STATE-OF-THE-ART REVIEW

Health Consequences of Environmental Exposures: Changing Global Patterns of Exposure and Disease



Philip J. Landrigan, MD, MSc, J. Leith Sly, PhD, Mathuros Ruchirawat, PhD, Emerson R. Silva, PhD, Xia Huo, MD, Fernando Diaz-Barriga, PhD, Heather J. Zar, MD, Malcolm King, PhD, Eun-Hee Ha, MD, Kwadwo Ansong Asante, DSc, Hamid Ahanchian, MD, Peter D. Sly, MD, DSc

New York, NY; Brisbane, Australia; Bangkok, Thailand; Caxias do Sul, Brazil; Shantou, China; San Luis Potosi, Mexico; Cape Town, South Africa; Burnaby, BC, Canada; Seoul, Republic of South Korea; Acra, Ghana; and Mashhad, Iran

Abstract

Environmental pollution is a major cause of disease and death. Exposures in early life are especially dangerous. Patterns of exposure vary greatly across countries. In low-income and lower middle income countries (LMICs), infectious, maternal, neonatal, and nutritional diseases are still major contributors to disease burden. By contrast, in upper middle income and high-income countries noncommunicable diseases predominate. To examine patterns of environmental exposure and disease and to relate these patterns to levels of income and development, we obtained publically available data in 12 countries at different levels of development through a global network of World Health Organization Collaborating Centres in Children's Environmental Health. Pollution exposures in early life contribute to both patterns. Chemical and pesticide pollution are increasing, especially in LMICs. Hazardous wastes, including electronic waste, are accumulating. Pollutionrelated chronic diseases are becoming epidemic. Future Global Burden of Disease estimates must pay increased attention to the short- and long-term consequences of environmental pollution.

KEY WORDS pollution, non-communicable disease, children, low and middle income countries, publich health

© 2016 The Authors. Published by Elsevier Inc. on behalf of Icahn School of Medicine at Mount Sinai. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

INTRODUCTION

Environmental pollution is a major cause of disease, death, and disability in countries around the world. The World Health Organization (WHO) calculates that pollution is responsible for approximately 7 million deaths per year, roughly equally attributable to ambient and indoor air pollution^{1,2}—a toll greater than the number of deaths caused by HIV/AIDS, malaria, and tuberculosis combined. The vast majority (94%) of these pollution-related deaths occur in low-income and lower middle income countries.

Exposures to environmental pollution in early life are especially hazardous.^{5,6} Susceptibility is greatest

No author has a conflict of interest with any material included in this article.

PDS and PJL conceived the concept for the article. All authors contributed data from their country, with data gaps filled by JLS from on-line sources. PJR wrote the first draft of the article, all authors gave comments and edits and PDS compiled the final version. All authors read and approved the final

From the Icahn School of Medicine at Mount Sinai, New York, NY (PJL); Children's Health and Environment Program, Queensland Children's Medical Research Institute, The University of Queensland, Brisbane, Australia (JLS, PDS); Chulabhorn Research Institute, Bangkok, Thailand (MR); University of Caxias do Sul, Caxias do Sul, Brazil (ERS); Shantou University Medical College, Shantou, China (XH); Universidad Autonoma de San Luis Potosi, San Luis Potosi, Mexico (FD-B); MRC Unit on Child & Adolescent Health, University of Cape Town, Cape Town, South Africa (HJZ); Faculty of Health Sciences, Simon Fraser University, Burnaby, BC, Canada (MK); Ewah Womans University, Seoul, Republic of South Korea (E-HH); CSIR Water Research Institute, Accra, Ghana (KAA); Ghaem Hospital, Mashhad, Iran (HA). Address correspondence to P.S. (p.sly@uq.edu.au).

during "windows of vulnerability"-brief, precisely timed periods in embryonic, fetal, and early postnatal life when vital organs are sculpted through complex, highly choreographed, and tightly scheduled developmental processes. Exposures to harmful environmental influences during these critical periods can cause permanent anatomic, functional, and metabolic changes. It is now understood from research in pediatric toxicology, nutritional epidemiology, and psychosocial epidemiology that even very low level exposures in early life to environmental pollutants, nutritional imbalance, or toxic stress can result in permanent alterations of organ function. 10 This dysfunction can manifest as acute or chronic disease at any point across the life span from early infancy to extreme old age. 11 Major acute diseases linked to environmental pollution in early life are pneumonia and diarrheal disease. Chronic, noncommunicable diseases (NCDs) linked to early environmental exposures include disorders of neurobehavioral development, adult and pediatric asthma, hypertension, obesity, diabetes, cardiovascular disease, and cancer. These associations are covered in more detail in the article by Sly et al published in this edition.¹²

Patterns of environmental pollution and of the diseases that it causes vary greatly from country to country. National income and level of development appear to be critical factors responsible for these sharp differences. 13,14 The goal of this report is to examine patterns of environmental pollution and pollution-related disease in different countries and to elucidate the links among those differing patterns, national income, and level of development. Specifically, the report examines the differences in environmental exposure and disease that exist in low-income countries (LICs), middleincome countries (MICs), and high-income countries (HICs). It will seek to elucidate links at each level of development between early exposures to environmental pollution and risk of disease across the life span. The report takes a broad health perspective, considering the acute health consequences in infancy and childhood of adverse exposures in early life as well as the long-term and delayed effects of early exposures that become manifest only in adult life. The report will focus especially on childhood conditions that WHO has designated as major contributors to burden of disease, including diarrheal diseases, lower respiratory infections, asthma, mental and behavioral diseases, complications of preterm birth, and transport injuries. The report argues that the magnitude of the impact of environmental pollution on disease is insufficiently appreciated and seriously undercounted and that future analyses of the global burden of disease must place greater emphasis on hazardous environmental exposures, especially those encountered in early life. Finally, the report will examine the question of whether populations around the world are adequately protected by current legislation against hazardous exposures in the environment.

