

# JEWISH GENETIC SENSITIVITY TO POLLUTION ACCENTUATED DISEASE

R.E. Ruthenberg 4/1/04

## **Introduction**

Disease is defined<sup>1</sup> as “a condition of an organ, part, structure or system of the body in which there is incorrect function resulting from the effect of heredity, infection, diet, or environment; illness; sickness; ailment.” Pollution in the human environment is understood to be a cause of disease and, it turns out, heredity appears to be an important factor related to one’s susceptibility to pollution effects. Jewish populations are at increased risk of pollution-caused disease due to genetic inheritances.

## **Background**

We all know that the human body has developed defense mechanisms against disease over eons of evolution. It is also quite understandable that variations in these mechanisms exist between individuals (as functions of one’s general health, parentage, etc.). But what is becoming increasingly known, with the explosion in genetic knowledge, is that an entire sub-population can be more susceptible to pollution-caused disease than others, due to genetic differences to the general population. Why is this?

When diseases take over the human body’s protective processes, they may do in a number of ways, including:

1) The processes are overwhelmed by the magnitude of the onslaught. If peak or average levels of environmental pollution exceed the ability of human processes to deal with them, then associated disease takes over. There is increased evidence that this is often the case in the general population. Further, it appears that many of the pollutants in our environment have been brought forth so quickly (primarily since the Industrial Revolution of the last century) that humans have not had sufficient time to evolve effective defense processes for these pollutants. Thus, whereas pollutants such as large diameter particulate matter (>10 micron) and background radiation (e.g. radon) are well tolerated (up to certain levels), small diameter particulate matter (<2.5 micron) from combustion processes and synthesized chemicals and by-products from modern day machines/factories e.g. airport facilities and aircraft jet engines, refineries, chemical plants, etc. would not be so well tolerated and in some cases, would be poisonous to our well being.

2) The defensive processes become broken or damaged, creating an increased or altered susceptibility to disease. This effect is gaining increased attention, particularly as related to genetic damage caused by pollutants. The discovery of DNA and the double-helix of genetic sequences continues to forge remarkable bridges of understanding of how environmental onslaughts can result in damage to individual gene sequences at a cellular level, with potentially disastrous results.

The human body has processes that normally go around “fixing” damaged DNA or otherwise “killing” the now-mutated cell structure, as it is important to do so before the damaged structure divides and replicates itself. When this repair capability is altered or decreased, either due to acute, chronic or genetic impacts, the mutations can propagate and create disease (cancer, etc.).

3) An ethnic group may possess an inherent genetic flaw, as compared to the general population, that causes reduced protective processes to exist for some types of pollution attacks e.g. genetically different lung structures could decrease the effectiveness of defense mechanisms against inhalants.

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<sup>1</sup> Webster’s Unabridged Dictionary

4) An ethnic predisposition to a disease can result in an effective sensitization of that ethnic group to pollution effects that worsen, change or otherwise interact with that predisposed disease. For example, if 20% of the Jewish population was at risk for cardiovascular disease, than they would be twice as likely to encounter pollution complications than another ethnic group that was only at 10% risk, where those pollution complications were highly correlated to cardiovascular disease interactions.

Thus, a first key question is whether or not there are significant genetic differences between Jewish populations and the general population (or other ethnic groups).

### **Jewish Genetics**

Though many people think of “Jewish” as strictly a religion, it turns out that there is a rather direct genetic relationship involved, which results from centuries of evolution.

Around the first century A.D. there were several large Jewish sects: the Pharisees, Sadducees, Zealots and Essenes. Of these, only the Pharisees survived; all Jewish groups today are descended from them. Christianity at one point was a Jewish messianic faction, but soon developed into a separate religion. Over time Jews developed into distinct ethnic groups.

### **Ethnic Divisions**

The commonly-used terms Ashkenazi and Sephardic refer both to a religious and an ethnic division. Some scholars hold that Ashkenazi Jews are descendants of those who originally followed the Palestinian Jewish religious tradition, and Sephardic Jews are descendants of those who originally followed the Babylonian religious tradition.

