANT campaign?

TOXI... WHAT?!

OH! I hear you with your FRIENDS on the PHONE...

“MAMI says: No PAINT FUMES in the HOUSE!”

“Use GREEN CLEANING PRODUCTS!”

“NO SMOKING!”

YEAH! And “Make PAPI take off his STINKY WORK CLOTHES outside the HOUSE!” (They DO smell BAD!)
Everyone Knows that Mom’s Smoking During Pregnancy is Bad for Baby, but...

DID YOU KNOW?

Dad’s Smoking Before Conception Can Harm the Child, too?

Mom’s smoking during pregnancy can cause: premature birth, birth defects, or even a miscarriage.

Dad’s smoking before conception can cause: childhood leukemia.

Moms or dads who smoke increase the amount of cancer-causing DNA changes in their children by 30%.

FUTURE PARENTS: Start Protecting Your Children’s Health BEFORE They Are Conceived!
Dr. Lopez includes information on the influence of toxic chemicals such as lead and the solvents in paints and other materials. She again mentions the important nutrition issues they had discussed earlier.

Watch: Chemicals and Infertility
Tracey J, Woodruff, PhD, MPH
Director, Program on Reproductive Health and the Environment; Professor in the Department of Obstetrics, Gynecology, and Reproductive Sciences at the University of California, San Francisco

Links:
- TEDx The Endocrine Disruption Exchange
- Generations at Risk Reproduction Health and the Environment
- CDC's Lead and Pregnancy

**KEY CONCEPT:**
Multiple environmental factors can influence reproductive health.

Environmental factors, alone or in combination with other variables, can have adverse impacts on reproductive health, increasing the risk of infertility, miscarriage, abnormal fetal growth, fetal death, preterm birth, birth defects or other developmental abnormalities.

In many cases, a specific cause of an adverse outcome cannot be identified. With the exception of birth defect registries in some states, lack of comprehensive data collection pertaining to most abnormal outcomes makes epidemiologic studies intended to identify causal factors difficult to conduct.

- **TOXICANTS** including: pesticides, endocrine disruptors, metals, air pollution, solvents
- **RADIATION**
- **STRESS**
- **NUTRITION**
- **CLIMATE CHANGE**
- **INFECTIOUS AGENTS** such as: Viruses: CMV, varicella, herpes, Bacteria: syphilis, listeria, Parasites: toxoplasmosis, Zika, rubella
CIRCLE at UC Berkeley
Catherine Metayer, Julia Vassey, Todd Whitehead (UC Berkeley), Brenda Giddings (CA Cancer Registry), Joe Wiemels (UCSF)

Western States Pediatric Environmental Health Specialty Unit
(WSPEHSU at UCSF)

Maria Valenti, Steve Burdick, Vickie Leonard, Sharyle Patton,
Jose Camacho, Richard Carlton

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