METHODS

This report presents data on patterns of environmental exposure and disease in 12 countries at different levels of development¹⁵—Australia, Brazil, Canada, China, Ghana, Iran, Mexico, South Africa, South Korea, Switzerland, Thailand, and the United States (Table 1). 16-19 These data were collected from publically available official sources in each country, the Institute for Health Metrics and Evaluation, or WHO sources by physicians and scientists who are members of global network of Collaborating Centres in Children's Environmental Health (CEH) that the WHO has constructed over the past decade in a wide range of countries at all levels of industrial and economic development. These Centres are now forming into a network to ensure effective collaboration and coordination of research efforts.²⁰ To date CEH Collaborating Centres have been designated in Australia, Brazil, Mexico, Japan, the Republic of Korea, Thailand, the United States, and Uruguay. The network is formally coordinated by the Collaborating Centre at the National Institute of Environmental Health Sciences.

Table 1. Ranking of 12 Countries on Human Development Index, 2014				
High Income	Australia	2		
	Switzerland	3		
	United States	5		
	Canada	8		
	Republic of Korea	15		
Upper Middle Income	Mexico	71		
	Iran	75		
	Brazil	79		
	Thailand	89		
	China	91		
Lower Middle Income	South Africa	118		
Low-Income	Ghana	138		

RESULTS

Differing Global Patterns of Environmental **Pollution.** Patterns of environmental pollution differ sharply across the 12 countries (Table 2). In low-income and lower middle income countries (LMICs), indoor air pollution and contaminated drinking water have traditionally been the major environmental risk factors for disease. 1,2,21 Among the 12 countries examined here, this pattern is seen most clearly in Ghana and South Africa. By contrast, in upper middle income countries and HICs, those traditional hazards have largely been controlled by the rise of public health systems and the construction of aqueducts, reservoirs, and sewer systems. Today, the principal environmental risk factors for children in HICs are ambient air pollution, toxic synthetic chemicals, pesticides, heavy metals, and the hazards of the urban built environment.

Toxic chemicals and pesticides have long been important pollutants in HICs. Many thousands of new chemicals and pesticides have been invented and disseminated widely into the environment over the past century.²² Most did not previously exist in nature. These chemicals are used today in millions of consumer products ranging from food packaging to clothing, building materials, motor fuels, cleaning products, cosmetics, toys, and baby bottles. They have become increasingly widely disseminated in the environment. Human exposure to these chemicals is widespread, and surveys in industrially developed countries have documented

measurable levels of more than 100 synthetic chemicals in the bodies of virtually all persons.²³ Synthetic chemicals have been linked to a wide array of disease.

Toxic chemicals and pesticides are today becoming increasingly important environmental pollutants in LMICs.²¹ Although not well publicized, the "chemical revolution" is one of the most important environmental changes that have transformed the developing world in the past half century. The movement of hazardous chemicals into LMICs is part of the overall globalization of the chemical manufacturing industry²⁴ and is being driven by the low labor costs in LMICs and the common absence of environmental protections.

Changing Global Patterns of Pollution-Related Disease. Patterns of disease show sharp differences across the 12 countries. These differences parallel the countries' very different patterns of environmental pollution. In LICs and LMICs, the principal diseases are those associated with indoor air pollution and water pollution—the ancient scourges of diarrhea and pneumonia—and although the incidence has fallen markedly, the millennium development goals targets will not be met by the end of 2015. 1,2,21 Infant mortality, maternal mortality, and malnutrition are common. Incidence and prevalence of vector-borne and parasitic diseases are high. Life expectancy is short.

In upper middle income and high-income countries a very different disease pattern predominates. As the result of environmental improvements plus vaccines and antibiotics, death rates in these

Country	Solid fuel use (% population) ¹⁶	Ambien pollution (annual μg/m³)	n ¹⁷ mean,	Improved water ¹⁸ (% population)	Improved sanitation ¹⁸ (% population)	Overweight ¹⁹ (% population)	Stunted ¹⁹ (% population)
		PM 10	PM 2.5				
Australia	0	10	6	100	100	No data	No data
Brazil	5.2	41	22	98	83	7.3	7.1
Canada	0	11	8	100	100	No data	No data
China	44.51	90	41	95	76	6.6	9.4
Ghana	82.58	98	49	89	15	2.6	22.7
Iran	0.01	127	76	96	90	No data	6.8
Mexico	15	79	27	96	85	9	13.6
South Africa	12.36	56	27	93	66	No data	23.9
South Korea	0.01	51	23	No data	100	6.7	2.5
Switzerland	0	23	15	100	100	No data	No data
Thailand	22.56	39	21	98	93	10.9	16.3
United States	0	20	12	99	100	6	2.1

