How You'll Live Longer, Smarter

The New Environmental Health

The Drive to Prevent:

- Cancer
- Heart Disease
- Alzheimer's
- Parkinson's
- and other chronic diseases

Can cloned genes be used to safety test chemicals?

As the environment gets healthier, so do we...

People born today, on average, have a life expectancy about twice that of folks just over a century ago. Most of those additional years have been gained by healthful environmental changes – including improved sanitation, purified water, cleaner air, the safer use of chemicals in our homes, gardens, factories and offices, and the restriction or elimination of unsafe practices.

In other health-promoting environmental steps, the United States and its states and cities, businesses and unions have worked together and:

- Removed lead from gasoline, and redesigned the gasoline pump to expose you to less benzene, which might increase your risk of cancer.
- Reduced smog, making your breathing easier.
- Removed from the market questionable products, such as a laxative ingredient that tests showed could cause cancer.
- Restricted or removed from commerce many workplace chemicals, food dyes and pesticides because they posed a risk of sterility, cancer or other diseases.
- Recommended healthier food habits – advising pregnant women, for example, to avoid eating certain large ocean fish, like shark and swordfish, in which mercury accumulates.

"If you want to learn about the health of a population, look at the air they breath, the water they drink, and the places where they live."

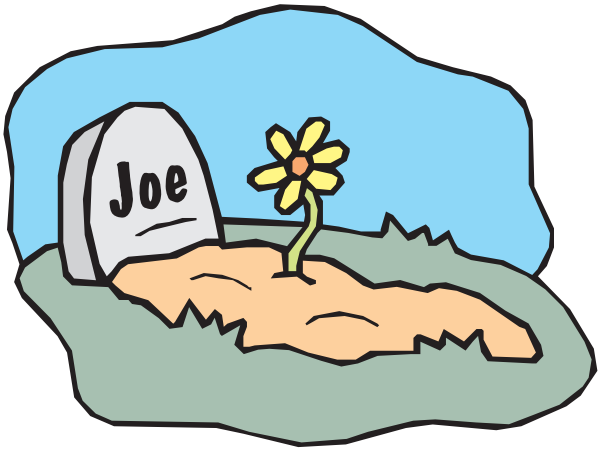
– Hippocrates, the Father of Medicine, in the Fifth Century BC.

In each case, these preventive measures did not just happen. They were put in place following studies...

...by the National Institute of Environmental Health Sciences, the National Toxicology Program (which is headquartered at NIEHS) and/or similar laboratories.

Great progress has been made since the 1962 book *Silent Spring* by Rachel Carson forecast that persistent pesticides would silence the world's birds – and perhaps make the world unlivable for humankind as well.

The book produced public support for the creation of NIEHS for research and, soon afterward, for the creation of the regulatory Environmental Protection Agency. Public support also developed for the creation of the National Toxicology Program. As one result of the interest and the ensuing research, DDT, dioxin, PCB's and other harmful and persistent chemicals have been banned in the United States and many other countries. These and the rest of the "dirty dozen" chemicals linked to cancer, birth defects and impaired reproduction are being curtailed internationally as well, under the Stockholm Convention on Persistent Organic Pollutants, to which the United States is a participant.



Too bad Joe didn't know what he was inhaling. We know now. Progress toward a healthier environment has been made since 1962's *Silent Spring*.

Progress has also been made in how we think about environmental health. Today, the environmental health sciences aren't entirely about pesticides and other chemical pollutants in our air and water. The definition of "environmental health" has broadened to include the environment we create for ourselves (by smoking or not smoking, and by our diet, for example). It also includes the medicines and other therapies we are prescribed, our occupations and places of work, and our lifestyles: Are we couch potatoes or joggers? Sexually reckless or responsible? Listening to loud music or keeping the volume down?

Some scientists even believe that a good view of nature, as opposed to a brick wall, may have a positive effect on our health.

