

Does Civilization cause Asthma? (Excerpted)

By Ellen Ruppel Shell

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Scott Schroeder, a pediatrician and an associate professor at Montefiore Medical Center, in the Bronx, is a rugged-looking man in his mid-forties who was good enough at basketball to have played in college but not, he says, for the pros. He has furnished his cramped office clubhouse-style, with sports paraphernalia and souvenirs. Its only window is an ersatz one, with curtains that Schroeder sketched on the cinder block in colored marker. When we met recently, his phone rang constantly with questions from anxious patients, and he answered each call with a jaunty mixture of benevolence and locker-room sarcasm. For Schroeder, who specializes in the treatment of asthma, taking on a patient means taking on a long-term relationship. His appointment book is full.

The Bronx is the U.S. epicenter of asthma. Rates of death from the disease are three times as high here as they are in the United States as a whole, and hospitalization rates are almost five times as high. In some Bronx neighborhoods 20 percent of the children have asthma, and so do a goodly number of adults. A local rap group wrote a song titled "Ventolin," named for a popular asthma reliever.

The Bronx may serve as a harbinger for the world. Australia, New Zealand, South Africa, Singapore, Hong Kong, parts of South America, and much of Western Europe struggle mightily with the disease. In the United States 15 million people have asthma, five to six million of them children -- more than double the number in 1980.

Asthma kills at least 5,000 Americans annually -- not a terribly large number compared with the toll other diseases take. But what the condition lacks in lethality, it more than makes up for in morbidity: it wears people down, crushes their spirits, and threatens their livelihoods. Asthma is the most common chronic disorder among children and the leading cause of both childhood hospitalizations and school absenteeism, robbing children of 10 million school days a year and their parents of an untold number of workdays. According to the Centers for Disease Control and Prevention, health-care costs associated with asthma will reach \$14.5 billion this year.

"When I first meet a patient, I spend an hour with him," Schroeder told me. "I can do this because I'm an academic physician who gets paid by the year, not by the patient. A general pediatrician working under managed care has to see four to six patients an hour -- he doesn't have the time to talk about diet, exercise, the kid's environment. And that's why these kids keep ending up in the ER. I was shocked when I first came here, because so many kids had been hospitalized fifteen or twenty times with asthma and had never seen a specialist."

Schroeder had to see a patient across town, so he offered me a lift and a quick tour of some of the region's asthma-ridden neighborhoods. The Bronx is the only one of the five New York City boroughs, he reminded me, that is part of the mainland, and for this reason it has long been a hub for trains and trucks delivering cargo. Whereas freight bound for Manhattan must be barged across the Hudson, trains can travel overland directly to the Bronx. When truck traffic largely supplanted train traffic, several decades ago, the trucks came roaring through too. Interstate 95, the major truck route from Florida to Maine, cuts straight through the Bronx, where it becomes the Cross Bronx Expressway and merges with a snarl of other full-throttle routes. Trucks make up a

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Schroeder can't be sure that the diesel fumes spewing from those eighteen-wheelers are

in any way responsible for the poor health of his patients. But he thinks they are, and so do other clinicians I spoke with. Scientists are equivocal. Studies done in the 1990s found that the former East Germany, with its heavy pollution from industry and domestic coal burning, had far less asthma than the ostensibly cleaner West Germany. Likewise, asthma is more common on the pristine, factory-free Isle of Skye, off the west coast of Scotland, than in Cardiff, the relatively gritty capital city of Wales. Douglas Dockery, a professor of environmental epidemiology at the Harvard School of Public Health, says that even if air pollution does not cause asthma, it can and does provoke symptoms in asthmatics. "It's very clear that in the United States asthma is worst in poor areas, and that we're seeing an increase of the disease in these areas," he says. "This makes us think that there must be environmental characteristics involved." Some scientists believe that diesel fumes are particularly potent asthma irritants, but most seem to agree with Dockery that symptoms are provoked by any number of pollutants, and that substances found indoors are often more irritating than auto and truck emissions. "It's tough to get a cab in the Bronx, and a lot of people don't have cars," Schroeder said. "So access is a problem. When kids have an asthma attack, their mothers call 911 and get an ambulance, which takes them to the emergency room. The kid is hospitalized, stabilized, given some medicine, and released. A few months later the kid is back."