countries have decreased by more than 50% compared with LICs. Life expectancy at birth has nearly doubled. Rates of pneumonia and diarrheal disease have fallen sharply. Infant mortality has decreased by 90%.²⁵ In the aftermath of this epidemiological transition, 26 the principal pediatric diseases seen today in HICs are chronic NCDs. 13 Asthma has more than doubled in incidence. 27 Birth defects are now the leading cause of infant death.²⁸ Neurodevelopmental disorders, including dyslexia, mental retardation, attention-deficit/hyperactivity disorder, and autism, have increased sharply in reported prevalence.²⁹ Leukemia and brain cancer in children have increased in incidence despite declining mortality. 30 Childhood obesity has more than tripled, 31 and its sequel, type 2 diabetes, has become epidemic. The major diseases of adults in these countries are also NCDs—heart disease, stroke, cancer, diabetes, and chronic lung disease.3

Specific information by disease is as follows.

Diarrheal disease. In all countries, death rates, as well as disease burden (years lived with disability [YLD]) from diarrheal disease, are highest in the age group younger than 5 years and decline with increasing age (Table 3). Highest death rates from diarrheal disease among the 12 countries examined here are seen in Ghana, Iran, and Mexico. The greatest burden of illness as a result of diarrheal disease is seen in Ghana, Iran, Mexico, Brazil, and South Africa. The difference in the death rate from diarrheal disease in the under-5 age group between Ghana (rate = 45.3), the country with the highest rate, and Australia (rate = 0.2), the country with the lowest rate, spans more than 2 orders of magnitude.

Lower respiratory infections and pneumonia. The pattern of lower respiratory infections and pneumonia is similar to that of diarrheal disease, with the greatest mortality and highest YLD in children younger than 5 years of age (Table 4). There are also great differences in the death rates, ranging from a rate of 137.6 per 100,000 in Ghana to 1.7 per 100,000 in Switzerland. The largest disease burden is seen in Mexico (YLD = 128.1/100,000) and the lowest in Canada (1.5/100,000). Interestingly, the YLD are higher in Australia than in Ghana and South Africa (Table 3).

Asthma. The pattern of disease caused by asthma is very different from that caused by diarrheal disease. Across all countries the greatest burden of childhood asthma is seen among children 10-14 years of age followed by 5-9 year olds (Table 5). The heaviest burden of asthmatic disease in all age groups is consistently seen in Australia, Brazil, and

Table 3. Age-Specific Diarrheal Disease Years Lived with Disability (YLD) in Different Countries; Rates/100,000, Listed from Highest to Lowest in Each Age Group

Age Group (y)	Country	Deaths	YLD
<5	Ghana	45.3	797.0
	Iran	7.8	797.0
	Mexico	15.5	766.8
	Brazil	18.2	719.8
	South Africa	202.9	675.4
	China	2.4	539.4
	South Korea	0.5	522.8
	Australia	0.2	495.6
	Switzerland	1.4	479.1
	Thailand	4.1	489.1
	United States	0.5	457.8
	Canada	0.4	450.0
5-9	South Africa	6.1	93.2
	Ghana	5.1	92.0
	Iran	0.3	83.3
	Mexico	0.6	82.5
	Brazil	0.4	80.0
	Thailand	0.4	67.7
	South Korea	0.02	60.8
	Ghana	5.1	57.0
	Switzerland	0.1	56.1
	Australia	0.02	56.0
	United States	0.03	55.3
	Canada	0.02	54.8
10-14	Ghana	2.5	67.8
	South Africa	2.9	64.7
	Iran	0.1	59.8
	Brazil	0.2	58.2
	Mexico	0.4	57.5
	Thailand	0.2	49.3
	United States	0.02	48.1
	Canada	0.02	47.4
	South Korea	0.01	43.6
	Australia	0.02	41.6
	China	0.04	41.2
	Switzerland	0.02	39.6
15-19	Ghana	5.4	56.4
	South Africa	5.5	51.3
	Iran	0.1	49.1
	Brazil	0.2	47.6
	United States	0.04	45.5
	Mexico	0.4	45.0
	Canada	0.03	44.8
	Thailand	0.2	40.6
	South Korea	0.02	35.3
	Australia	0.02	35.1
	China	0.04	33.6
	Switzerland	0.04	31.9
	JWIGCHAIN	0.04	31.3

Canada, followed by the United States, Switzerland, and Canada. The overall burden of asthmatic disease is lowest in Iran, China, Mexico, and Ghana.

Table 4. Age-Specific Lower Respiratory Infections Years Lived with Disability (YLD) in Different Countries; Rates/ 100,000, Listed from Highest to Lowest in Each Age Group