The environmental health sciences also look at socioeconomic status – that is, how the workplace, neighborhood and home environment of many poor Americans produce disease, disability and premature deaths.

The environments we personally create for ourselves, through our habits, diet and lifestyle are now seen as very important.

Ironically, though today's pesticides are safer and our air and water cleaner, the new, broader definition of environmental health adds to the numbers of diseases that are considered to be related to the environment. For cancer, the environment-related contribution has thus "increased" from an estimated 3 or 4 percent or so, when synthetic chemicals were the issue, to as much as 80 percent under the broader definition.

There has also been a revolution in how we measure and study the impact of environmental agents on our health. Indeed, the chemists and water-testers of yesterday would be surprised by the scenes at environmental health research centers today:

- Cloned human genes are being set out in clusters on a glass slide to test suspect poisons. In the future, such techniques – using clones of your genes – may help predict how you, as an individual, will react to a drug or other chemical.
- The blood and urine of groups of people representing the population as a whole are being tested to see what chemicals these people have individually absorbed.
- And the genes of similar, representative groups are being studied to see what slight changes in their so-called "susceptibility" genes make them more – or less – susceptible to cigarette smoke, industrial chemicals, pesticides and sunlight.

Environmental health has taken a new turn now that the human genome has been sequenced or "mapped." The environmental health sciences have taken up the advanced tools of genetic research and moved into a new phase that intrigues many of our best scientists.

We and others are reaching deep into the human cell to find the changes that, in response to an environmental assault, tip that cell toward cancer, Parkinson's, Alzheimer's or other diseases. We are re-sequencing, or re-mapping, the human genome in a cross-section of Americans so we can see how their genes vary and how those variations make some people more susceptible – and others, less – to the substances around us.

At what point does the cell tip toward cancer, Parkinson's or Alzheimer's?

This kind of research is so new, so cutting-edge that scientists often have to compound new words (like "toxicogenomics") to describe what they're doing. Yet it is typical of what goes on today at the National Institute of Environmental Health Sciences and the National Toxicology Program. This whiz bang work – alongside more traditional studies of lead poisoning, pesticides, mercury and diesel exhaust particulates – is also carried out by the NIEHS' 20-plus university-based centers in communities across the United States, from Boston's Harvard to Berkeley, Calif., and from New York's Columbia University/Harlem, to the Mexican border work of Texas A & M.

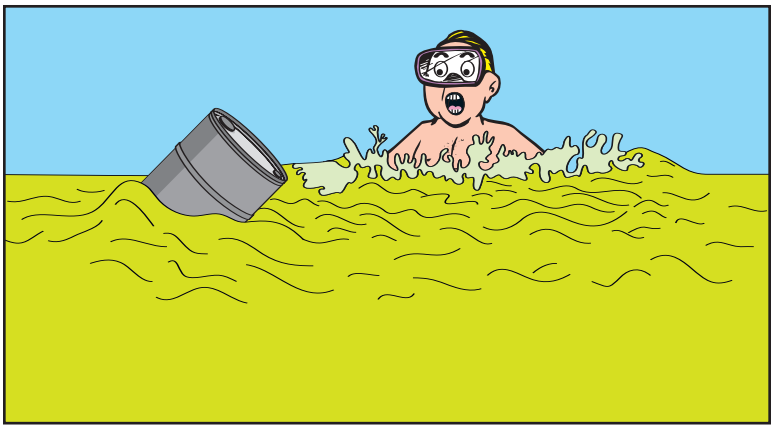
Technologies developed for the international genome project are now being used to study toxins and other environmental factors, and our susceptibility to them.

Whether you're a healthy man or woman – or one facing prostate cancer or Parkinson's, breast cancer or Alzheimer's – whether you're a couple with children – or having no success in conceiving them, the new environmental health sciences are important to you.

