RGA

Re-flections

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LETTER FROM THE EDITOR

Dear Readers:

The broad theme of this issue of *Re-flections* concerns the interplay between our environment and disease. The human genome project has focused a great deal of attention on the relationship between an individual's genome and the propensity to develop specific diseases or conditions; however it is ultimately the interplay between the genome and the environment that determines the nature of the disease that eventually leads to one's demise.

In the premodern era in developed countries, the leading causes of death have been directly attributed to: famine, pestilence, war and strife. These factors substantially held world population in balance for many years. Most of the recent advances in human mortality have been due to improvements in sanitation, vaccinations, food treatment and production, and antibiotics.

Our culture has developed around high-intensity cultivation of soil. During the last century this has led to the rapid relocation of most of the population into large urban areas, since fewer farmers per capita are needed to support the population's food needs. While this has concentrated a huge amount of intellectual talent into creative urban centers, it has also taxed our ability to provide a clean environment in which to live. In addition, it has created an ideal environment for microbes in need of a large number of potential host organisms living in proximity. The challenge in years to come will be to maintain the integrity of our atmosphere and water supply, as well as to prevent soil depletion from intensive agriculture.

How we live within our environment will also determine the types of disease processes that will be seen. The use of tobacco and alcohol products has played a significant role in disease distribution. Equally, so has the reliance on automobiles. While internal combustion engines have played an integral role in our ability to distribute the products necessary for modern living, they represent a double-edged sword. The sedentary living associated with use of the automobile has no doubt contributed to the plague of obesity that we are now experiencing in many countires, and may even be secondarily related to the increase in the incidence of Type 2 diabetes. It is also contributing to global warming.

Other environmental factors not faced in the past include ozone depletion and the potential development of 'super-microbes'. The development and impact of genetically modified foods has yet to be determined. Likewise, our dependence on highly processed foods may prove to be contributory to certain diseases.

The leading causes of death at the end of the 20th century are listed to the right. What will this pattern look like over the next 20 – 50 years? Will the diseases of degeneration, sedentary living and damaged immunity take the upper hand? Only one thing is certain, the pattern will likely change, and as insurers, we must try to anticipate the change and prepare for the consequences.

Sincerely,
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> Table B

Table B. Percent of total deaths, death rates, age-adjusted death rates for 1997, percent change in age-adjusted death rates from 1996 to 1997 and 1979 to 1997, and ratio of age-adjusted death rates by race and sex for the 15 leading causes of death for the population in 1997
[Death rates on an annual basis per 100,000 population; age-adjusted rates per 100,000 U.S. standard population]

Rank1	Cause of death (codes on the Ninth Revision International Classification of Diseases, 1975)	Percent of total deaths	Death rate	Age-adjusted death rate				
				1997	Percent change 1996 to 1997	Percent change 1979 to 1997	Ratio Male to female	Ratio Black to white
...	All causes	100.0	864.7	479.1	-2.5	-17.0	1.6	1.5
1	Diseases of heart	31.4	271.6	130.5	-3.0	-34.6	1.8	1.5
2	Malignant neoplasms, including neoplasms of lymphatic and hematopoietic tissues	23.3	201.6	125.6	-1.8	-4.0	1.4	1.3
3	Cerebrovascular diseases	6.9	59.7	25.9	-1.9	-37.7	1.2	1.8
4	Chronic obstructive pulmonary diseases and allied conditions	4.7	40.7	21.1	0.5	44.5	1.5	0.8
5	Accidents and adverse effects	4.1	35.7	30.1	-1.0	-29.8	2.4	1.2
...	Motor vehicle accidents	1.9	16.2	15.9	-1.9	-31.5	2.1	1.1
...	All other accidents and adverse affects	2.3	19.5	14.2	-	-27.6	2.8	1.4
6	Pneumonia and influenza	3.7	32.3	12.9	0.8	15.2	1.5	1.4
7	Diabetes mellitus	2.7	23.4	13.5	-0.7	37.8	1.2	2.4
8	Suicide	1.3	11.4	10.6	-1.9	-9.4	4.2	0.6
9	Nephritis, nephrotic syndrome, and nephrosis	1.1	9.5	4.4	2.3	2.3	1.5	2.6
10	Chronic liver disease and cirrhosis	1.1	9.4	7.4	-1.3	-38.3	2.3	1.2
11	Alzheimer's disease	1.0	8.4	2.7	-	1,250.0	0.9	0.7
12	Septicemia	1.0	8.4	4.2	2.4	82.6	1.2	2.8
13	Homicide and legal intervention	0.9	7.4	8.0	-5.9	-21.6	3.8	6.0
14	Human immunodeficiency virus infection	0.7	6.2	5.8	-47.7	...	3.5	7.5
15	Atherosclerosis	0.7	6.0	2.1	-4.5	-63.2	1.3	1.0
...	All other causes	15.4	132.9	...	...	...	...	...