Jews have historically been divided into four major ethnic groups:

Ashkenazi (Jews who lived in Germany or France before migrating to Eastern Europe)

Sephardic (Jews who lived in Spain or Portugal)

Oriental Jews (Jews who lived in the Middle East and North Africa, but later spread to Central Asia and South Asia). Note that in common usage, most Oriental Jews are called Sephardic, as the religious rites of Oriental Jews and Sephardic Jews are essentially the same.

The Yemenite Jews (also known as Teimanim). These are Oriental Jews whose geographical and social isolation from the rest of the Jewish community allowed them to develop a liturgy and set of practices sufficiently distinct from other Oriental Jewish groups so as to be recognized as a different group.

Smaller groups of Jews include the following:

The Ethiopian Jews, also known as the Falasha or Beta Israel.

The Bene Israel, i.e. Jews who lived in Bombay, India.

The Romaniotes, i.e. Greek speaking Jews living in the Balkans from the Hellenistic era until today (almost 6,000 worldwide)

Following the Spanish Inquisition the Sephardic Jews were dispersed, some migrating to Europe, where they were assimilated into the Ashkenazi, with others migrating to the Middle East where they were assimilated into the Oriental Jews. Most Oriental Jews practice Sephardic rite and are therefore sometimes referred to as Sephardic. Ashkenazi Jews practice Ashkenazi rite.

Out of these communities, the largest by far are the Ashkenazim, comprising ~80% of the Jewish total, with Oriental Jews comprising most of the remainder.

Sub-groups of Jews include the Gruzim (Georgian Jews from the Caucasus), Juhurim (Mountain Jews from Daghستان and Azerbaijan in the eastern Caucasus), Maghrebim (North African Jews), and Abayudaya (Ugandan Jews).

Thus, it is clear that Jewish ness is strongly ethnic related, continually enhanced by marriage within the religion, resulting in about 80% Ashkenazi worldwide and near 90% in North America.

### **CONCLUSIONS: Jewish Genetics and Environmentally Influenced Disease**

Is there then evidence that genetic differences result in disease and disease sensitivity differences between Jewish populations and others, particularly as related to environmental pollution exposure? The straight answer is: Yes. Selected reference information below is quoted to support that conclusion.

The impact of this conclusion is that it is entirely possible and even probable that higher levels of pollution-induced or related disease could be experienced in communities with high percentages of Jewish population and in that regard, Environmental Justice\* parameters of environmental regulation might apply to such communities to the extent they are being placed in harm's way by major polluters<sup>2</sup>.

\*Environmental Justice - The fair treatment of people of all races, cultures, and income with respect to the development, implementation, and enforcement of environmental laws, regulations, programs, and policies. Fair treatment means that no racial, ethnic, or socioeconomic group should bear a disproportionate share of the negative environmental consequences resulting from the operation of industrial, municipal, and commercial enterprises and from the execution of federal, state, local, and tribal programs and policies<sup>3, 4</sup>.  
EPA

Notwithstanding any environmental regulatory situations, Jewish people might be well advised to consider themselves one of the "environmentally sensitive" groups (typically implied to be children,

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<sup>2</sup> The issue becomes more complicated in that many major polluters, such as airports and their aircraft operations, are not openly identified to the public. Thus, populations in the area/region may not be aware of the degree of nearby pollution danger, especially considering that most dangerous pollutants are not sensory detectable (odor, visibility, etc.) at or near their dangerous concentration levels.

<sup>3</sup> Ref. [www.epa.gov/compliance/environmentaljustice/index.html](http://www.epa.gov/compliance/environmentaljustice/index.html)

<sup>4</sup> A case could be made that the environmental justice definition should also include groups that are particularly sensitive to pollution effects e.g. pregnant women, babies, immune compromised or chemically sensitive individuals, asthmatics, etc. That is, the traditional "minority" classifications need to be extended to embrace pollution sensitivity associations in addition to racial, ethnic or socioeconomic factors.

aged and infirm) that the EPA often refers to when putting out warnings of impending dangerous air quality conditions, such as this EPA ozone alert:

Ground-level ozone is a respiratory irritant that causes health problems by damaging lung tissue and reducing lung function. Exposure to ground-level ozone causes coughing, headaches, nausea, and may cause premature aging of the lung. Poor air quality can affect everyone, but *groups that are particularly sensitive* to ozone include children who are active outdoors, outdoor workers, and people with respiratory disease, such as asthma.