Our Chemical World, and our Dilemma

Chemicals are the basis of our way of life – and health – today. There are about 15,000 chemicals made and used in high volume in the United States. (One of our center directors has figured that when we roast coffee for our morning jump-start, we end up with more than 1,000 chemicals right there in our cup!) And there are many natural products – herbal products, for example – that have become widely marketed and used without testing.

Synthetic chemicals, used on our farms, not only help feed us cheaply and well, they help feed much of the rest of the world as well. Chemical fibers clothe us. Chemicals cure us. They form key parts of our cars and our phones and computers, many building materials, rugs and other furnishings – you name it. Little wonder that U.S. production of these synthetic chemicals has climbed, almost without pause, from 10 million pounds in 1918 to well over 300 billion pounds in recent years.



Per person, we make and/or use more than 1,500 pounds of chemical products a year. They help feed, clothe, transport and house us.

Just as fire can burn us as well as warm us, some chemicals, natural as well as man-made, can cause diseases. Most of us are familiar, at least in a general way, with the evidence that tobacco smoking is a major cause of lung cancer and other diseases. Similar data in test animals as well as population studies showed that asbestos causes mesothelioma (an unusual tumor of the linings of the chest and abdominal cavity) and lung cancer and increases in gastrointestinal cancer. Another condition caused by asbestos is a chronic fibrous disease of the lung aptly called asbestosis.

Scientists also discovered that a number of chemicals, including the pesticides kepone and dibromochloropropane, were causing workers to become sterile.

Some chemicals also can cause nerve damage. This resulted, in the case of kepone, in workers at a plant suffering nervous tremors, twitching and flickering eyes. That's history today. The State of Virginia ordered the last U.S. production to be terminated in 1975. In other cases, when we've learned of problems, businesses, labor unions and federal government regulators have stepped in to remove or restrict the hazard. Of course, we need to continue testing novel new chemicals and some old chemicals as well.

A major question today is how quickly can our testing discover problems? Can we predict – before anybody's hurt – whether a chemical will have a harmful health effect?

Basically, there have been two ways to determine the causes of cancer and other diseases suspected of being caused by chemicals. One is by studying groups of people – like the classic studies comparing the illnesses of cigarette smokers with the experience of nonsmokers. The other way is by studying laboratory animals. Both methods have strengths and weaknesses.

Epidemiology - Studying Disease Rates

Epidemiology – EP-eh-DEEM-ee-oll-o-jee – is the study of the occurrence of disease in large numbers of people. It attempts to link an exposure some of them have had to a subsequent disease. Sometimes this can be straightforward: In 1775, Sir Percival Pott of England reported that chimney sweeps had a very high incidence of cancer of the scrotum, the pouch of skin containing the testes. His report of a disease related to an environment (chimneys full of soot) was an early example of an epidemiological study.

Because it makes such good sense, epidemiology is easily understood and accepted by the public. Most health regulations today are based on epidemiological studies.

But they do have some limitations. Since people get exposed to all kinds of things, pinning down which exposure caused an illness, especially an illness that occurs 10 or 20 years later, can be very difficult. Usually, people do not know the chemicals they have been exposed to, or in what amounts. Newer epidemiological studies try to get around this problem by testing people for residues of chemicals that have collected in body fat. For example, tests for DDE, a substance that DDT breaks down to in the body, can indicate past exposure to the pesticide.

In terms of protecting people, the most significant problem is that epidemiology is entirely an after-the-fact science. It can link exposures to disease only after people have experienced the exposures and the illness – and sometimes death.

Thus, we often turn to ways to screen substances before people are exposed. The foremost methods are animal studies:

For about 80 years, scientists have made use of laboratory animals, mostly rats and mice, for studies. These studies are not the simple observation of a dozen rats in a shoe box. A good animal study requires care in its planning, carrying out, observation and evaluation. The "gold standard" of animal tests for cancer-causing agents exposes rodents for two years and takes a year or two longer when you add in the planning of the study and its careful, microscopic evaluation.