Roaches and Dust Mites

SCHROEDER dropped me off at the Albert Einstein College of Medicine, where I was to meet David Rosenstreich, a professor of medicine, the director of the division of allergy and immunology, and one of the country's leading experts on asthma allergens. Rosenstreich had just returned from a meeting in Colorado, where he had delivered a lecture on cockroaches and asthma symptoms; he published what is widely regarded as the definitive study on the subject in a 1997 issue of *The New England Journal of Medicine*. He showed me slides of three of the 300 known cockroach species. Under magnification they appeared monstrous. "Wherever people go, from the Arctic to Antarctica, there are roaches," Rosenstreich told me. "They are really difficult to get rid of, particularly in multiple-family dwellings, because when you clean out one apartment, they simply move on to the next one, and then, when the coast is clear, they return." Children in infested homes are much likelier to show an allergic reaction to cockroaches than children who grow up without them, and are much likelier to have asthma attacks triggered by exposure to them. Rosenstreich said that roaches are by no means the

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only culprit. Fecal material produced by dust mites is also extremely allergenic, and given that dust mites require only heat, humidity, and dust (the major component of which is shed human skin) to survive, they are just as hard to get rid of as cockroaches. "Every square meter of mattress has twenty-four dust mites, and each dust mite produces seven fecal particles a day," Rosenstreich told me. "There's a quarter of a million fecal particles in every ounce of mattress dust. So you can see the difficulty." Many homes in and around Hunts Point and other inner-city neighborhoods have all the qualities associated with high asthma rates: poor ventilation, uncontrollable heating systems, and water damage that leads to the growth of molds, which are another important allergen. Carpets, Rosenstreich said, are breeding grounds for all sorts of nasty things, as are upholstered furniture and the piles of clothes that tend to accumulate when many people crowd into tight quarters without sufficient storage space.

"Five or more might share an apartment with a single bedroom," he said. "When you have so many crowded into such a tight space, you have lots of people showering, cooking, boiling water. That adds to the humidity, which of course is great for roaches."

Given the association of cockroaches and dust mites and mold with asthma, it may seem paradoxical that outside the United States asthma is a disease of affluence. There is, for example, almost no asthma in rural China or sub-Saharan Africa (apart from South Africa), yet it is rampant in Sweden and New Zealand and Australia. One possible explanation is that rugs, upholstery, and other items in which insects might want to nest are still luxuries in the developing world. This theory begins to break down, however, when one considers that there are plenty of dust mites and cockroaches in rural China, and that Australians are not notably partial to upholstery or wall-to-wall carpeting. More likely, cockroaches, dust mites, diesel fumes, tobacco smoke, dog hair, mold, and any number of other things are triggers of asthma -- but they do not cause it. Spending nearly all of one's time in a poorly ventilated home, as many inner-city American children do -- will surely aggravate asthma, but will probably not bring on the disease in someone not prone to it. What will bring it on? That, says Louise Cohen, the director of the New York City Childhood Asthma Initiative, is "the sixty-four-thousand-dollar question."

Immunity and Genes

ONLY recently have we understood what asthma is, let alone what causes it. Asthma was traditionally considered a simple allergic reaction that provoked spasms and constriction of the bronchial passages, resulting in wheezing and shortness of breath. But over the past twenty years it has become clear that although asthma attacks are episodic, the inflammation associated with them is chronic, and requires long-term management with anti-inflammatory medication -- in some cases for life. Scientists now believe that this chronic state is brought on by something that prevents the immune system from developing properly in the first months of life.

Starting out life with a naive immune system is not a bad thing. Were a fetus to have a mature immune system, it would almost certainly regard the mother as a foreign invader and reject her. A baby is protected for some time by antibodies passed to it through the placenta and, later, in breast milk. At about three months the immune system begins to mature in most infants. But in people who go on to develop asthma, the immune system seems to mature too slowly to be able to differentiate between annoying and serious irritants. As a result, the infant's system musters an armada of antibodies to fight cockroaches or dust mites as though they were deadly microbes. This results in an allergic reaction that constricts the airways and leads to hyper-responsive, or "twitchy,"

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lungs (*asthma* means "panting" in Greek). Not all infants with twitchy lungs show symptoms to the same degree; it is thought that the minority of asthmatics who develop the disease later in life may actually have had mild, undetected asthma from early infancy. In severe asthmatic episodes a minor irritant can set off an immune response that shuts down the airways completely, resulting in respiratory arrest and, in extreme cases, death. Richard Green, the chancellor of the New York City school system, died in such an episode eleven years ago.