- Quantity zero.
... Category not applicable.
--- Data not available.
Rank 1 based on number of deaths.

UNDERWRITING FOODBORNE ILLNESSES IN THE NEW MILLENNIUM

Food for Thought

Millions of people suffer from foodborne illnesses yearly. Bacteria, viruses, helminthes and fungi cause most foodborne illnesses. While most people only experience self-limiting events, others suffer from more serious forms of the disease. During the past 20 years, the epidemiology of foodborne diseases has evolved as new pathogens and transmission factors have emerged. Evidence supports these diseases are more prevalent in developing countries. Serious diseases such as cholera, typhoid fever and liver fluke infections have been virtually eliminated in developed countries. The incidence of foodborne disease is, however, increasing in both developed and developing countries. The problems are complex and compounded by growing international trade in foodstuffs and the transborder movement of vast numbers of consumers with varied tastes and lifestyles.

In industrialized countries, up to 10% of the population may suffer annually from a foodborne illness. Consumers as a result have become increasingly interested in topical issues such as transgenic foods, toxic contaminants in foods, irradiation of foodstuffs for preservation and the potential for transmission of "Mad Cow" disease through consumption of beef. Food safety has consequently increased in visibility and priority and is likely to continue to do so in the foreseeable future. Global changes, however, are likely to have direct, predominately adverse effects. The risk of foodborne disease is substantially increased by biological and chemical contamination of areas where food is produced, processed and consumed. Population growth with unplanned migration from rural to urban areas, consequently leading to slum formation, cause pollution problems. Drinking-water supplies and waste-disposal systems are under intense pressure, especially in developing countries, and foodstuffs produced there carry a greater risk for spread of foodborne pathogens.

An increasing number of illnesses are international in scope, with contamination in a food product in one country affecting persons in several other countries. Similarly, tourists affected abroad return home to potentially transmit the pathogen to others. The expansion of international trade in human and animal foodstuffs can be expected to increase the risk that contaminants can be spread rapidly worldwide.

By 2020, the human population is expected to reach 8.5 billion, 80% of which is expected to be in developing countries. This compares with 5.8 billion in 1996. In developed countries the proportion of people over age 60 will rise from over 17% currently to 25% by 2025. This trend is also occurring to a more limited extent in developing countries resulting in the emergence of many people with reduced resistance to disease, including foodborne illnesses.

Who is at the greatest risk of serious illness and mortality from water and foodborne enteric microorganisms? This group includes the very young, the elderly, pregnant women and the immunocompromised. This population segment in the U.S. is currently 20% and increasing. More than half of documented deaths from gastroenteritis and Hepatitis A occur in the elderly in developed countries. The overall case fatality rate for foodborne gastroenteritis outbreaks in nursing homes is 10 times greater than that of the general population. Cancer patients undergoing chemotherapy, and transplant patients are also at significantly greater risk of dying from enteric infections than the general population.

Several factors contribute to the increased risk of foodborne illness in susceptible populations. These include an age-associated decrease in humoral and cellular immunity, age-related decreased production of gastric acid, decreased intestinal motility, malnutrition, lack of exercise, entry into nursing homes and excessive use of antibiotics. Globally, Salmonella is still the most serious agent causing acute disease, with S. enteriditis and S. typhimurium being of most concern. Foods of animal origin, particularly meat and eggs, are most often implicated. Incidents most frequently occur in homes and restaurants, and the main factors contributing to outbreaks are poor temperature control in preparing, cooking, and storing food.

The risky practice of eating shellfish and other foods in the raw state is increasingly common in affluent societies where consumers are demanding minimally processed foods with long shelf lives, no preservatives and low salt and sugar content. Under such conditions, pathogens are more likely to arise, even at proper preparation temperatures, causing the probability of infection to increase. Consumer concerns regarding food irradiation, which is an affordable means of sterilizing food products, are likely to decline given the intrinsic merits of the technology, its safety and the efforts of public health educators. In fact, it is projected to be one of the most significant contributions to public health since the introductions of pasteurization and chlorination of water.