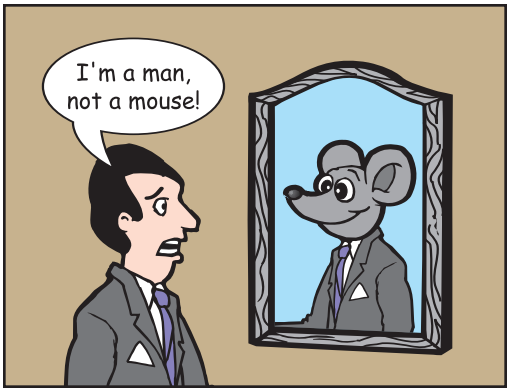
Such studies have produced much of the evidence that has led to the listing of more than 200 drugs, pesticides, metals, chemicals and other substances in the federal government's Report on Carcinogens. As requested by Congress, the report is produced by the National Toxicology Program at NIEHS to alert members of Congress, regulators and the public to these substances and their current regulation.

In 1775, a study of chimney sweeps in England linked their sooty environment to cancer.

Some of the advantages of a carefully planned animal study over a human study are obvious: The genetic makeup of laboratory mice and rats can be controlled. They are specially bred for uniformity. The environment and exposures also can be carefully controlled, so that cause and effect can be demonstrated more easily. Generally, three or more different doses of a substance are used on different groups of rodents. If a resulting cancer or other disease occurs at highest rates among the highest-dosed rodents, and less and less at the lower dosages, that reinforces a cause-and-effect relationship. If a test rodent is known to handle a chemical in its body the way a human does, that also is important evidence.

In some of the newest studies, these rodents are modified to carry human-like genes carrying increased susceptibility to diseases, such as cancer.

Skeptics may cry, "I'm a man (or woman), not a mouse!" And they're right. But genome studies have demonstrated that there is less difference than we might think.



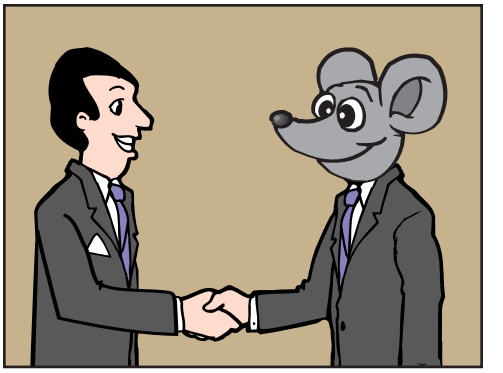
But you share many genes and bodily mechanisms!

And look at the test results: Almost always, compounds that have proved to cause cancer in humans also have caused cancer in test animals.

While there are exceptions and some animals may be more sensitive to a substance than a human is, a carefully done animal study can often tell a lot. Vinyl chloride was discovered to cause cancer in animal studies before such effects were observed in factory workers in Louisville, Ky. Aflatoxin, which is a product of a fungus that can grow on peanuts, corn and other grains, was first observed to cause cancer in trout, then in lab animals and finally in epidemiological studies of human populations.

Sometimes the result of an animal study is a bit off, much as weather forecasts sometimes miss, but we live in an imperfect world where we prefer a weather forecast with its occasional false alarm, to no forecast at all.

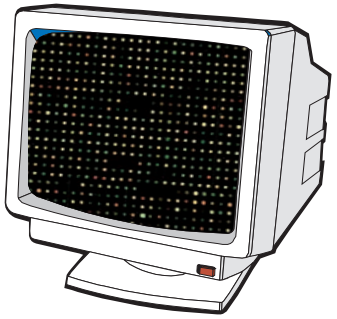
There are other helpful methods for screening chemicals. For example, you can compare their molecular structures. If a new chemical looks structurally like a known problem-substance, then the new chemical becomes a prime target for further tests.



Hazards to both animals and humans have been discovered -- and restricted or eliminated.