100,000, Listed Iro	m nighest to Lowe	st iii Eatii Age	Group
Age Group (y)	Country	Deaths	YLD
<5	Mexico	38.4	128.1
	Iran	32.2	102.6
	Brazil	32.7	102.6
	China	32.7	94.5
	Australia	1.8	68.9
	Ghana	137.6	56.3
	South Korea	2.5	52.3
	South Africa	118.6	46.8
	United States	2.9	38.7
	Thailand	26.5	33.0
	Switzerland	1.7	24.3
	Canada	2.5	1.5
5-9	Mexico	1.2	67.4
	Iran	1.0	51.9
	Brazil	1.6	43.0
	China	1.1	37.9
	Ghana	4.1	30.1
	South Korea	0.2	27.4
	Australia	0.1	25.3
	South Africa	3.0	24.5
	Thailand	2.8	17.7
	United States	0.3	17.6
	Switzerland	0.1	8.8
	Canada	0.2	0.7
10-14	Mexico	1.1	21.5
	Iran	0.6	14.6
	Brazil	1.6	11.9
	Ghana	2.2	8.7
	South Africa	2.3	7.7
	China	0.6	7.5
	South Korea	0.2	7.2
	Australia	0.1	6.3
	United States	0.3	5.3
	Thailand	2.1	5.1
	Switzerland	0.1	2.7
	Canada	0.1	2.7
15-19	Mexico	1.6	16.7
	Iran	0.7	10.9
	Brazil	2.6	9.1
	Ghana	8.9	7.1
	South Africa	7.8	6.4
	South Korea	0.2	4.6
	Australia	0.1	4.3
	United States	0.5	4.0
	Thailand	3.0	4.0
	Switzerland	0.2	2.4
	Canada	0.4	0.2

In sharp contrast to the data on asthma morbidity, however, the highest death rates as a result of early childhood asthma (<5 years) are seen in Ghana and asthma severity appears to be increased in LMICs.

Mental and behavioral disorders. Mental and behavioral disorders of childhood increase in prevalence with advancing age to reach their highest levels in 15-19 year olds (Table 6). Highest rates of morbidity (YLD) from mental and behavioral disorders are seen among 15-19 year olds in the United States, Brazil, Switzerland, Australia, and Canada. Brazil, Switzerland, and the United States also report the highest burden of disease from these disorders among 10- to 14-year-old children. Highest death rates from mental and behavioral disorders are seen among 15-19 year olds in South Africa followed by the United States. Disease burden as a result of these conditions is consistently lowest in Mexico, China, and Iran. However, these data must be considered with caution because the documentation of mental and behavioral disorders is less reliable in LMICs and fewer resources are devoted to mental disorders in these countries.

Preterm complications. Deaths from preterm birth complications, as defined in official statistics, are seen exclusively in the age group younger than 5 years (Table 7). By contrast, morbidity from preterm birth complications extends across childhood and adolescence. Deaths from preterm birth complications are reported most commonly in Ghana, South Africa, Brazil, and Iran. Morbidity from preterm birth complications is consistently highest across age groups of childhood in the United States, followed by Brazil, Mexico, South Africa, and Iran.

Transport injuries. The WHO includes deaths and injuries from road traffic collisions in its list of environmental exposures. Rates of death and injury from transport injuries are generally highest in 15-19 year olds, followed by 10-14 year olds (Table 8). The major risk factors for transport injuries among young children in South Africa are lack of infant seats and seatbelts. Among children 0-5 years of age, the highest death rates from transport injuries are reported from Iran, Ghana, China, and Thailand.

DISCUSSION

The data presented in this report indicate that environmental exposure is a major cause of disease, death, and disability in countries around the world. However, the specific types of pollution, the routes of exposure, the specific toxicants, and the resulting patterns of disease vary greatly from country to country. Income and level of development are major determinants of these different patterns of environmental pollution and disease. ^{13,14} Deep social and economic

Table 5. Age-Specific Asthma Years Lived with Disability (YLD) in Different Countries; Rates/100,000, Listed from Highest to Lowest in Each Age Group

Age Group (y)	Country	Deaths	YLD
<5	Brazil	0.5	168.1
	Australia	0.1	157.0
	Canada	0.1	112.8
	South Africa	0.7	94.2
	United States	0.2	90.9
	Thailand	1.1	76.4
	Switzerland	1.5	65.00
	South Korea	0.3	55.90
	Ghana	1.8	35.30
	Mexico	0.6	31.50
	China	0.1	17.60
	Iran	0.4	5.00
5-9	Australia	0.1	1037.2
	Brazil	0.1	917.5
	Canada	0.1	765.2
	United States	0.2	608.0
	South Africa	0.3	555.6
	Switzerland	0.3	545.9
	Thailand	0.3	444.8
	South Korea	0.04	346.9
	Ghana	0.3	246.5
	Mexico	0.2	175.1
	China	0.05	120.7
	Iran	0.1	40.2
10-14	Australia	0.10	1291.9
	Brazil	0.10	1060.1
	Canada	0.10	958.5
	United States	0.3	764.9
	Switzerland	0.40	691.8
	South Africa	0.30	668.4
	Thailand	0.3	531.0
	South Korea	0.03	441.5
	Ghana	0.30	314.4
	Mexico	0.20	206.4
	China	0.04	147.1
	Iran	0.1	50.8
15-19	Australia	0.20	839.9
	Brazil	0.10	612.6
	Canada	0.10	579.4
	Switzerland	0.60	469.4
	United States	0.30	463.0
	South Africa	1.20	395.5
	Thailand	0.3	300.1
	South Korea	0.04	239.5
	Ghana	0.70	176.0
	Mexico	0.20	117.4
	China	0.10	77.6
	Iran	0.1	60.9

injustices underlie and shape global patterns of pollution. In LICs and LMICs, the predominant environmental pollutants are contaminated indoor

Table 6. Age-Specific Mental and Behavioral Disorders Years Lived with Disability (YLD) in Different Countries; Rates/ 100,000, Listed from Highest to Lowest

