Asthma’s Inner World

Researchers follow the disease’s roots not to the lungs, but to the gut.
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We live in a sea of chemicals.

Synthetic organic chemicals make modern life possible, prevent injury and treat disease. When humans are exposed to them in ways not originally intended, however, they may have consequences that are not so beneficial. And exposure is exactly what is happening; these chemicals permeate daily life. They occupy the air we breathe, the water we drink, the food we eat, the clothes we wear and the toys our children play with.

The proof is in our blood. Exquisitely sensitive modern analytic techniques can detect more than 200 chemicals in human umbilical cord blood—evidence that mothers share more than essential nutrients with a developing fetus. Because the prevalence of childhood conditions such as asthma, food allergies and autism spectrum disorders is increasing markedly, the role of fetal exposure to a variety of chemical compounds clearly is cause for concern. Is this increase linked to chemical exposures? We do not know. Given the beneficial effects of chemicals, it’s hard to imagine living without them. However, until we know the risks of exposure, we cannot make informed decisions about their use.

This issue of Johns Hopkins Public Health highlights work by the Bloomberg School’s Janet DiPietro and her colleagues on the effects of exposure to organochlorines—insecticides, polychlorobenzenes and other synthetic compounds—during fetal development. This pilot study, the first of its kind to measure maternal chemicals at the same time that fetal behavior is measured, suggests that organochlorines may affect fetal movement. This is crucial research, and the next step is to determine whether children’s long-term health is affected. (For more about this research, read the fascinating story on page 4.)

Much more research on the developing human fetus is necessary to fully understand the impact of chemicals on human health, individually and in mixtures. It’s an incredibly difficult area of study requiring new modes of measurement and analysis. Children and babies are also of special concern because their organ systems are still developing, which puts them at high risk.

One need only look at the sad history of lead exposure to observe the damage chemicals can inflict on young lives. Lead was once ubiquitous in our society, showing up most notoriously in gasoline and household paint. Children who ingested lead paint suffered intellectual disabilities as well as an increased risk of hypertension, cardiovascular disease and kidney disease. Generations suffered exposure before long-delayed removal of lead from paint and gasoline resulted in a dramatic fall in lead intoxication, lead poisoning and the resultant harmful effects. Even so, far too many children still have dangerous blood lead levels.

The larger question for us today is, what other “leads” are out there? Is exposure to synthetic organic chemicals also having deleterious effects on human health and development? Which chemicals pose the greatest threats? Does the interaction of exposure to multiple chemicals magnify their effects?

In addition to being critical public health questions, these issues have been a matter of great personal importance to me. My daughter, Sarah, was diagnosed with an autism spectrum disorder in 1995 at age 5. My late wife Wendy devoted her life to making sure that Sarah reached her maximum potential. After Wendy’s death in 2006, family and friends gave generously to a memorial fund in her memory that enabled us to support students to study developmental disabilities. We are now building on these activities to create the Wendy Klag Center for Autism and Developmental Disabilities at the Bloomberg School.

The Center, led by Mental Health chair M. Daniele Fallin with associate dean for Research Janet DiPietro as associate director, officially launches on October 15, 2013. It has a bold mission that includes identifying the etiologies of developmental disabilities like autism, devising the best possible treatment and prevention programs, and advancing policies that maximize health and minimize harm.

To accomplish this ambitious agenda, we intend to take advantage of the depth and breadth of expertise in the Johns Hopkins environment to create new synergies that will more effectively address the issue of developmental disabilities. We will bring together epidemiologists to assess and track prevalence of conditions in populations, geneticists to identify candidate genes, laboratory scientists to measure chemicals and other prenatal exposures, developmental psychologists to assess cognitive and other impairments, biostatisticians to develop new methods of detecting important signals in huge amounts of data from brain imaging tests and genomic analysis, experts to devise optimal policies to care for and support individuals with developmental disabilities, and clinicians at the cutting edge of screening and care to develop new strategies for early detection—all working on a common problem.