The human "costs" of foodborne illnesses, as estimated in the U.S., stemming from seven foodborne pathogens (Campylobacter, Clostridium, E. Coli 0157:H7, Listeria, Salmonella, Staphylococcus, and Toxoplasma), cause an estimated 3.3 – 12.3 million cases of illness and up to 3900 deaths. These seven pathogens are estimated to cost the U.S. $6.5 – 34.9 billion annually.

It is highly probable that food safety will decline in the first part of the 21st century because of unfavorable environmental and human factors. Matters should improve incrementally thereafter, thanks to scientific, technological and educational efforts in public health. For individuals, while it is impossible to turn back the clock, a healthy lifestyle with regular exercise, maintaining a balanced diet, receiving regular health care, paying attention to personal hygiene, and practicing safe food preparation and handling should lead to a reduced incidence of foodborne illness, morbidity and mortality.

Richard G. Rougeau, M.D.

SOME THOUGHTS ON THE ENVIRONMENT AND ILLNESS

You can't believe everything you read (unless, of course, if it's in *Re-flections*), but some things cause one to stop and think. Several months ago, The New England Journal of Medicine published two interesting, seemingly unrelated articles. These articles caused me to consider the affects the environment has on our health. The first article, from Scandinavia, proposed that environmental insults, not genetics, are the principle cause of cancer. The second article, from Arizona, stated that early daycare and multiple siblings protect children from developing asthma as adolescents. In the first article, environmental challenges had a negative impact on human health. In the second article, the environment had a positive affect on human health. Is it possible to create a scientific, evidence-based explanation for these observations?

In the first article, an analysis of 44,788 pairs of twins from Finland and Sweden found that the environment is the primary determinant in the development of various types of common cancers.[1] In 58-84% of the cases, it was found that environmental factors contributed to cancer of the GI tract, breast and prostate, while genetics was only a factor in 10-20% of the cases. This implies that genes play a minor role in the development of these serious diseases.

What can we do to decrease the risk of cancer? We can easily reduce some environmental cancer-causing exposures, such as tobacco, poor diet, and drug abuse, from our daily lives. However, there are many other exposures that are more difficult to prevent, for example: secondary smoke, human papillary virus, H. pylori, and UV radiation. The Journal's editorial pointed out that these environmental observations should expand our knowledge of genetic factors.[2] That is, identification of the genes damaged by the environment should help us identify other potentially avoidable exposures. Also, since these cancers seem so heavily influenced by our surroundings, something we can usually modify, we should focus our resources on decreasing these environmental dangers (e.g., secondhand smoke). It also pointed out that there are other unknown influences on the development of cancer beyond the nature v. nuture argument, as evidenced that a woman's risk of contralateral breast cancer is only 0.8% per year, despite the fact that both breasts shared an identical genome and environment.

In the second article, Ball and colleagues followed 1035 children from birth to age 13, tracking the development of asthma and/or asthmatic symptoms[3]. Their data showed that attendance in daycare before the age of six months, or having two or more siblings, decreased the relative risk of developing asthma as young adolescents. Furthermore, each of these factors was additive (those children with both early daycare and multiple siblings had less asthma than children with either factor alone). Similar to most previous studies, early daycare attendance and siblings increased the frequency of upper respiratory infections, and led to an increase in wheezing associated with these infections. But these challenges to the young immune systems were seemingly protective of wheezing and asthma associated with atopy later in life.

An accompanying editorial, subtitled "Please, sneeze on my child," points out that there is a clear scientific rationale behind these observations.[4] More than likely, environmental exposures to the developing immune system affect its response to future challenges. Evidently, there are two phenotypes of helper T-cells in neonates—Th1 and Th2—which produce different types of cytokines. The Th2 cells release proinflammatory interluekins-4, -5, and interluekin-13, which cause eosinophilia and airway hyperreactivity. The Th2 phenotype is present at birth, but is typically replaced by Th1 cells. Those children with a family history of atopy have a delayed Th2 to Th1 transition, and thus the proinflammatory and hyperreactive responses persist. It is felt that exposure to microbes is an important signal for the development of the mature, Th1 response. It follows that the more infections a young child gets, which is clearly associated with both daycare and siblings, the quicker the helper T-cells "mature."