Age Group (y)	Country	Deaths	YLD
<5	United States	0.2	109.9
	Canada	0.2	98.7
	China	0.6	95.6
	South Africa	17.9	94.5
	Thailand	0.2	92.3
	South Korea	0.1	92.7
	Australia	0.2	91.5
	Ghana	0.6	90.6
	Switzerland	0.1	90.0
	Iran	0.8	88.3
	Brazil	0.3	86.9
	Mexico	0.6	83.8
5-9	Iran	0.2	1186.7
	Brazil	0.05	1070.1
	Switzerland	0.03	1037.7
	Thailand	0.1	989.4
	South Africa	1.2	948.0
	Ghana	0.1	930.3
	Canada	0.04	924.6
	Australia	0.05	863.5
	China	0.03	811.0
	Mexico	0.1	815.1
	South Korea	0.01	807.9
10-14	Iran	0.01	2514.4
10-14	Brazil		
		0.06	2171.7
	Switzerland	0.04	2167.1
	United States	0.1	2044.8
	Thailand	0.1	1958.5
	South Africa	0.9	1895.9
	Ghana	0.1	1850.4
	Canada	0.1	1804.7
	Australia	0.1	1763.4
	South Korea	0.03	1600.8
	Mexico	0.1	1489.1
	China	0.1	1446.9
15-19	Iran	0.7	3488.1
	United States	2.1	3392.6
	Brazil	0.4	3318.1
	Switzerland	0.8	3236.6
	Australia	1.6	3029.7
	Canada	0.8	2946.5
	South Africa	4.5	2799.5
	Thailand	0.1	2756.7
	South Korea	0.1	2609.7
	Ghana	0.3	2536.1
	Mexico	0.7	2227.3
	China	0.2	2112.8

air and contaminated drinking water. ^{1,2} The resulting diseases are pneumonia and diarrhea, along with high rates of infant, child, and maternal mortality. In high-income and upper middle

Table 7. Age-Specific Preterm Complications Years Lived with Disability (YLD) in Different Countries; Rates/100,000, Listed from Highest to Lowest

Age Group (y)	Country	Deaths	YLD
<5	United States	47.4	65.4
	Thailand	49.1	63.4
	Brazil	99.7	50.1
	Mexico	59.4	48.4
	Iran	99.2	45.4
	South Africa	113.0	45.1
	Ghana	129.3	43.4
	Australia	26.6	43.0
	China	33.6	42.3
	Canada	31.8	40.3
	South Korea	17.6	34.9
	Switzerland	18.7	32.4
5-9	United States	_	63.0
	Thailand	_	60.2
	Brazil	_	47.4
	Mexico	_	46.6
	Iran	_	43.3
	South Africa	_	43.0
	Ghana	_	42.5
	Australia	_	41.5
	China	_	40.6
	Canada	_	38.8
	South Korea	_	33.4
	Switzerland	_	31.5
10-14	United States	_	60.9
	Thailand	_	58.4
	Brazil	_	45.5
	Mexico	_	45.0
	South Africa	_	41.9
	Iran	_	41.8
	Ghana	_	41.2
	Australia	_	40.0
	China	_	39.7
	Canada	_	37.6
	South Korea	_	32.3
	Switzerland	_	30.9
15-19	United States	_	59.4
	Thailand	_	57.3
	Brazil	_	45.1
	Mexico	_	43.8
	Iran	_	40.8
	South Africa	_	40.8
	Ghana	_	40.4
	Australia	_	39.5
	China	_	38.8
	Canada	_	36.7
	South Korea	_	31.6
	Switzerland		30.4

income countries, by contrast, ambient air pollution, toxic chemicals, and pesticides are the dominant environmental hazards, and NCDs have

Table 8. Age-Specific Transport Injuries Years Lived with Disability (YLD) in Different Countries; Rates/100,000, Listed from Highest to Lowest

Age Group (y)	Country	Deaths	YLD
<5	Canada	2.6	27.0
	South Africa	3.0	19.4
	Iran	23.3	10.4
	Australia	2.9	10.4
	Switzerland	2.6	9.1
	China	6.8	8.7
	Thailand	6.5	7.4
	Ghana	9.7	7.3
	Brazil	4.6	6.4
	South Korea	4.4	6.3
	South Africa	3.0	5.9
	Mexico	6.7	4.6
	United States	3.7	4.4
5-9	South Africa	2.5	149.4
	South Korea	1.7	76.1
	Iran	12.2	55.8
	Australia	1.7	54.9
	Switzerland	1.9	49.9
	China	3.6	45.5
	Thailand	4.2	37.7
	Ghana	5.2	37.6
	South Korea	2.6	34.2
	Brazil	4.4	33.3
	South Africa	2.5	33.3
	Mexico	4.0	24.3
	Canada	2.0	24.3
	United States	2.8	23.3
	Iran	12.2	10.0
10-14	South Africa	2.3	253.3
	South Korea	6.9	131.5
	Australia	2.2	117.6
	Switzerland	1.1	117.0
	Iran	8.8	115.6
	China	3.0	95.9
	Thailand	8.3	83.7
	Ghana	4.2	79.7
	South Africa	2.3	77.5
	South Korea	1.6	76.1
	Brazil	5.8	72.0
	Canada	18.7	53.3
	Mexico	5.3	52.9
	United States	3.7	52.4
	Iran	8.8	20.0
15-19	Switzerland	9.8	200.7
.5 15	Iran	20.3	200.7
	Australia	14.0	198.5
	China	13.1	163.3
	Thailand	38.4	150.3
	South Africa		
	Ghana	12.6	146.0
		16.8	136.2
	South Korea	6.9	131.5
		(continued on n	ext page)