By bringing the best and brightest together, the Wendy Klag Center will catalyze research that has a purpose: to identify what may be harming our children and to protect the next generation. ♦
An advocate with a passion for evidence, Jose "Oying" Rimon II leads the world’s largest family planning conference.
The population of Ethiopia’s capital city will suddenly surge on November 11. More than 3,000 researchers, government ministers, students and NGO leaders from 100 countries will gather in Addis Ababa for the 2013 International Conference on Family Planning (ICFP). It’s yet another sign that family planning—once relegated to the global agenda’s hinterlands—is back. Two previous conferences led by the Bloomberg School’s Bill and Melinda Gates Institute for Population and Reproductive Health (Kampala in 2009 and Dakar in 2011) helped restore the field’s prominence. Then, at last year’s London Summit, governments and NGOs committed to delivering contraceptives to an additional 120 million women by 2020, and donors pledged $2.6 billion to do so.

Orchestrating the Addis conference’s 750 presentations in 150 panels, and hundreds of parliamentarians and policymakers, is Jose “Oyin” Rimon II, MA, Gates Institute deputy director. Rimon returned to the School in 2012 after five years at the Bill & Melinda Gates Foundation. Dubbed a “positive disruptor” by a former boss, Rimon is an exuberant, outspoken advocate with a passion for evidence. He recently shared his vision for ICFP 2013 and his thoughts on global family planning with Johns Hopkins Public Health editor Brian W. Simpson, MPH ’13.

How do you plan a conference of this size?
You need vision and logistics. If it’s all vision without logistics, it’s going to fail. If it’s all logistics without the vision, it will just be another meeting.

Why does the field need another conference after the success of the London summit?
There’s some momentum after London, but that momentum needs to be substantive in terms of, is the money that the donors pledged actually flowing and how is that money going to be used. And on the other side, are the developing countries owning this issue and allocating the right resources or implementing the right policies to their own situation. That’s still needed in a big way.

220 million women who do not want to become pregnant are not using contraception. What are the barriers to fulfilling this unmet need?
One is supply, the other one is demand. On the supply side, how do you make sure that the contraceptives that are needed for both spacing and limiting are actually available to the people who want them, when they want them? That means making sure that the stock-outs [when facilities run out of contraceptives] don’t occur as often as they do. In her field visits, Melinda [Gates] was surprised to observe that while there are no stock-outs for HIV/AIDS drugs or for vaccines, you have stock-outs for contraceptives. There’s something wrong with that picture, you know?

What’s the solution?
The tech experts call one solution the informed push model. That’s a complicated way of describing the Coca-Cola model: There is an established supply, and the suppliers just go and restock to the level determined for that area. If a store is supposed to have 1,000 bottles of Coke and there are only 400, they just stock it up to 1,000 and keep moving. It’s not rocket science.

And how do you address the demand side?
Especially in sub-Saharan Africa, there are still many countries where there is demand for high fertility among mothers and fathers. So Africans themselves have to work on educating people in terms of their options. And in virtually all of these countries, the desired number of children by mothers is almost always below the actual number of children in the family. Wouldn’t it be great if mothers could actually have the number of children they want? So behavior change, educational programs, outreach and counseling are key to addressing the issue of demand, the issue of misinformation and misconceptions, the fear of side effects, and oftentimes just the ignorance of where to go to get services.

How does a conference like the ICFP really effect change?
At many levels. When there is no sense of a community and there’s a feeling of abandonment, it’s like we can’t achieve anything. So this conference changes that perspective. It also brings in the exchange of best practices: What did Ethiopia do? Why are they successful? The reason we picked Addis is that we want to celebrate a little this time around. Ethiopia from 2005 to 2011 had an increase of almost 100 percent of their CPR [contraceptive prevalence rate]: Modern methods went from 14 percent to 27 percent.

How did Ethiopia achieve this?
They did this by political commitment at all levels, delivering services through a powerful health extension workers program and shifting tasks so a health extension worker can provide a contraceptive injection. It doesn’t have to be a nurse or a physician.