Another screening method uses bacteria. This method, the Ames test (named for and developed by NIEHS center director Bruce Ames) tests for mutations in bacteria exposed to the substance being tested. Many chemicals that cause cancer also cause such mutations or changes in DNA. The test is not perfect but it provides an inexpensive indicator for further tests. Examples: AF-2, a food additive once used widely in Japan, and safrole, a naturally occurring flavoring agent once added to root beer, were positive on the Ames test and, after additional studies, were banned.

The Tests of the Future

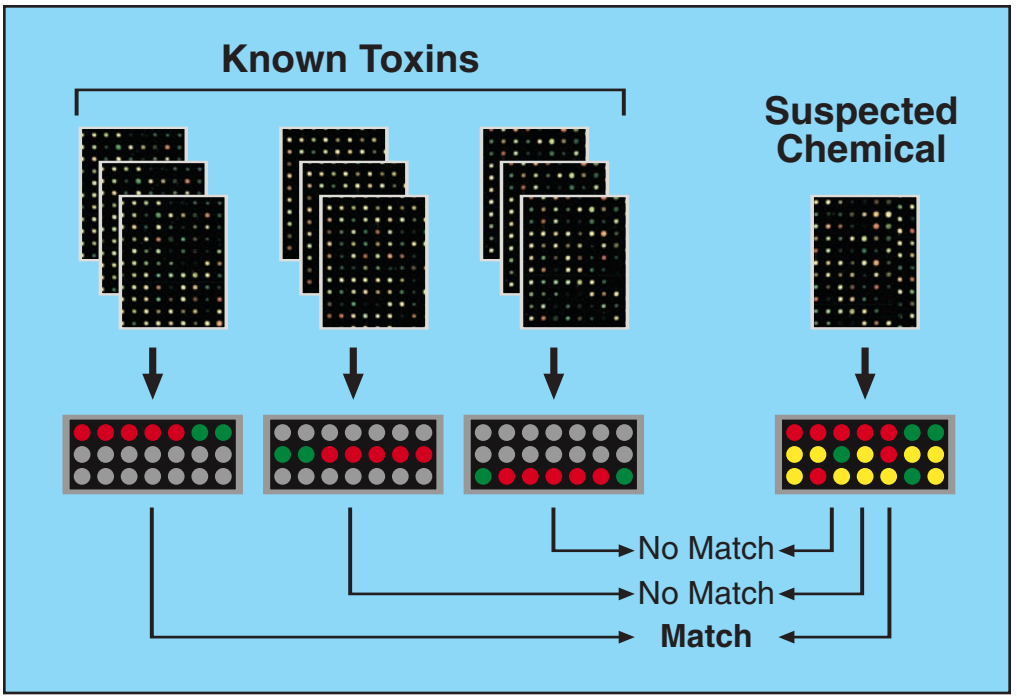


Genes turned on or off show up as glowing red or green dots on a computer screen.

What if we could clone human genes, separate them into piles on a glass slide, and use them to screen chemicals? We're beginning to do that at the NIEHS/NTP's National Toxicogenomics Center and at associated centers. ("Toxico-genomics" combines the word for the study of toxins or poisons with the word for genetic studies.)

We're developing a "library" of the patterns of genes turned on or off by known toxins. We'll then screen suspect chemicals to see if they produce the same patterns of turned on/turned off genes.

That's our hope and plan because there are thousands of potentially useful drugs and chemicals out there – and a full animal study may take years and quite a lot of dollars – $2 million to $6 million per chemical tested.



Screening with cloned genes whose reactions are read by computer – this technique we call toxicogenomics – could speed the testing of new, life-saving drugs as well as other chemicals that are to be marketed or used in manufacturing.

The use of cloned genes and computers also may tell us a lot about now-mysterious diseases, and our varying susceptibility to them. While animal tests can say, yes (it causes cancer) or no (it does not cause cancer), the use of cloned genes promises to provide more information, such as *how* a chemical causes disease.

