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INTERFACE:
GENES AND THE ENVIRONMENT

CENTER FOR ENVIRONMENTAL GENETICS UNIVERSITY OF CINCINNATI Fall 1996

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Environmental Pollution and Child Health in Central and Eastern Europe

Central and Eastern Europe are facing enormous challenges today, in the aftermath of the collapse of the Soviet Union. Economic disruption and high levels of unemployment are widespread, during this period of transition from a highly-centralized economy to one of local autonomy. Public and environmental health problems are also widely scattered. Some countries--such as Poland and the Czech Republic--have well-educated populace and are making the transition more smoothly than other countries such as Bulgaria, Romania, Albania and Slovakia.

The World Health Organization (WHO) and several United States federal agencies (*i.e.* the National Institute of Environmental Health Sciences [NIEHS], the National Institutes of Health International Fogarty Center [IFC], the U.S. Environmental Protection Agency [EPA], and the U.S. Department of Energy [DOE]) are responding to the needs of these countries through sponsorship of a number of international workshops and exchange programs. For example, in May 1996 **Robert L. Bornschein** and **C. Scott Clark** (Department of Environmental Health, University of Cincinnati College of Medicine) participated in an international conference (held in Sosnowiec, Poland), entitled**:** "***Environmental Pollution and Child Health: Critical Needs and Issues for Central and Eastern Europe***." The goals of this NIEHS/WHO/IFC-sponsored conference were**: [a]** to provide scientists, physicians and other health professionals from Central and Eastern Europe with information to help them address their own environmental health problems; **[b]** to standardize data-collection methods; and **[c]** to foster collaborative research among scientists from Eastern and Central Europe and their counterparts in Western Europe and North America.

The May 1996 conference focused on**:** 1) lead exposure assessments and health effects, 2) air pollution, 3) birth malformations, 4) reproductive outcomes, and 5) childhood cancers and national cancer registries. This meeting has resulted in several initiatives at the **University of Cincinnati Department of Environmental Health** [UC Dept EH].

International outreach activities

The UC Dept EH has had a long-standing relationship with environmental health scientists in Poland and several other Central European countries. In the 1970's, for example, five junior and senior scientists from the **Nofer Institute of Occupational Medicine** (in Lodz, Poland) received advanced training in Occupational Medicine, Industrial Hygiene and Toxicology while studying in the UC Dept EH. Many of these individuals now hold prominent positions at the Nofer Institute, the WHO, and the **Institute of Occupational Medicine and Environmental Health** (IOMEH) in Sosnowiec, Poland. This latter Institute is now directed by **Jerzy Sokal**, a former Visiting Fellow at the University of Cincinnati.

The last 3 years have seen an increase in scientific exchanges between the UC Dept EH and the Institutes in Lodz and Sosnowiec. In 1994, **Eula Bingham**, **C. Scott Clark, Grace Lemasters** and **Jon Reid**--with support from the U.S. State Department and the U.S. EPA--offered a course in applied risk assessment at the Nofer Institute. **Clark**, **Reid** and **Rubin Mazon** from the UC Dept EH offered the course again at the Nofer Institute in July 1996. In addition, at the 3rd International Conference on Environmental Contaminations in Central and Eastern Europe, held in Warsaw, Poland (July 1996), **Mazon** presented a paper titled "A hazard-ranking system for developing countries." Moreover, **Reid** conducted a workshop on "Risk assess-

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ment and the application of Monte Carlo techniques in the field of exposure modeling" in Sosnowiec, Poland (September 1996). Professors **Bornschein** and **Bingham** have been members of our **Center for Environmental Genetics** (CEG) since its inception in June 1992.