What do most people not understand about global family planning?
When I was at the Gates Foundation, we commissioned a series of surveys [of Americans] on international family planning. One of the major conclusions was that if you are advocating for family planning as an end to itself—that family planning is good—it doesn’t resonate as well with the American public because they think you have a hidden agenda like population control. But if family planning is positioned as reducing maternal mortality, infant mortality, unintended pregnancies and abortions, if you put it in that context, boom! Then all of a sudden you have overwhelming support.

So the field should be doing more to emphasize that family planning prevents maternal and child mortality?
Oh yeah. That’s the main argument now based on evidence. In The Lancet special issue on family planning last year, Saifuddin Ahmed [an associate professor in Population, Family and Reproductive Health] was the key author of a research paper that essentially said that satisfying the unmet need for contraception can prevent an additional 29 percent of maternal deaths per year. Other studies document a 19 percent reduction in infant deaths. It’s huge. I mean what other low-cost intervention could do that?
Steven S. An, PhD, associate professor, Environmental Health Sciences (EHS), was elected program chair-elect of the Respiratory Structure and Function Assembly of the American Thoracic Society.

Carolyn Cumpsty-Fowler, PhD, MPH '96, assistant professor, Nursing and Health Policy and Management (HPM); Andrea Gielen, ScD '89, ScM '79, professor, Health, Behavior and Society (HBS), and the current director of the Johns Hopkins Center for Injury Research and Policy; and Susan P. Baker, MPH '69, professor, HPM, and founding director of the Johns Hopkins Center for Injury Research and Policy; and

Timothy D. Baker, MD, MPH '54, professor, International Health (IH), received the Baltimore City Medical Society Lifetime Achievement Award.

Chris Beyrer, MD, MPH '91, professor, Epidemiology, and director of the Center for Public Health and Human Rights, has been named International Chair of the 8th International AIDS Society Conference on HIV Pathogenesis, Treatment, and Prevention, to be held in 2015 in Vancouver.

Kay Dickersin, PhD ’89, MA, professor, Epidemiology, was awarded the 2013 Valkhof Chair at Radboud University Nijmegen Medical Centre in the Netherlands.

Fang Han, PhD candidate, Biostatistics, received a 2013 Global Google PhD Fellowship which recognizes innovation, creativity and leadership in promising young academicians.

D.A. Henderson, MD, MPH ’60, University Distinguished Service Professor, and Dean Emeritus of the Bloomberg School, was presented with the Order of Brilliant Star with Grand Cordon by Ma Ying-jeou, President of the Republic of China (Taiwan).

David Holtgrave, PhD, professor and chair, HBS, has been appointed again to serve a two-year term on the President's Advisory Council on HIV/AIDS (PACHA).

Sheppard G. Kellam, MD, professor emeritus, Mental Health (MH), was elected a Society for Prevention Research Fellow for lifetime contributions to prevention science.

Michael J. Klag, MD, MPH ’87, Dean of the Bloomberg School, was named a 2013 "Kidney Champion" by the National Kidney Foundation of Maryland for his contributions to the prevention and epidemiology of kidney disease.

After a 21-year absence from the Bloomberg School, Karen Davis, PhD, says that the timing of her return couldn’t be better.

The new director of the Roger C. Lipitz Center for Integrated Health Care predicts that the Center can play a key role as the U.S. health care system readies to meet the needs of the aging baby boom generation.

“As the boomer generation moves into their 70s and starts to deal with more health issues, we really want to identify innovative models of integrated care and delivery that work for patients, family members and caregivers,” says Davis, the Eugene and Mildred Lipitz Professor in Health Policy and Management (HPM).

Davis, who returned to the School in January after two decades as president of the Commonwealth Fund, is up to the challenge.
Before leading the Commonwealth Fund, she held high-level positions in the U.S. Department of Health and Human Services and chaired HPM from 1983 to 1992.

“When Washington has questions about health insurance models, they look to Karen’s research for answers,” said HPM chair Ellen MacKenzie, PhD ’79, MSc ’75, at Davis’ May installation as the Lipitz Professor. “Her focus on patient-centered care, creating a data-driven voice and building a high-performance health care system has changed the way people think about health policy.”

In July, Davis received the American Hospital Association’s 2013 TRUST Award for vision and leadership in improving health care quality and practice.