#### REFERENCE

##### **Scientists Discover Protein Identifies Damage To DNA**

CHAPEL HILL -- Scientists at the University of North Carolina at Chapel Hill have identified a protein that becomes part of the critical process by which the genetic information called DNA repairs itself following damage by sunlight, pollution or other trauma.

The protein, which is called ATR and already was known, senses damage to DNA so that the body's natural repair system can kick into action, the researchers found.

A report on the UNC School of Medicine findings appears in the May 14 issue of the Proceedings of the National Academy of Sciences. Authors are postdoctoral associates Keziban Unsal-Kacmaz and Alexander M. Makhov and Drs. Jack D. Griffith and Aziz Sancar, Kenan professor of microbiology and immunology and Kenan professor of biophysics and biochemistry, respectively.

Ultraviolet radiation, pollution and chemotherapy cause mistakes in DNA that must be repaired before the cell divides and propagates the mutations as cancer or other problems, Sancar said. Redundant proofreading and repair systems exist that pinpoint the affected genetic sequences, cut them away and build them back right.

"Little is known, however, about how this molecular fix-it team recognizes the problem," Sancar said. "In this new work, we report that we have identified one piece of the molecular alarm system that starts the cascade of DNA repair and cell cycle checkpoint."

The downstream effects of the ATR alarm protein were already known, but it was unclear if ATR sensed damaged DNA directly or if it was just part of the cascade, activated by another sensing protein upstream from it, he said.

"To find out if ATR directly sensed damaged DNA, we put a molecular tag on the ATR protein and purified it," Sancar said. "We incubated the tagged protein with either bits of DNA that were normal or damaged by UV radiation. ATR bound more often to damaged DNA than to undamaged DNA.

"Also, upon interaction with damaged DNA, ATR's activity increased," he said. "These results suggest that ATR senses damaged DNA and helps to start the cascade of DNA lesion repair."

Scientists call the natural mechanism the DNA damage checkpoint system. The researcher who discovered it originally, Dr. Leland Hartwell, received the Nobel Prize last year for his work.

"This is a very important phenomenon in both normal and cancerous cells, and there has been a great deal of research about it," Sancar said. "ATR appears to act as a switch that starts the repair process

and also stops cells from proliferating while they are being repaired. This new work is not going to cure cancer by itself, but it is a significant step forward."

Now that the protein's role is known, other scientists can screen for drugs that act on it.

Griffith and Sancar are members of the UNC Lineberger Comprehensive Cancer Center. They and their postdoctoral fellows worked on human cells known as fibroblasts.

The National Institutes of Health supports the research.

**Stanford Research Points To Chance As Cause Of Genetic Diseases In Ashkenazi Jews**

Source: Stanford University Medical Center

Date: 2003-02-28

STANFORD, Calif. - A population of Jewish people known as the Ashkenazi Jews have an unusually high risk of several genetic diseases, and up until now, no one has understood why. Was it random chance that made mutations so common or did evolution play a role in keeping mutations around?

The answer to this question, said researchers at Stanford University Medical Center, appears to be chance. Their findings appear in the March online issue of the American Journal of Human Genetics and in the journal's April print edition.

Some disease mutations unusually common in Ashkenazi Jews, who make up 90 percent of the American Jewish population, include Tay-Sachs disease and some forms of breast cancer, high cholesterol and hemophilia. Four of these disorders, including Tay-Sachs disease, are in a class of diseases called lysosomal storage diseases. People with these disorders lack enzymes that break down toxins into harmless compounds. Instead, the toxins are stored in cellular compartments called lysosomes, where they can build up to high levels and eventually damage the cell.