Omer G. Berger, UC Professor of Clinical Pediatrics and Medical Director for the NIEHS-sponsored clinical trial of ***succimer*** (the new oral lead-chelating agent), traveled to Romania in October 1996. There, he met with pediatricians who have been treating children who have marked elevations in blood lead [average = 35 µg/dl, many greater than 50 µg/dl; 10 micrograms per deciliter is considered by the U.S. CDC to be dangerous]. These children live in the copper-smelting town of Zlatna. The town has no access to chelation therapy and, until recently, no lead-screening program or education about exposure-reduction techniques. Hopefully, the information provided by **Berger** will begin to improve this situation.

Professor **Klaus Willeke**, UC Dept EH Director of the Aerosol Research and Exposure Assessment Laboratory, has sponsored several Visiting Scientists and graduate students from Poland, Lithuania, and the Ukraine--during the last 7 years since the collapse of the Soviet Union. **Willeke** has also helped to set up a Western-style Ph.D. program in Lithuania and continues to serve on the thesis committees of graduate students in Lithuania.

Professor **Sokal**, Director of IOMEH, has begun sending a new generation of Visiting Scientists from Poland to the University of Cincinnati for advanced training in toxicology and occupational medicine. This will afford them the opportunity to become acquainted with recent developments in genetic toxicology and environmental genetics. Two physicians, both recent graduates of the IOMEH in Sosnowiec, will visit Cincinnati in the spring of 1997. They will receive additional training in the evaluation and treatment of lead-exposed children and occupationally-exposed workers. Professor **Sokal** and the UC Dept EH have signed a "Memorandum of Understanding," which will lay the groundwork for a Risk Assessment Summer School in 1998. This school will host scientists and risk managers who will be coming from locations throughout Central and Eastern Europe.

New UC courses being offered

The research and teaching activities of the **CEG faculty** in the international arena are part of a broader Department of Environmental Health and University of Cincinnati initiative. The University, with about 2,000 full-time faculty, currently has an enrollment of about 36,000 students. Approximately 1,300 foreign students--from more than 80 countries--attend classes at UC, many of them with support from Fulbright or other prestigious international awards. In a 1994 report issued by **Joseph A. Steger**, UC president, the ***Globalization Initiative*** was identified as one of five major focus areas for education, research and outreach at our institution. As a result, during the spring quarter of 1996, twenty-seven faculty received grants from the University to enhance teaching and research on international topics. For example, **Grace Lemasters**, our current CEG Deputy Director, received funds to facilitate the development of a new course on "Global epidemiology." Visiting scientists from Central Europe, and Central and South America will participate, along with UC medical and graduate students.

In the spring of 1997, Professors **Lemasters** and **Bornschein**--with the assistance of graduate students Tina Lawson and Tania Carreon--will offer their newly-developed course, titled "Global environmental epidemiology." This course is designed to**:** 1) increase the students' awareness of the role played by global differences in social, economic and genetic background in the expression of environmental diseases; 2) foster an appreciation of the differences in the practice of environmental epidemiology necessitated by international differences in available resources and political and ethical contexts; and 3) provide an overview of environmental medicine problems associated with specific exposures in selected countries.

Childhood lead (Pb^{++}) poisoning

The continued usage of lead in gasoline, the overuse and misuse of pesticides, the lack of proper emission controls, and the inappropriate disposal of hazardous wastes--place the population of Central and Eastern Europe at high risk for environmentally-induced diseases. This burden is not borne equally by all countries, or even by regions within a country.

Due to the presence of a well-trained scientific and medical community in **Poland**, more is known about the extent of the problems in this country than in most of the more heavily polluted countries of Eastern Europe. Within Poland, there is considerable variation in regional pollution levels. For example, nowhere in Poland is pollution more widespread than in the densely-populated urban area known as the **Upper Silesian Industrial Zone**. This region, located in South Central Poland, is home to 4 million people (10% of the total population of Poland). It is the most industrialized region in the country (75% of all heavy industry)--with extensive coal mining, numerous lead, zinc and copper mines, smelters, and several very large steel mills (Figure 1).