Davis looks forward to close collaborations with colleagues at the schools of Nursing and Medicine and at Johns Hopkins Bayview who are designing clinical care models to help older people maintain their independence.

She points out that Medicare does not cover some key services that could make this happen—social worker home visits to help with dementia care and home safety renovations, for example. “What the Lipitz Center brings is the economic analysis to show that it really pays, in terms of reducing hospital stays and delayed admissions to nursing homes, if these types of services are in fact covered,” Davis says.

It’s analysis that can effect policy change, she says, and turn a pilot study into standard practice throughout the Medicare program.

—Jackie Powder

Anthony K. L. Leung, PhD, assistant professor, Biochemistry and Molecular Biology, is a finalist for the 2013 Agilent Early Career Professor award for original research contribution enabling measurements of importance.

Dan Morhaim, MD, associate, HPM, received the New York Medical College Jackson E. Spears Community Service Award for his long tenure as a physician/member of the Maryland legislature.

George Rebok, PhD, MA, professor, MH, spoke at a White House meeting on Psychological Science and Behavioral Economics in the Service of Public Policy; and became an American Institutes for Research (AIR) Institute Fellow.

Anne W. Riley, PhD, professor, Population, Family and Reproductive Health (PFRH), has had a student fellowship named in her honor to support students to work at Maryland Advocates for Children and Youth in legislative advocacy and evaluation.

Noel R. Rose, MD, PhD, professor, Pathology, Molecular Microbiology and Immunology (MMI), and director, Johns Hopkins Center for Autoimmune Disease Research, was elected to foreign membership in the Polish Academy of Sciences.

Alfred Sommer, MD, MHS ’73, University Distinguished Service Professor, and Dean Emeritus of the Bloomberg School, was honored as a 2013 Dan David Prize Laureate and shared the $1 million prize for “his unexpected and striking discovery in demonstrating that vitamin A has the power to save children’s lives.”

Adam P. Spira, PhD, assistant professor, MH, received the 2013 Barry Lebowitz Early Career Scientist Award from the American Association for Geriatric Psychiatry, and the 2013 Insomnia Section Investigator Award from the American Academy of Sleep Medicine.

Moyses Szklo, MD, DrPH ’74, MPH ’72, professor, Epidemiology and Medicine, received the Robert S. Gordon Jr. lectureship award from NIH, and was selected to present the 157th Cutter Lecture on Preventive Medicine at the Harvard School of Public Health. He also received a special award from the Brazilian Minister of Health during the 12th Brazilian ExpoEpi on Successful Experiences in Epidemiology, Prevention and Disease Control.

Maria Trent, MD, MPH, associate professor, PFRH, and Pediatrics, received the 2013 National Medical Association Council on Concerns of Women Physicians (CCWP) Research Award.

Laurie Schwab Zabin, PhD ’79, professor emeritus, PFRH, and founding director, Bill and Melinda Gates Institute for Population and Reproductive Health, received the American Academy of Pediatrics’ 2013 Founders of Adolescent Health Award from the Section on Adolescent Health.

Jonathan Zenilman, MD, professor, PFRH, MMI, IH and Epidemiology, received a Distinguished Career Award from the American Sexually Transmitted Diseases Association.
limitation on growing these bacteria, she had to devise strategies that did require laboratory culture.

In recent studies, Wills-Karp examined whether the clostridia-related bacteria could indeed be driving the immune change behind severe asthma. Because of the bacteria’s growing constraints, for these experiments she had to devise strategies.

In one experiment, for instance, her team called upon a Japanese company that had developed special mice that have absolutely no germs in their bodies except for the clostridia-related bacteria. They collected fecal material from the mice and shipped it to Wills-Karp’s lab. Presumably, the fecal material would contain the clostridia-related bacteria. Wills-Karp’s team transplanted the fecal material into a common breed of laboratory mice that scientists had shown were free of the clostridia-related bacteria. They then compared the rate of asthma symptoms in those mice to a comparable group of mice that had not received the fecal transplants.


Strange or not, the experiment proved useful. The mice receiving the fecal transplants went on to develop severe asthma, a finding that, along with other results, provided strong evidence that this member of the microbiome may drive severe asthma.