"It's been known for a long time that Ashkenazi Jews have a high risk of these lysosomal storage diseases," said Neil Risch, PhD, professor of genetics, statistics, and health research and policy at the School of Medicine and one of the senior authors on the study. "The majority opinion has been that there must be some selective advantage for those mutations."

Researchers had suspected that lysosomal storage diseases may be similar to sickle cell anemia, in which people who carry two mutated copies of the gene have a disease, but those who inherit one copy of the mutation are protected against malaria. Those people - called carriers - are more likely to be healthy, have more children and pass their mutation on to future generations.

If carriers of lysosomal storage mutations were protected against other diseases, then those mutations should be more common in Ashkenazi Jewish populations than mutations that cause diseases unrelated to lysosomal storage. Risch and his colleagues analyzed DNA sequences from Ashkenazi Jewish people and compared how common mutations were in lysosomal storage disease genes vs. other disease genes.

The researchers found that mutations in lysosomal storage disease genes are no more common than mutations that cause other inherited diseases in the Ashkenazi Jewish population. This suggests that carriers for lysosomal storage mutations had no benefit over their peers. Instead, Risch said, these

mutations were probably present in the Jews who coalesced into the Ashkenazi Jewish population 900 years ago.

"The mutations that persisted represent whatever the people who had the most children happened to be carrying," Risch said. It just happened that those who founded the Ashkenazi Jewish population had disease mutations and passed them along to their children. Because Ashkenazi Jews tend to marry within their own population, those mutations remained common.

Risch also looked at the regional distribution of mutations in Ashkenazi Jews, and the age of those mutations. He found three points in time when mutations entered the population. One mutation has been in the Jewish population for 120 generations - around the time that the Jewish people formed a distinct population in the Middle East. This mutation causes a type of hemophilia called Factor 11 deficiency type II.

The majority of the mutations - including all of the mutations in lysosomal storage genes - entered the population when the Ashkenazi Jews formed a coherent group about 50 generations ago. The final mutations cropped up in the Lithuanian Ashkenazi Jews about 12 generations ago.

### **New UCLA Program To Study The Possible Environmental Causes Of Cancer**

Source: University Of California, Los Angeles, Health Sciences

Date: 2003-03-13

A new program at UCLA's Jonsson Cancer Center and the School of Public Health will seek to discover subtle variations in the human genetic blueprint that predispose some individuals to develop cancer after contact with environmental pollutants.

The program will explore, for example, why some individuals exposed to second-hand cigarette smoke develop lung cancer, while others do not. Bringing together the best environmental researchers and molecular biologists at UCLA, the program seeks to shed new light on how pollutants interact with genetics to cause a variety of cancers.

The \$1 million effort is being funded with a leadership gift from Pacific Palisades resident Art Alper, who made the donation in memory of his wife, Ann Fitzpatrick Alper, who died last year from complications of lung cancer. The Ann Fitzpatrick Alper Program in Environmental Genomics will be headed by Dr. Robert H. Schiestl, a professor of pathology, environmental health and radiation oncology.

"We'll investigate the molecular mechanism by which environmental agents such as air pollution, pesticides and radiation cause cancer and why a certain sub-population of people are more sensitive to these environmental exposures than the general population," Schiestl said. "With knowledge about the mechanism of this interaction between environmental exposure and genetic predisposition, it's our goal to develop improved biomarkers of exposure, to identify people at increased risk and to design nutritional and chemical interventions to counteract the development of cancer, especially in those with increased sensitivity."

The environmental genomics program will focus on six research projects that seek to:

\* Characterize genetically the effects of air pollution particles on the makeup of human cells. \* Understand the relationship of environmental exposures and a non-smoker's susceptibility to lung cancer. \* Identify the specific protein that prevents a cancer-causing enzyme from activating potent carcinogens found in smog, cooked foods and cigarette smoke. \* Investigate the molecular mechanism responsible for higher incidence of prostate cancer for men exposed to pesticides in California. \* Characterize genetically the molecular basis of hypersensitivity to radiation treatment in certain cancer patients. \* Characterize the mechanism that makes boron a dietary element that appears to prevent or reduce the risk of prostate cancer.