Table 8. continued					
Age Group (y)	Country	Deaths	YLD		
	Brazil	21.3	124.0		
	Canada	15.9	94.3		
	United States	21.6	92.6		
	Mexico	17.1	92.6		
	South Africa	12.6	86.7		
	South Korea	2.6	34.3		

become the principal causes of morbidity and mortality. 26

Exposures to environmental pollutants in early life are especially dangerous and can cause acute infections, morbidity, or death in infancy and childhood as well as chronic NCDs that can become manifest at any point across the human life span. 11,12 Rates of asthma are increased in children exposed to urban air pollution.³³ Prenatal exposure to polychlorinated biphenyls is linked to reductions in IQ scores.³⁴ Prenatal exposure to the organophosphate insecticide chlorpyrifos is associated with reduced head circumference at birth and developmental delays, reduced IQ, and pervasive developmental disorder. 35,36 Baby boys exposed in utero to phthalates appear to be at increased risk of developing behavioral abnormalities resembling attention-deficit/hyperactivity disorder.37 Prenatal exposure to phthalates has also been linked to shortening of the anogenital distance in baby boys, a marker of feminization.³⁸ Prenatal exposure to bisphenol A is linked to behavioral abnormalities.³⁹ Prenatal exposure to brominated flame retardants has been linked to reductions in IQ.40 Prenatal exposures to the metals arsenic and manganese are linked to reductions in IQ, cancer, and neurodevelopmental disorders. 41,42 Prenatal exposures to the perfluorinated chemicals PFOA and PFOS have been linked to decreased birth weight and reduced head circumference in newborn infants. 43 A large number of the synthetic chemicals in widest use have never undergone any safety testing and their potential toxicity is therefore not known.²² Only about 20% have been screened for developmental toxicity. Even less is known about the possible synergistic effects of simultaneous exposures to multiple untested synthetic chemicals. Likelihood is high that there are other still undiscovered diseases and disabilities caused by widely used synthetic chemicals whose toxicity has not yet been recognized.¹¹

The data presented indicate that the once very separate patterns of disease in LMICs and HICs are converging.⁴⁴ With globalization of trade,

spread of the "western lifestyle," and increasing globalization of the chemical manufacturing industry, the new reality in global health is that NCDs are becoming a major problem in countries around the world. Toxic chemicals and other environmental hazards that previously were found only in developed countries are now pouring into LMICs with ever increasing rapidity. Production and use of synthetic chemicals were initially concentrated in HICs. This reflected the origins of the chemical manufacturing industry in Western Europe in the late 19th and early 20th centuries and its spread in the 20th century to North America, Japan, and Australia. Today, however, the chemical manufacturing industry is highly globalized, and the manufacture and use of chemicals are shifting increasingly to LMICs²³ where labor costs are low and environmental protections few. Tragic episodes of occupational and environmental exposure to toxic chemicals have resulted from the movement of the chemical industry to LMICs and have caused great damage. These include acute episodes such as the Bhopal disaster in India, where thousands of people of all ages died and were severely injured after acute exposure to methyl isocyanate after an explosion in a pesticide manufacturing facility, 44 as well as chronic, slowly unfolding tragedies such as the current exposure of more than 1 million persons in China, South and Southeast Asia, and sub-Saharan Africa to chrysotile asbestos.4

The data presented here indicate that environmental pollution is insufficiently appreciated and inadequately quantified as a cause of disease. As is detailed by Sly et al¹² in this edition, one reason why pollution is undercounted as a risk factor is that a very high standard of proof is required to establish etiologic associations between pollution and illness. 46 A second reason is that the various components of pollution such as air pollution, water pollution, asbestos, and lead have traditionally been counted separately, one at a time. This disaggregated approach reflects the typical approach to environmental health research and also is consistent with the structure of most public health and environmental protection agencies, which typically have separate bureaus for air, water, and solid waste. However, an unintended consequence of this fragmentation is that it minimizes the total impact of pollution and thus fails to give pollution the attention it deserves in planning and policymaking.

To confront the global problem of disease caused by pollution of all types, improved programs of public health and environmental protection are needed in countries at every level of economic development. Pollution control strategies and technologies that have been developed and successfully deployed in HICs need to be transferred to low- and middle-income countries and their implementation needs to be adequately funded. These strategies have succeeded by controlling exposures at source. Lead has been removed from gasoline. Asbestos use has been sharply curtailed and in some countries banned. Air and water pollution have been reduced. Highly toxic pesticides have been replaced. These actions have produced tangible benefits for human health and the environment. They are highly cost effective and have lifted the economies of entire nations.