Further studies revealed another interesting aspect of this process. “In mice, this bacteria is cleared during weaning or maturation,” says Wills-Karp. Her initial experiments involved young mice, those still colonized by the clostridia-related bacteria. So her group did a series of experiments to determine whether the immune changes brought about by the bacteria endure.

Indeed they do, her studies showed. “We see that past the time of clearance of that bacteria, this Th17 response persists,” says Wills-Karp. “Whatever happens is changing the immune response indefinitely.”

Her studies suggest that the presence of the bacteria in the guts of young mice gets communicated to the bone marrow, the site of immune cell production. This information skews the immune system’s normal balance, biasing it in favor of the production of Th17 cells.

It’s easy to see how the same scenario might occur in people, says Wills-Karp.

“The going assumption with asthma is that the first year of life is critical to the establishment of the disease,” she says. Certain events early in life can disrupt the gut’s normal microbial balance. If a child receives repeated courses of antibiotics, for example, those medicines might skew the balance in a way that allows a clostridia-related species to flourish. As in the mouse, that information would get telegraphed to the immune system, and so on.

A Proof of Concept

Wills-Karp’s findings demonstrate something that no scientist has shown before, says Richard Markham, MD, a Bloomberg School professor of Molecular Microbiology and Immunology and an expert in sequencing technology essential to much microbiome research.

“They suggest for the first time that the presence of a single species of bacteria has influence on whether an individual can develop asthma,” he says.

Markham and Wills-Karp add that asthma may not be the only disease that follows this pattern. Th17 cells have also been associated with arthritis, multiple sclerosis, Crohn’s disease and other autoimmune conditions. The microbiota may underlie those diseases as well.

Her results, says Wills-Karp, “are proof of concept.” One big unknown is whether the human disease truly does parallel the mouse pattern. Patients with severe asthma do have elevated levels of Th17 cells, scientists have found. But no one has shown that the clostridia-related bacteria underlie those cases.

Wills-Karp is starting to address this question in a study with Stacey Burgess, PhD, a former student and now an infectious disease researcher at the University of Virginia. The pair will examine whether the clostridia-related bacteria are more prevalent in children with asthma. This and Wills-Karp’s other studies could help guide the way toward new asthma treatments—perhaps a drug that dampens or eliminates the clostridia-related bacteria or a new and improved probiotic.

Of course, preventing asthma in the first place would be even better. Here, too, growing knowledge about the microbiome might offer some guidance. Research implies that microbially rich environments reduce asthma risk. So does it make sense to raise your kids on a farm or simply not wash off the pacifier after it falls on the floor, five-second rule or no? The New York Times Magazine recently ran a story on the microbiome; the opening photo showed a baby slathered in mud, mouthing a grimy toy car that was clenched in a dirt-encrusted fist.

Wills-Karp won’t go so far as to endorse muddy playtime, although she observes that there is an evolutionary argument to be made for this practice: “Kids when they are young touch everything and put it all in their mouths. Maybe there’s a reason for that.” She would, however, advise germophobic parents to temper their fear, saying, “I would tell parents not to go overboard with the hand sanitizers. Babies do need some kind of exposure to the environment.”

Greater understanding of the microbiome’s role in asthma may help scientists refine such prevention strategies, as well as develop new treatments for those already afflicted. The microbiota may contribute a little or a lot to asthma, says Wills-Karp. “We don’t yet know. Microbiome research is in the early stages.”

The microbiome mystery continues.

Asthma’s Inner World

(Continued from page 31)
A Great Journey

One evening in late March 2009, I started on a journey.

That evening, I listened to my first lecture in a graduate public health course, Public Health Biology. David Sullivan, an associate professor in Molecular Microbiology and Immunology, and guest lecturers led the class through a fascinating tour of bacteria, viruses and parasites, and their pernicious effects on human health.

I was hooked. I took more courses as a nondegree-seeking student, then as part of a certificate program. Environmental health. Biostats. Epi. Health and human rights. Human physiology. (Sweat literally beaded on my forehead when I saw the final exam’s first question.) Then I was accepted to the part-time MPH program. I loved the intensive problem-solving course that MPH students start with—a kind of public health boot camp.