As a pediatrician and father of three young children, I have always stressed my firm belief in the protective power of the immune system. We share cups and water bottles, and we are not reluctant to eat cookies off the floor, yet my kids don't get sick. Is this because, as my wife thinks, I ignore all symptoms except arterial bleeding, compound fractures and shock, or is it because I have wisely primed my children's innocent, immature, immune systems? I think it's a little of both, but this study made me feel better and supported my assertion that I am doing these things for the welfare of my children.

So where do we go from here? How do we change our lives and influence the lives of those we love (and those we insure) to minimize disease? The World Health Organization recently confirmed what our mothers have been telling us for years: "eat your vegetables." The world's largest study of diet and cancer development confirmed that the consumption of vegetables decreased the risk of cancer by 40%, while those who consumed the most red meat increased their cancer risk by the same margin.[5] Yet this sound advice goes largely ignored. Sixty-four percent of Americans (including over half of the polled senior citizens) prefer to take vitamins and nutritional supplements rather than change their eating habits.[6] Multivitamins are perceived to be a "quick fix," and taste better than eating vegetables. The fact that the long-term health affects of such dietary supplementation is unknown is evidently not a concern to most people.

As found in both articles, external environmental forces affect our health and well-being. As far as I'm concerned, I will continue to control what I can in my environment. Today's air quality is good, so I will put on sunscreen and go for a run. Then I will have a salad for dinner at a smoke-free restaurant. If I do get sick, I can blame it on my children for infecting me with germs that they brought home from school.

Robert J. Profumo, M.D.

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While it is quite clear that an individual's genetic make-up is a major contributor to their susceptibility to disease, it is ultimately the interplay between the environment and genotype that determines the outcome of a person's reaction to the various toxins, radiation sources and microorganisms encountered in daily living.

It is difficult to predict what physical conditions will eventually lead to a person's demise. This task may be compounded by the myriad possible changes in environment that a person is exposed to during life. It may, however, be possible in some cases to reach reasonable conclusions about future mortality trends within populations at large. Some changes in our environment have been well studied and these changes will predictably alter the incidence of specific diseases within the population. It is important, from a pricing viewpoint, that we anticipate these trends and adjust for them when necessary.

One such environmental change that has been extensively studied is the depletion of stratospheric ozone. This atmospheric substance normally absorbs a significant amount of solar radiation, which is a major source of ultraviolet (UV) radiation. UV radiation affects human health, crop production and the biological food web in marine ecosystems. Any of these factors can ultimately lead to changes in disease incidence. Exposure to UV radiation has been specifically linked to skin cancer (including melanoma), cataract formation, aging of the skin, and possible weakening of the immune system. Changes in crop production and the marine ecosystem may also lead to complex changes in disease incidence.

The United Nations Environment Program has estimated that about 200,000 malignant melanomas occur globally each year. This dangerous skin cancer is not distributed evenly among insured populations worldwide. It is apparent that factors such as the latitude of sun exposure can affect the incidence of melanoma, since ozone depletion is most prominent in polar regions. For example, in Australia the incidence of melanoma is 53.5/100,000 person years in Queensland (lat. 12 – 28 S), as compared to 30.3/100,000 in Victoria (lat. 36 – 38 S). Fortunately, the Australians have recognized the importance of avoidance of excessive UV exposure, especially exposure leading to sunburn during childhood. The successful adoption of public health programs has contributed to a downward mortality and incidence trend in melanoma, at least in younger females.

What is the American experience with melanoma? Melanoma is increasing in incidence. In the 1930's the lifetime risk of developing invasive melanoma was one in 1,500. Currently the risk is one in 74. Not only is the incidence increasing, but the mortality rate is also increasing about two percent per year, primarily due to the increasing incidence. Fortunately, the five-year survival is improving, mostly because of the advances made in early detection of this disease and the increasing awareness of surveillance of suspicious lesions. The five-year survival in the 1940's was only about 40%, whereas it is currently 90%.

The trend of increasing melanoma incidence is just one example of how changes in the environment can affect human health. Although the example of the increasing melanoma incidence and mortality may have a negative impact on overall mortality (if we ignore the lessons that the Australians have learned), there are also examples of how human manipulation of the environment can favorably improve mortality (for example: improved sanitation and water purification). Some changes, such as genetically modified foods are perhaps too recent to allow us to speculate how they might impact disease incidence. As we become more aware of the changes in our environment (both of the man-made variety and those that are part of natural cycles), it is obvious that we may expect changes in the distribution of a variety of disease entities. It is in our own best interest to develop the skills necessary to prepare for the future.

Dr. Carl Holowaty, M.D.

References for the articles in this issue are available upon request.