Pollution control needs to receive a higher priority in the international development agenda, a level at least the equivalent of that assigned to HIV/AIDS, malaria, and tuberculosis control. The lack of attention given to pollution in the program priorities of major international organizations is striking, especially given the substantial impact and favorable cost/benefit ratio of pollution control programs. Pollution protections are especially urgently needed in LMICs, where chemical production and use are rapidly increasing and environmental and occupational safeguards are too often few. Current legal structures in many countries fail to adequately protect workers, children, and other vulnerable populations against environmental threats to health. ²²

Construction of strong public health and environmental protection programs will require several elements at the country level. Tracking systems to monitor environmental pollution and disease provide an essential foundation for these systems. Training of physicians and other health care providers to recognize and manage diseases caused by environmental

pollution is a second essential need. Legally mandated safety testing of new chemicals before they are introduced to commercial markets and of existing chemicals is a third essential pillar of chemical control at the country level.²² Assessment of toxicity must be followed by governmental regulation. Voluntary controls appear to be of little value.

At the international level, an argument can be made for the formation of a new international clearinghouse focused on defining the health effects of environmental pollution. This new agency could be modeled on the International Agency for Research on Cancer. It would assess industrial chemicals and other forms of pollution for potential health effects using a precautionary approach that emphasizes prevention and does not require absolute proof of toxicity. It will facilitate and coordinate epidemiological and toxicological studies and will lead the urgently needed global programs for pollution prevention.

CONCLUSIONS

The adverse health consequences of exposure to environmental toxicants are major and growing problems, yet receive insufficient attention. It is time to focus the world's attention on the great and growing global problem of environmental pollution. It is time to set hard but feasible numerical targets for pollution control. Pollution, of all types, deserves as much attention as infectious diseases and the global response to pollution deserves the same degree of rigor as has been applied to AIDS, tuberculosis, and malaria. Focus by the international community on environmental pollution can save the lives of millions of people, cost effectively and predictably. The need is great, and the time is now.

REFERENCES

- 1. World Health Organization. 7 million deaths annual linked to air pollution. Geneva: WHO; Available at: http://www.who.int/phe/health_topics/out doorair/databases/en/. Accessed July 9, 2014.
- World Health Organization. Burden of disease from household air pollution for 2012. Geneva: WHO. Available at: http://www.who.int/phe/health_topics /outdoorair/databases/FINAL_HAP_ AAP_BoD_24March2014.pdf?ua=1; 2014. Accessed July 9, 2014.
- 3. World Health Organization. Data on the size of the HIV/AIDS epidemic:

- number of deaths due to HIV/AIDS. Global Health Observatory Data Repository. Geneva: WHO; 2014.
- World Health Organization. Deaths: estimated deaths, data by region. Global Health Observatory Data Repository. Geneva: WHO. Available at: http://apps.who.int/gho/data/view. main.14117?lang=en; 2014. Accessed July 9, 2014.
- 5. Hubel D, Wiesel T. Brain mechanisms of vision. Sci Am 1979;241:150–62.
- World Health Organization. Environmental Health Criteria 237. Principles for evaluating health risks in children
- associated with exposure to chemicals. Geneva: WHO. Available at: http://www.who.int/ipcs/publications/ehc/ehc237.pdf; 2006. Accessed November 28, 2014.
- Miller RW. How environmental hazards in childhood have been discovered: carcinogens, teratogens, neurotoxicants, and others. Pediatrics 2004;113(4 Suppl): 945-51.
- 8. Barker DJ. The developmental origins of adult disease. J Am Coll Nutr 2004;23(6 Suppl):588S—95S.
- Shonkoff JP, Garner AS. Committee on Psychosocial Aspects of Child

Landrigan et al.

- and Family Health, Committee on Early Childhood, Adoption, and Dependent Care, Section on Developmental and Behavioral Pediatrics. The lifelong effects of early childhood adversity and toxic stress. Pediatrics 2012;129:e232–46.
- 10. World Health Organization and United Nations Environment Programme. State of the Science on Endocrine Disrupting Chemicals. Geneva: WHO. Available at: http://www.environmentalhealthnews.org/ehs/news/2013/pdf-links/EDC%20 summary%201ayout%20040213-3.pdf; 2012. Accessed November 28, 2014.
- Grandjean P, Landrigan PJ. Neurobehavioural effects of developmental toxicity. Lancet Neurol 2014;13:330–8.
- 12. Sly PD, Carpenter DO, Van den Berg M, et al. Health consequences of environmental exposures: causal thinking in global epidemiology. Annals of Global Health 2016;82(1): 3-9.
- Barreto ML. The globalization of epidemiology: critical thoughts from Latin America. Int J Epidemiol 2004;33:1132-7.
- 14. De Maio FG. Understanding chronic non-communicable diseases in Latin America: towards an equity based research agenda. Globaliz Health 2011:7:36.
- United Nations Development Programme. Human Development Index. New York: UN. Available at: https://data.undp.org/dataset/HDI-Indicators-By-Country-2014/5tuc-d2a9?. Accessed December 1, 2014.
- 16. World Health Organization Global Health Observatory. Population Using Solid Fuels 2013. Geneva: WHO. Available at: http://apps.who.int/gho/athena/data/download.xsl?format=xml&target=GHO/WHS5_512&profile=excel&filter=COUNTRY:*;REGION; 2014. Accessed February 26, 2015.
- 17. World Health Organization Ambient Air Pollution Database 2014. Country Level PM10 and PM 2.5. Available at: http://www.who.int/phe/health_topics/ outdoorair/databases/AAP_database_ results_2014.pdf. Accessed July 29, 2015.
- UNICEF and World Health Organization. 25 Years of Progress on Sanitation and Drinking Water: 2015
 Update and MDG Assessment. New York: World Health Organization Press; 2015.
- UNICEF, World Health Organization, and World Bank. Joint UNICEF, WHO and World Bank child malnutrition estimates. Geneva: WHO; 2014 Available at: data. unicef.org, who.int/nutgrowthdb/estimates, or data.worldbank.org. Accessed July 28, 2015