By using clones of your genes – cloning them from a sample of your cells – future physicians may be able to determine which cancer drug or other therapy is best for you as opposed to which drug should be avoided because it may, in you, have intolerable side effects.

Susceptibility – the 'Why me?' question

Many scientists at NIEHS/NTP believe that one day soon we will be able to solve the riddle of susceptibility – why one person may be so much more susceptible to radiation or chemicals than another person. This is the "Why me?" question that patients so often ask and that physicians can seldom answer. Some examples:

- You may be hurt by a chemical that doesn't bother most people.
- Your co-workers may fall ill and you are fine. You may be more resistant than most people.

This varying susceptibility is a major interest of environmental health scientists today. The National Institute of Environmental Health Sciences is looking at susceptibility via what's called the *Environmental* Genome Project. Under this umbrella, scientists look at a group of known "susceptibility" genes from the tissue of groups of people – representative of the population as a whole. The idea is to see how these genes vary from person to person, and to match these variations with our varying susceptibility to chemicals and diseases.

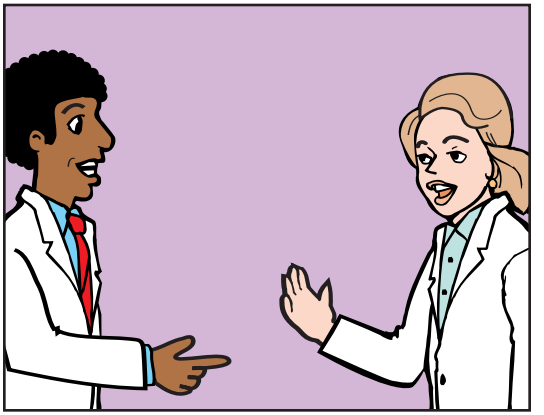
(These "susceptibility" genes are different from some disease genes identified in sequencing the human genome under the *Human* Genome Project. That project has identified some few single genes that cause some diseases almost invariably and directly, without an environmental trigger. There don't appear many of these "act alone" genes. Most genes act with one or more other genes and the environment, and most diseases are produced that way.)

Susceptibility.

Why do 16 percent of heavy cigarette smokers succumb to lung cancer - while others don't? Why do some factory workers exposed to a chemical become sterile, while other exposed workers sire ten kids?

When genetic variations are matched to a demonstrated increase or decrease in vulnerability we may learn more about why Uncle John and Uncle Pete reacted so differently to the chemicals in tobacco smoke – why Uncle John is dead of lung cancer while Pete keeps on trucking, with only a raspy voice and a little cough.

With such knowledge, we should be able to fine tune regulations so that they are not needlessly restrictive but do protect the most susceptible.



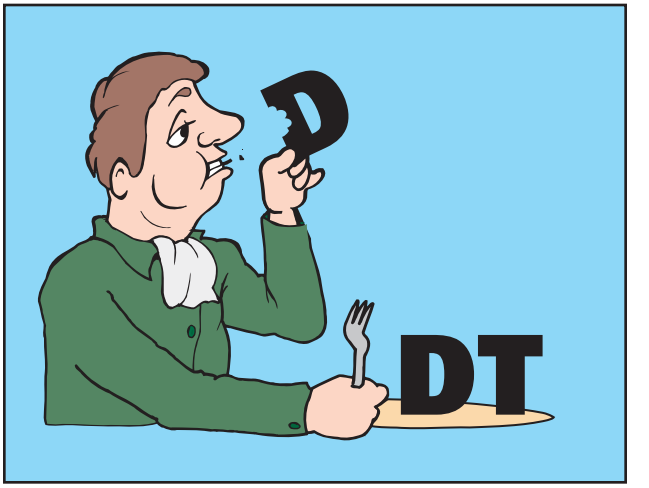
Why are some people more susceptible to some exposures than others? The answer could help find the best drug for you - the one that cures with few side-effects.