"This program promises to be a unique effort that we hope will unravel many of the mysteries surrounding the interaction of genes and environment in the development of cancer," said Judith C. Gasson, a scientist and director of UCLA's Jonsson Cancer Center. "This work will reflect Ann's passion for a safer environment along with her hope that future generations will not suffer the devastation of cancer."

Cancer occurs when changes in our genetic blueprint, or DNA, cause certain genes to become altered in cells, which then grow out of control. In some people, exposure to environmental pollutants may trigger these changes or genetic mutations.

"Before we had the new tools of the genome revolution, disease was considered to be either environmentally or genetically caused," said Linda Rosenstock, dean of the School of Public Health, who will oversee the new program. "But now we know that most diseases are the result of an interaction between genetics and the environment. At UCLA, we are fortunate to have the top scientific minds in both environmental research and molecular biology, which uniquely positions us to tackle these emerging issues."

Understanding the processes and genetic alterations involved in the development of various cancers has already resulted in targeted therapies that attack what is broken in cancer cells, leaving healthy tissues alone and resulting in less toxic treatments for patients. The same promise holds true for the environmental genomics program, Rosenstock said.

"Perhaps by understanding the genetic risks posed by environmental pollutants, we can tailor drugs to help prevent cancer," she said. "Or, more likely, we can try to control the environmental factors for those people at risk for cancer."

An environmental activist who drove a hybrid car, Ann Fitzpatrick Alper developed lung cancer although she had not smoked since she was a college student in the early 1950s. Smoking alone could have caused her cancer, or it may have been a combination of other environmental factors.

About 95 percent of the nearly 2.5 million Americans who will be diagnosed with cancer this year have no known genetic predisposition to the disease. Researchers believe these people develop malignancies due to complex interactions between their genes and their environment. If scientists can uncover the chemical and biological cascade that results in cancer, they can potentially stop the disease before it occurs. The goal is to discover what specific combination of an individual's genetics and factors such as diet, air pollution, exposure to tobacco, sensitivity to sunlight, etc., result in disease.

"The key to the future is to understand why certain people develop certain cancers," Rosenstock said. "Through this kind of research, merging environmental factors and molecular genetics, we may be able to find the answers."

Art Alper's gift is being augmented with a gift from the Kenneth Jonsson Family Foundation. UCLA's Jonsson Cancer Center Foundation is also augmenting the donation, bringing the gift to \$1 million.

Additional donations for the Ann Fitzpatrick Alper Program in Environmental Genomics may be sent to the Jonsson Cancer Center Foundation at 8-950 Factor Building, Box 951780, Los Angeles, CA, 90095-1780.

-UCLA-

For more information about UCLA's Jonsson Cancer Center, its people and resources, visit our web site at <http://www.cancer.mednet.ucla.edu>

### **Trends in Breast Cancer Incidence and Mortality**

Leslie A. Gaudette, Carol Silberberger, Chris A. Altmayer, Ru-Nie Gao\*

[www.statcan.ca/english/indepth/82-003/archive/1996/hrar1996008002s0a04.pdf](http://www.statcan.ca/english/indepth/82-003/archive/1996/hrar1996008002s0a04.pdf)

### Genetics Overview

DNA (deoxyribonucleic acid), a chemical found on cell chromosomes, is responsible for carrying genetic information. Chromosomes are threadlike structures present within the nuclei of cells. DNA's double helix structure allows the chromosomes to be replicated during cell division. Genes (segments of DNA) contain instructions for controlling when cells should grow, divide, and die. Certain genes called tumor suppressors slow down the process of cell division, causing cells to die.