Fernando Martinez, the director of respiratory sciences at the University of Arizona, trained in Italy as a pediatrician but decided to do research on asthma when he realized how many of his patients had it. "It was extraordinary, a huge problem," he told me recently. "Like most people, I assumed tobacco smoke and pollution were the problem - - this was the politically correct way to think. But these factors turned out not to play a major role. In high-pollution areas, in low-pollution areas, among all ethnic groups, there was asthma. Clearly, something else was involved."

Martinez, who came to the United States after launching his career in asthma research, is one of a number of specialists who believe that modern life may be responsible for the developed world's asthma rates -- but in a very unexpected way. It is not tobacco

smoke

or pollution that is at the heart of the problem, these specialists believe, but modern hygiene practices and antibiotics that foreclose the need for the young immune system to tackle microbial and parasitic challenges. "Just as you need to use your eyes to develop sight and your legs to develop the muscles to walk," Martinez said, "your immune system develops through its experience. By legitimately protecting our kids from dangerous infections we may have kept parts of their immune systems from maturing."

This could explain why children in the developing world, who are repeatedly infected by bacteria and parasites, are unlikely to contract asthma, whereas children in the developed world, who are inoculated against infectious diseases and frequently given antibiotics, are contracting asthma in ever greater numbers. (Martinez quoted estimates that an astonishing 40 percent of children in the United States are given antibiotics for a period of a month or more in their first year of life.)

Yet most children in the United States do not get asthma, probably because most do not have the genetic constitution for it. It is well known that African-Americans and Hispanic Americans have a significantly higher rate of asthma than Caucasian Americans, and that this is at least in part a consequence of genetic predisposition. African-Americans on average have a smaller lung capacity than Caucasians, for example; some scientists think this increases their asthma risk. It is very difficult to determine which factors in these groups may have a genetic underpinning and which are caused by something other than genes. Hispanics and African-Americans tend to have relatively high rates of premature birth, for example, which might predispose infants toward asthma.

Carole Ober, a professor of human genetics at the University of Chicago, has made a relatively homogeneous group, the Hutterites of South Dakota, a focus of her asthma work. The Hutterites are members of a religious sect that began in the Tyrolean Alps in the 1500s. In the 1870s a group emigrated to what is now South Dakota. For the past fifteen years Ober has studied 1,500 of their descendants, all of whom can trace their heritage to sixty-four ancestors. Of the 750 with whom her asthma work is concerned, all live on nine communal farms, nearly all eat a high-fat diet, and none smoke. Most mothers in this group breast-feed their newborns for at least nine months. None of this

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is surprising in a religious sect with Western European roots. What is perhaps surprising is that roughly 15 percent of these Hutterites have asthma -- the same rate found in poor inner-city children in a related study in Chicago.

Because the Hutterites are genetically homogeneous, Ober and her team have been able to compare the genetic material of those who have asthma with material from those who don't, and to distinguish several genes associated with the disease. Ober has studied the genetic material of her Chicago population for similarities. So far, the genes linked to asthma in the Hutterites appear also to be associated with asthma in the Chicago population. The disease differs greatly between the two groups, however, in terms of symptoms. Asthma in the Hutterites is mild -- so mild that before Ober's study it often went unnoticed and undiagnosed. Very few Hutterites require steroids, a fairly routine treatment for moderate to severe cases elsewhere. And even fewer are hospitalized for the disease.

Ober and her colleagues have tried to tease out what it is about the Hutterites' lives that makes their experience of asthma so much less traumatic than that of urban dwellers. The ways of life differ dramatically, of course, but what stands out is that Hutterites live close to nature and far from the stresses of the modern world. It has long been observed that stress can bring on asthma attacks. Perhaps even more important is t

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"The data in support of a protective effect [of farm animals] are looking increasingly good," says Patrick Holt, an immunologist who specializes in asthma at the TVW Telethon Institute for Child Health Research, in West Perth, Australia. "Such stimuli may aid in the normal postnatal maturation of the immune system and help it to correctly program immune responses against other agents, such as environmental allergens."

This is perhaps why the Hutterites, who rely on farm animals for their livelihood, do not have life-threatening asthma despite their genetic predisposition to the disease.