There may also be instances when simple tests will reveal people who are susceptible to environmental substances – certain substances in foods, for example – and who can then be advised to avoid them.

In another big project, the National Toxicology Program is working with the Centers for Disease Control to test blood and urine from representative people to see just what chemicals they have been exposed to and absorbed.

PBS Commentator Bill Moyers got himself tested at a hospital for chemicals in his system and observed that most of the chemicals found in him wouldn't have been in his grandfather, because they didn't exist then.

On the other hand, as some testing shows, Moyers' levels of chemicals were probably lower than his father's, the generation between, because of the phasing out of a dozen or more of the bad actors.



DDT levels in blood and urine have greatly declined since the 1960's.

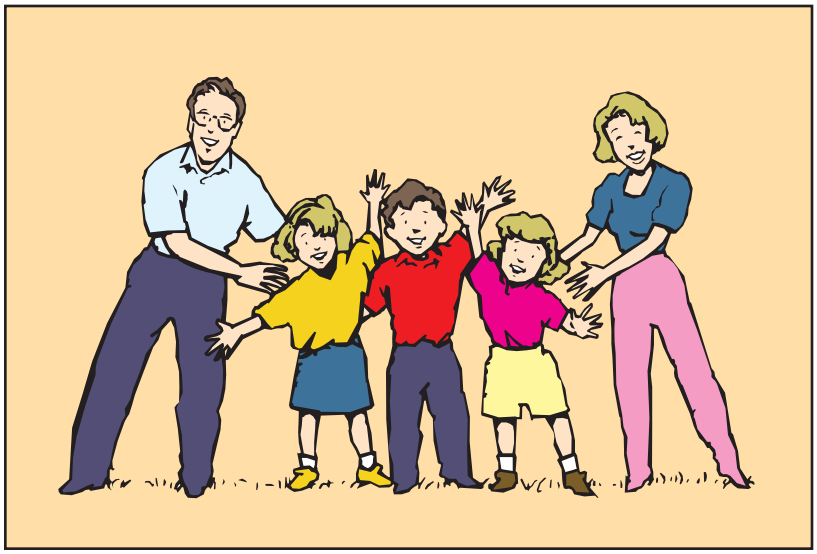
Like people doing a jigsaw puzzle, scientists are fitting together all this new data from their exciting new scientific tools. We're struggling to look at where genetics and the environment interact in the human cell, causing a molecule to change that starts a kind of chain reaction leading to disease. Scientists liken the changes to a cascade – a series of ever-larger waterfalls of cellular changes – that may lead to cancer, Parkinson's, arthritis, heart disease or other diseases.

We sometimes compare our heredity, or genes, to a loaded gun, and the environment to that gun's trigger.

Though we still do not understand the root causes of many of these serious, chronic diseases, we suspect they can be caused or triggered by chemicals and other environmental exposures from years before. We think these diseases may be influenced by a lot of things – several genes, perhaps, and various environmental exposures or conditions, our age and stage of development, our nutritional status.

We sometimes compare our heredity, or genes, to a loaded gun, and the environment to that gun's trigger.

The environment, in some cases, can also load the gun. It can change (mutate) or damage a gene. Or it can damage the system that corrects occasional errors in the reproduction of our DNA – much like damaging the spellcheck program on a computer.



Using many of the same new tools that have been used to explore the human genome, environmental health scientists want to see how this damage occurs. We want to see how an exposure 30 years in

the past can produce a cancer today. Or how a combination of pesticide exposures might, decades later, contribute to Parkinson's.

And, of course, armed with the "how" and the "why" of these diseases, we want to prevent them.

Indeed, prevention is where the environmental health sciences are focused today. It's an exciting place to be! Along with the Human Genome Project, this environment-related work will revolutionize medicine – especially preventive medicine – and that will mean that all of us, and our children and grandchildren, will be healthier and more active for many more years.

What You Can Do for Yourself Now!