Changes in DNA can sometimes cause normal cells to become cancerous by de-activating the tumor suppressor genes. Researchers are still investigating how and why some genes mutate but have discovered that inherited DNA changes may cause cancers to occur more frequently in some families. *However, most DNA mutations that cause breast cancer are not inherited; they occur during a woman's life and may be caused by a variety of factors (many still unknown to medical experts). These factors may include exposure to certain chemicals (such as Aldrin, Alachlor, and Acetamide), high dose radiation (from atomic bombs or from certain types of radiation therapy used to treat other cancers), other environmental exposures, diet, and smoking.*

BRCA1 (breast cancer gene 1) and BRCA2 (breast cancer gene 2) are two tumor suppressor genes that, when functioning normally, help repair damage to DNA (a process that also prevents tumor development). In 1994, researchers discovered that women who carry mutations of BRCA1 or BRCA2 are at higher risk of developing both breast and ovarian cancer than women who do not have these genetic mutations. Currently, women with BRCA1 mutations account for 5% of all breast cancer cases.

Dr. Sandhya Pruthi, MD, a Breast Health Specialist at the Mayo Clinic, estimates that 20% of women who carry BRCA1 mutations will develop breast cancer by age forty, 51% by age fifty, and 87% by age sixty.

*{Ed. Comment}*

*There is considerable research that appears to demonstrate that pollution can damage human DNA, resulting in cancer, including breast cancer. Damaged DNA is normally fixed by human immune repair processes and there appears to be a "susceptibility" factor involved i.e. some*



people may be more susceptible to contracting cancer than others. It is unclear whether increased susceptibility is due to a degrading of the repair process or an overwhelming of an otherwise normally functioning system i.e. one persons repair robustness may be less than another's. Given this, it may also be that the susceptibility factor(s) vary by race, ethnicity or inheritance. Thus, Jewish people may be more (or less) susceptible to air pollution carcinogens than, say, Hispanics, due to either immune system differences or thresholds of failure, or both. It is already well known that Ashkenazi Jews are particularly prone to mutations of the BRCA1/BRCA2 genes.

**Risk factors for breast cancer in women**

Factor	High-risk group	Low-risk group
<b>High relative risk (&gt; 4.0)</b>		
Age	Old	Young
Country of birth	North America, Northern Europe	Asia, Africa
Family history (mother and sister with breast cancer)	Yes	No
<b>Moderate relative risk (2.1-4.0)</b>		
History of cancer in one breast	Yes	No
Family history (mother or sister with breast cancer)	Yes	No
Biopsy - confirmed benign proliferative disease	Yes	No
Chest X-ray (moderate to high doses)	Yes	No
<b>Minor relative risk(1.1-2.0)</b>		
Socioeconomic status	High	Low
Marital status	Never-married	Ever-married
Place of residence	Urban	Rural
Religion	Jewish	Seventh-Day Adventist, Mormon
Age at first full-term pregnancy	≥ 30 years	<20 years
Age at menarche (first menstruation)	≤ 11 years	≥15 years
Age at menopause	≥ 55 years	<45 years
Obesity		
Breast cancer ≥ 50 years of age	Obese	Thin
Breast cancer < 50 years of age	Thin	Obese

Source: Adapted from Kelsey JL. Breast cancer epidemiology: Summary and future directions. *Epidemiologic Reviews* 1993; 15(1): 256-63.

Genetic testing of families with hereditary diseases is discussed in a letter in JAMA 276 (9 Oct. 1996). A letter criticizing the statement by Hubbard R, & Lewontin RC. (Pitfalls of genetic testing. NEJM 334 (1996), 1192-4), that "DNA tests cannot usually help clinicians or benefit patients" is in NEJM 335 (1996), 1235-7. It was in response to the doctors offering 185delAG testing in BRCA1 gene to Jewish people. They make a point that testing for a predisposition to cancer must not be restricted by self-interest to the research and bioethics communities. Uncertainty over the use of results of tests for BRCA1 and BRCA2, linked to hereditary breast and ovarian cancer, is raising questions, Science 274 (1996), 496-498; Nature Genetics 14 (1996), 185-7, 188-90; Lancet 348 (1996), 760, 965. There are now questions about whether Jewish women will be discriminated against in insurance in the USA, following the publication of genetic studies.