Although members of the sect do take antibiotics and are inoculated against childhood infections, their immune systems may benefit from early and frequent exposure to the parasites and microbes associated with farm animals. Evolutionarily speaking, this seems ideal: an immune system so vigilant that it is poised to overreact but whose responses are tempered by gentle exposure to the everyday grunge of the natural world. Such exposure is certainly not what most Western parents desire for their children. "If there is one thing that characterizes American culture, it's obsessive cleanliness," says Scott Weiss, a pulmonary epidemiologist and the chief of environmental and respiratory epidemiology at Harvard University's Channing Laboratory. "There may be some optimal timing when exposure to infection should occur, but because parasitic infection is so uncommon in the Western world, and other infections are prevented with vaccines or squashed by antibiotics, we're essentially preventing children from getting that exposure."

A concurrent rise in allergies, including food allergies, Weiss says, suggests that the Western diet may also play a role in rising asthma rates. Several preliminary studies have shown that the children of mothers who eat fatty fish and leafy green vegetables have less asthma than do other children. Weiss is currently doing a study of 6,000

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pregnant women to test this finding. He says, "One thing we do know: as the Western diet spreads around the world, so does asthma."

Another hallmark of the Western urban lifestyle is a markedly low level of physical activity. Watching television is by far the most frequent childhood pastime, and cyber-

play is beginning to take up the rest of what might be outdoor playtime. Thomas Platts-Mills, a professor of medicine in the division of allergy and immunology at the University of Virginia Medical Center, says that this trend may be making its own contribution to the asthma epidemic. "The question is," he says, "what is it about children running around for hours that might protect them from asthma?" Platts-Mills says that studies have shown that lungs are more likely to become twitchy if people go a half hour or more without taking deep breaths. Taking deep breaths, he says, is what children used to do when they scurried around the playground or chased their siblings. It seems that the fruits of progress -- inoculation against microbes, protection from parasites, and a life of leisure spent in climate-controlled comfort -- have had the unfelicitous and certainly unanticipated side effect of making us more vulnerable to a chronic lung disease.

Treatment and Prevention

THERE is no comprehensive surveillance of trends in asthma at the state or local level, although the National Center for Health Statistics conducts annual surveys that determine, among other things, asthma prevalence. It is hard to know for sure which lifestyle or environmental factors might be important in spreading the disease. At the International Conference of the American Lung Association and American Thoracic Society held last year, Surgeon General David Satcher singled out asthma as a condition for which current public-health measures were clearly not effective. "We're moving in the wrong direction, especially among minority children in the urban communities," he said, adding that the federal government is now making a major financial commitment to support research and programs aimed at intervention and prevention.

The toll of asthma continues to increase, despite important advances in diagnosis and treatment. Michael Rich, a pediatrician and a child-health researcher at Harvard Medical School, says this is no mystery, given how little we know about the causes of asthma and how to prevent it. "Billions of dollars are being spent on this disease, and we know a lot about it, yet it's getting worse, because we're not asking the right questions," Rich told me recently. "The real question is, what stands in the way of knowledge being translated into behavior?"

While scientists are scrambling to find the underlying reason for the explosion in asthma, and federal health agencies are devoting tens of millions of dollars to these efforts, society is exploring a means by which to contain the disease. The Department of Housing and Urban Development and the Centers for Disease Control have made public their deep concern about asthma. Earlier this year HUD awarded \$4.5 million in grants to help inner-city residents clean, repair, and maintain their homes in order to reduce asthma triggers. Whether this will dramatically reduce asthma symptoms is unclear, but it is doubtless a good first step. And more needs to be done. A study published last September in the *Journal of Pediatrics* found that severe asthma symptoms and hospitalizations are significantly reduced when families are given regular access to specially trained social workers. Though of great benefit, such farsighted grassroots efforts have so far been scarce and sporadic, because of costs in time and money. "This is a chronic disease that requires comprehensive management," says Virginia

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Taggart, the health-science administrator with the division of lung diseases at the National Heart, Lung, and Blood Institute. "If anything, our patients are getting less time. Our health-care system is working against us."

As chronic diseases become an ever-greater part of the health-care burden, a change in emphasis from emergency treatment to long-term care seems an obvious step. Yet the American health-care system is designed to treat people as quickly and expeditiously as

possible, not necessarily to care for them. Until the system is reconfigured to deliver more than palliative care, asthma will continue to take a tragic toll.