- Sly PD, Neira M, Collman G, et al. Networking to advance progress in children's environmental health. Lancet Global Health 2014;2:e129–30.
- Pronczuk J, Bruné M-N, Gore F. Children's environmental health in developing countries. In: Nriagu JO, ed. Encyclopedia of Environmental Health. Burlington: Elsevier; 2011:601–10.
- Landrigan PJ, Goldman LR. Children's vulnerability to toxic chemicals: a challenge and opportunity for health and environmental policy. Health Aff 2011;30:842-50.
- Centers for Disease Control and Prevention. Fourth National Report on Human Exposure to Environmental Chemicals, 2010. Atlanta, GA: CDC. Available at: http://www.cdc. gov/exposurereport/; 2010. Accessed July 29, 2015.
- 24. Spitz PH, ed. Chemical industry at the millennium. Maturity, restructuring and globalization. Philadelphia: Chemical Heritage Foundation; 2003.
- Mathews TJ, Miniño AM, Osterman MJ, Strobino DM, Guyer B. Annual summary of vital statistics: 2008. Pediatrics 2011;127:146–57.
- Omran AR. The epidemiologic transition: a theory of the epidemiology of population change. Milbank Mem Fund Q 1971;49:509

 –38.
- 27. US Environmental Protection Agency. America's Children and the Environment. Percentage of Children with Asthma. Available at: http://www.epa.gov/economics/children/child_illness/d1-graph.html. Accessed July 29, 2015.
- Centers for Disease Control and Prevention. Improved national prevalence estimates for 18 selected major birth defects—United States, 1999-2001.
 Morb Mortal Wkly Rep 2006;54: 1301-5.
- Centers for Disease Control and Prevention. Prevalence of autism spectrum disorder among children aged 8 years—Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2010. MMWR Surveill Summ 2014;63(SS02):1–21.
- National Cancer Institute. SEER
 Database. Bethesda, MD: National
 Institutes of Health. Available at:
 http://seer.cancer.gov/. Accessed July
 29, 2015.
- 31. Centers for Disease Control and Prevention. Overweight and obesity. Childhood obesity facts. Prevalence of childhood obesity in the United States, 2011-2012. Atlanta, GA: CDC. Available at: http://www.cdc.gov/obesity/data/childhood.html; 2013. Accessed November 9, 2014.
- 32. Kelly BB, Narula J, Fuster V. Recognizing global burden of cardiovascular disease and related chronic diseases. Mt Sinai J Med 2012;79:632–40.

- Gauderman WJ, Avol E, Gilliland F, et al. The effect of air pollution on lung development from 10 to 18 years of age. N Engl J Med 2004;351: 1057–67.
- Jacobson JL, Jacobson SW. Intellectual impairment in children exposed to polychlorinated biphenyls in utero. N Engl J Med 1996;335:783—9.
- 35. Rauh V, Arunajadai S, Horton M, et al. 7-year neurodevelopmental scores and prenatal exposure to chlorpyrifos, a common agricultural pesticide. Environ Health Perspect 2011;119:1196–201.
- 36. Bouchard MF, Chevrier J, Harley KG, et al. Prenatal exposure to organophosphate pesticides and IQ in 7-year old children. Environ Health Perspect 2011;119:1189—95.
- Engel SM, Miodovnik A, Canfield RL, et al. Prenatal phthalate exposure is associated with childhood behavior and executive functioning. Environ Health Perspect 2010;118:565-71.
- Swan SH. Environmental phthalate exposure in relation to reproductive outcomes and other health endpoints in humans. Environ Res 2008;108: 177–84.
- Braun JM, Yolton K, Dietrich KN, et al. Prenatal bisphenol A exposure and early childhood behavior. Environ Health Perspect 2009;117:1945–52.
- 40. Herbstman JB, Sjödin A, Kurzon M, et al. Prenatal exposure to PBDEs and neurodevelopment. Environ Health Perspect 2010;118:712—9.
- Wasserman GA, Liu X, Parvez F, et al. Water arsenic exposure and intellectual function in 6-year-old children in Araihazar, Bangladesh. Environ Health Perspect 2007;115:285—9.
- 42. Wasserman GA, Liu X, Parvez F, et al. Water manganese exposure and children's intellectual function in Araihazar, Bangladesh. Environ Health Perspect 2006;114:124–9.
- 43. Apelberg BJ, Witter FR, Herbstman JB, et al. Cord serum concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in relation to weight and size at birth. Environ Health Perspect 2007;115:1670–6.
- 44. Dhara VR, Dhara R, Acquilla SD, Cullinan P. Personal exposure and long-term health effects in survivors of the union carbide disaster at Bhopal. Environ Health Perspect 2002;110:487–500.
- Frank A, Joshi TK. The global spread of asbestos. Ann Global Health 2014;80:257-62.
- Murray CJ, Ezzati M, Flaxman AD, et al. Global Burden of Disease 2010: a multi-investigator collaboration for global comparative descriptive epidemiology. Lancet 2012;380:2055

 –8.