**Genetic makeup given larger role in some cancers  
Risk is seen for women no matter family history**

By Rick Weiss The Washington Post October 24, 2003

Women who inherit mutated versions of either of the two major genes linked to breast and

ovarian cancer face extremely high odds of getting one of those cancers even if there is no history of either disease in their families, according to a landmark study of cancer genetics.

The finding removes what scientists now say was a false sense of security among women who carry one of the gene mutations but have no cases of breast or ovarian cancer in their families. Based on previous studies that had analyzed the question differently, some doctors have been counseling such women that the cancer genes were less of a threat to them, perhaps because their genetic lineage conferred some compensatory protection.

The new findings, appearing in Friday's issue of the journal *Science*, lend support to the idea that most Ashkenazi Jewish women--an ethnic group in which 1 in 40 women carries the mutations--ought to get tested to see if they carry mutated versions of either gene, known as BRCA1 and BRCA2. Those who test positive, several researchers and doctors said, should seriously consider having their ovaries removed when they're finished having children.

That operation not only brings the risk of ovarian cancer down to about zero, but it also has been shown to reduce the incidence of breast cancer by about 50 percent.

For all the newfound potency of those cancer genes, however, the study also offers evidence of the powerful influence that non-genetic factors can have.

The study shows, for example, that moderate exercise and maintaining normal weight can significantly delay the onset of breast cancer, even in women who inherit the most dangerous mutations. *The report also finds an enormous increase in the risk of breast cancer in American women with the mutations who were born after 1940, as compared to those born with the same mutations before 1940. That suggests that changes in American women's environment or lifestyle have vastly increased the basic risk conferred by these genes.*

The positive side of that finding, said study leader Mary-Claire King of the University of Washington in Seattle, is that cancer risk could probably be lowered a lot if those factors were identified and reduced.

*"This suggests we need to be thinking more about interactions between genes and environment, even for mutations that have the very dramatic effects that these do," King said.*

The new findings come from a study that began with 1,008 Ashkenazi women diagnosed with breast cancer at a dozen cancer centers in the New York City area between 1996 and 2000. Among them, 104 tested positive for mutations in the BRCA1 or 2--the two genes most heavily implicated in breast and ovarian cancer. Ashkenazim, whose ancestry is European, represent the vast majority of U.S. Jews. They are ideal subjects in studies of breast and ovarian cancer genetics in part because they are about 20 times more likely than U.S. women overall to carry mutated versions of BRCA 1 or 2.

It was in cancer-prone Ashkenazi families that these genes were first discovered. While the average U.S. woman has about a 10 percent chance of getting breast cancer in her lifetime, the risk for women with BRCA mutations in those initial studies was about 80 percent.

But it was unclear whether other women harboring these mutations faced such steep risks, or whether that was true only for carriers who, like those in the first studies, also had multiple family members with breast or ovarian cancer. Indeed, some studies in recent years had suggested that carriers without such family histories might have only modest additional risk.

The new study improved on previous ones by conducting genetic tests on all of the patients' extended family members. It showed that fully half of all cancer patients with BRCA mutations had no history of ovarian or breast cancer in their family--simply because of chance events. In most cases, it was because the mutation was passed down silently through fathers, in whom it usually has no effects.

But regardless of family history, the study showed, all women bearing BRCA1 or 2 mutations have the same extremely high risks of developing breast cancer: 20 percent by age 40, 55 percent by age 60, and greater than

80 percent by age 80. For ovarian cancer, lifetime risk was 54 percent for mutations in BRCA1 and 23 percent for BRCA2, compared to a typical U.S. risk of less than 2 percent.

But genes are not destiny, the study also showed. Women whose lifestyles in their teens and 20s included moderate exercise pushed back by many years the onset of the disease. Avoiding obesity also helped substantially.