Each course, led by the Bloomberg School’s terrific faculty, enthralled me and helped me in my goal of mastering the fundamentals of public health. As part of my MPH capstone, I worked with colleagues to interview Frederick, Maryland, residents and public health experts about a cancer cluster investigation there. (You may have read our article in the special 2013 issue on death, “It Would Break Your Heart.”)

The MPH was one of the most rewarding challenges of my life. I spent a lot of hours at home hunkered over my laptop, reading, studying and participating in online “live talks” for courses. My wife and kids patiently respected Dad’s study times on weekends and weekday evenings. I won’t kid you, it was hard—especially for a former journalist and English major more familiar with Tom Wolfe and Wallace Stevens than John Snow and Sir Richard Doll—but I savored the bracing intellectual challenge.

On May 21, 2013, I found myself in Joseph Meyerhoff Symphony Hall for the School’s convocation. (In front of me sat Varsha Ramakrishnan, our inaugural Johns Hopkins-Pulitzer Center Global Health Reporting Fellow. She wrote the remarkable story about dowry violence in India on page 38.)

On that day last May, 535 very happy people walked the stage and graduated from the School. I’ll always be proud that I was one of them. When Dean Klag shook my hand and gave me my diploma, I knew a great journey was both ending and beginning.

BRIAN W. SIMPSON, MPH ’13
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Letters to the Editor

Crediting Carl Taylor
I very much enjoyed the 2013 Special Issue of Johns Hopkins Public Health. Of special interest to me was the article “Speak and Save” on verbal autopsies by Richard Byrne. The Department of International Health, at the time chaired by Carl Taylor, was very much involved in the development and, I believe, first use of the method back in 1971. That information was missing in the story, and I think it should have been part of it, if only to give credit to Dr. Carl Taylor, under whose guidance highly motivating working and research conditions were provided in the Narangwal Rural Health Research Centre in 25 villages in rural Punjab, North India.

Ardy Kielmann, MDCM, DrPH
Cotignac, France

Defining Public Health
To assert that the practice of surgery equals the practice of public health [“Operation Health,” Spring 2013] brings the meaning of the words “public health” even closer to oblivion. The cover artwork and cover storyblur distinctions that need to be made in order to keep the public aware of what the practice of public health is and what it has done for them.

A surgeon saved my life once and I thanked him. Public health practitioners save my life every single day and I don’t know whom to thank. The growth of public spending on clinical care while public health budgets stagnate suggests that our fellow citizens are only capable of thanking the life-savers they can see. Promoting the image of the heroic surgeon as the face of public health worsens confusion over what it means to create health at the population level. A circumcision program is public health, a circumcision is a surgery.

Words matter. Your magazine is one of few places where one expects to find clear words about what is involved in the practice of public health. Equating surgery and public health was a setback.

David Bishai, MD, PhD, MPH, Professor, Population, Family, and Reproductive Health, Bloomberg School

But What About Those Masks?
I enjoyed the article “Operation Health” in the recent magazine, but I wanted to comment on the photo of the two surgeons. The purpose of the surgical mask is to cover both the nose and the mouth. In the photo one of the surgeons has his nose exposed. I doubt this is a lesson Hopkins wishes to exemplify.

N. Lynn Eckhert, MD, DrPH, MPH
Partners HealthCare International
Boston, Massachusetts

[Adam L. Kushner, MD, MPH, associate, International Health, and faculty, Center for Refugee and Disaster Response, responds: I agree that this is certainly not behavior to condone; the photo in fact demonstrates not only a lack of proper procedure, but also shows that the nurse is not wearing appropriate eye protection. Studies have shown that as few as 18 percent of hospitals in developing countries have proper eye protection. The photo was meant to highlight that there are many deficiencies in operating rooms in developing countries [ranging] from knowledge and use of proper techniques to proper safety precautions and resources. It is hoped that by bringing attention to the need for improving surgical care, additional resources can be devoted to the safety of patients and providers.]