Good things happen when we act on the knowledge that our environment is our health!

The removal of lead from paint and gasoline has actually helped younger generations measure higher on IQ tests! Adding folate (also called folic acid) to our diets has reduced one class of debilitating birth defects. Simply washing our hands regularly – in home and commercial kitchens, day-care centers and hospitals – has prevented countless cases of illnesses and death.

But we can't let our guard down: Lead in old painted surfaces can still cause problems when an old building is demolished or children are housed in old homes. The deteriorating paint flakes and crumbles into a dangerous dust. Testing potentially exposed kids is an important way to catch problems early. Learn more at 1-800-LEAD-FYI.

- **"Read the label, Mabel,"** (and Harry, too) and avoid spraying pesticides so they land where kids crawl or wallow – whether that's the lawn or the living room rug. Don't misuse pesticides meant for flowers on your tomato plants or chard, or let it drift over to them either. Per acre, many gardeners use more chemicals on their flowers and lawns than farmers do on their crops! The run-off from such use can threaten waterways and public health, so use no more than absolutely necessary.
- Wear gloves and protective clothing if you use these or other chemicals – and, in case of a spill, wash the chemicals off your skin or out of your eyes (or your kids') immediately.
- **Wear UV-absorbing sunglasses** and a hat, clothing and/or sun block to reduce your risk of cataracts, ordinary skin cancer, malignant moles and wrinkles.
- **Learn about radon** at 1-800-SOS-RADON.
- There's no need to wait for further discoveries about susceptibility – or until many of your friends have lung cancer, a hacking cough, bronchitis or emphysema: Quit smoking now for the health of yourself and your family. Insist on a smoke-free home and support a smoke-free workplace. Don't subject others, especially children, to smoke.
- **Don't "top" your gas tank** or spill gasoline or other evaporating fluids that can produce ozone and smog and that, in turn, can hurt your lung capacity.
- Eat five or more servings of fruits and vegetables a day – and if you're female, beginning in your early teens, **take an ordinary daily vitamin pill containing folate;** it reduces your chance of having a deformed child (and it's good for you, too).
- On hikes, take pure water along or a disinfection kit. That crystal-clear stream can harbor bacteria that can turn your insides out.
- Jog away from traffic and jog in the mornings or evenings to avoid heat and auto pollution.
- As a medical employee or patient, take the recommended radiation precautions.
- Protect your own and your children's hearing from loud and persistent noises.
- **Make use of proven safety measures** – automobile seat and shoulder belts, car seats for kids, helmets and shin and knee pads and athletic cups, as appropriate. Learn how to avoid the kinds of movements at work that can lead to disabilities.

- If you're pregnant, eat good foods (but not everything in sight), and check with your employer or union about any chemicals or radiation in your job you may need to avoid or handle differently, and make sure your significant other, if working with chemicals and pesticides, showers and washes his work clothes separately from other clothes.

- At all times, male or female, be moderate if you drink alcohol. (If you're pregnant, most authorities suggest you should not drink at all).

- **Male or female, take a tip from our lab mice** who live longer and healthier when on reduced-calorie diets. Tobacco, excess alcohol and too many calories (along with too few of the right nutrients) are considered leading environmental causes of disease and disability today. The experts who say this may be spoilsports – but they have a lot of good evidence on their side. Your body fat, among other things, stores up many pollutants.

- Grow some plants. Indoors and out, they clean the air.

- Don't get stressed out by all this. That ain't healthy either. Relax and enjoy life. Hike and canoe in the Great Outdoors. Take your dog for a stroll (or your best gal or guy!)

And while you're strolling, have a listen. Hear that? Those – thank you Rachel Carson! – are birds singing.

Photos by Steven R. McCaw, Image Associates, Inc.

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To receive occasional news bulletins on NIEHS's activities by email, go to the News page and sign up.

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NIEHS is one of the National Institutes of Health within the U.S. Department of Health and Human Services

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