### GENERAL REFERENCE

Book:

Jewish Genetic Disorders: A Layman's Guide  
by Ernest L. Abel 2001

Geared to consumers, this superb guide clearly answers questions about genetic diseases common to the Jewish people. The outstanding writing and well-organized text combine to make difficult material accessible to a broad audience. Arranged in three sections, the book begins with an overview of the basics of genetics and genetic disease, followed by a chapter on how and why some diseases occur more often among the Ashkenazi, Sephardi, and Oriental Jewish populations. The largest section comprises a wealth of information about the specific genetic diseases, arranged by body system (e.g., gastrointestinal, central nervous system diseases), and the cancers. Additionally, a helpful glossary, a list of screening centers, and suggestions for further reading are provided. Abel (obstetrics/gynecology, Wayne State Univ.) shows great skill in weaving together sometimes heartbreaking facts with a gentle hand. Because of its well-written, current, and comprehensive coverage, this title would be exceptional even if there were tons of books on this topic (which there aren't). A first-choice selection for all consumer health and larger public library collections. Gail Hendler, NYU Medical Ctr. Lib., New York  
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Reference:

<http://www.mazornet.com/genetics/index.asp>

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Glossary of terms:

**Amniocentesis**

A procedure used for prenatal diagnosis. The amniocentesis procedure involves the insertion of a needle through the abdomen into the amniotic sac from which a small amount of amniotic fluid is obtained. Nowadays, the amniocentesis is performed while using ultrasound as guidance. The amniotic fluid, which includes the fetus' DNA, is used for testing. Amniocentesis is usually performed between 16 and 18 weeks of pregnancy.

**Cell Nucleus**

Inside the cell nucleus, 6 feet of DNA are packaged into 23 pairs of chromosomes (one chromosome in each pair coming from each parent).

**Chorionic Villus Sampling (CVS)**

A procedure used for prenatal diagnosis. The CVS procedure involves the insertion of a needle through the abdomen into fingerlike projections of the placenta which are called chorionic villi. This procedure is also performed while using ultrasound as guidance. The chorionic villi obtained is used for DNA testing. CVS is usually performed at 10 to 12 weeks of pregnancy.

### Chromosome

The structures found in the nucleus of the cell, called the chromosomes, contain genetic (inherited) information. Human cells contain 23 pairs of chromosomes, a total of 46 chromosomes. Twenty-two pairs of chromosomes are referred to as autosomes, since they do not determine the sex of an individual. The twenty-third pair is the sex chromosomes, generally referred to as the X and Y chromosomes. Each chromosome contains thousands of individual genes. These genes determine an individual's characteristics.

### Deoxyribonucleic Acid (DNA)

The DNA is the chemical sequence found in genes. These sequences allow for the transmission of inherited information from generation to generation.

### Enzyme

A substance that in small amounts increases the rate of a specific biochemical reaction is called the enzyme. Enzymes are usually required for the normal metabolism, or breakdown, of substances in the body.

### Gene

Each gene is a segment of double-stranded DNA that holds the recipe for making a specific molecule, usually a protein. These recipes are spelled out in varying sequences of the four chemical bases in DNA: adenine (A), thymine (T), guanine (G) and cytosine (C). The bases form interlocking pairs that can fit together in only one way: A pairs with T; G pairs with C.

### Human Cell

Each of the 100 trillion cells in the human body (except blood cells contains the entire human genome--all the genetic information necessary to build a human being. This information is encoded in 6 billion base pairs, subunits of DNA. (Egg and sperm cells each have half this amount of DNA.)

### Mutation

A mutation is a change in the sequence of DNA. Many mutations are "silent" and do not cause disease. When mutations occur in genes and disrupt the production of a functional protein, they may lead to genetic disease.

### Protein

Proteins, which are made up of amino acids, are the body's workhorses--essential components of all organs and chemical activities. Their function depends on their shapes, which are determined by the 50,000 to 100,000 genes in the cell nucleus.

#### Contact Information:

Center for the Study and Treatment of Jewish Genetic Diseases at the University of Pittsburgh Medical Center Health Systems

For information on testing call: Erin O'Rourke, M.S., Tel: 1-800-334—7980,  
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*\*The author of this report hopes that the information is useful to stimulation of pollution/health discussion within Jewish communities with resulting actions designed to better characterize current and future surrounding pollution environments and to enact any action plans to better the community environment.\**