The impact of this intense, poorly-regulated industrialization is reflected in the blood lead levels of children living in the region. The prevalence of blood lead levels of 15 µg/dl or higher ranges from 16-27% near smelters, in contrast to a prevalence of 3% in non-urban areas. [In contrast, the prevalence is about 1% in a random sample of U.S. children aged 6-11 years old.] The elevated blood lead levels in children living in the Upper Silesian

Fig. 1. The Central and Eastern European countries described in the text. Upper Silesia is denoted by the *shaded area.*

Industrial Zone are the result of high ambient air lead levels [1.0-3.4 $\mu g/m^3$; most U.S. urban areas < 0.2 $\mu g/m^3$], high soil and dust lead concentrations [>1,000 ppm] and high levels of lead in food [daily intake is about 80 $\mu g\ Pb^{++}$/day; U.S. average dietary intake is <10 $\mu g\ Pb^{++}$/day].

Childhood asthma

There is also evidence that local air pollution is having an adverse impact on the respiratory health of children in the region. Approximately 20% of all sulfur dioxide, nitrogen dioxide and particulate emissions in Poland are concentrated in Upper Silesia--in an area that comprises about 2% of the total area of Poland. Since coal is the primary domestic heat and energy source, sulfur dioxide levels are highest during the winter and are associated with an increased frequency of asthma and reduced peak-expiratory-flow rates in children. The IOMEH in Sosnowiec has studies underway to assess the impact of long-term exposure to air pollution on the respiratory health of a cohort of 4,500 children from four communities in Poland.

It is important to note that--while there is ample evidence of environmental pollution in the region--other factors such as lifestyle, exercise, diet and smoking habits are undoubtedly also contributing to the poor health status of the population. Whereas chemical pollution is the predominant concern in Central Europe, there is the added problem in Eastern Europe of microbial pollution--due to poor (or nonexistent) treatment of sewage and drinking water.

Plans for the future

During the last year, Professors **Clark** and **Bornschein** have held several planning sessions with physicians and environmental health scientists in Upper Silesia. Plans have been outlined for an "exposure-interventions" trial--to be implemented in communities that are adjacent to a copper smelter which emits lead and arsenic pollution, and a lead/zinc smelter which produces lead, cadmium and zinc pollution (in addition to high levels of sulfur dioxide and particulate emissions). **Clark** and **Bornschein** are expecting to return to Poland in early 1997 in order to continue these planning sessions. We hope very much that techniques for reducing residential dust, which have been developed during the UC course of prospective studies (such as the NIEHS-sponsored Cincinnati Childhood Lead Study, the EPA-sponsored Cincinnati Soil Lead-Abatement Study, and the NIEHS-sponsored Treatment of Lead-Exposed Children), can be implemented successfully in the Upper Silesian Industrial Zone of South Central Poland, where 4 million people live.

---Contributed by Bob Bornschein, Scott Clark and Klaus Willeke

LETTERS TO THE EDITOR

RESPONSES TO VARIOUS QUESTIONS

Q **A recent article in the *Lexington Herald-Leader* describes the new revolution in genetic testing, but then discusses the "dark side" of this new revolution--*i.e.*, the fear that test results might be used to discriminate against people seeking insurance or employment. What is your Center doing to address these ethical issues?**

A *Because this has been a sufficiently frequently asked question, we have decided to devote the Lead Article of Issue #10 to this topic. We very much appreciate everyone's concerns on this subject.*

Q **First, the U.S. Pentagon says there is no evidence of any exposure to nerve gas during the 1991 Gulf War, then they say there might have been very low levels of exposure. And now John C. Bailar III (epidemiologist who chaired the National Academy of Science's Institute of**

Medicine Committee on the Gulf War Syndrome) says there is scant scientific evidence of any unique Gulf War Syndrome, that this was just a "stress syndrome" as the result of military combat. What can we believe?

A *The "Gulf War Syndrome" represents a collection of illnesses (chronic fatigue, joint pains, upper respiratory congestion, rashes and memory loss), affecting at least 1% of the Gulf War military population due to "unknown environmental agents"--possibly including nitrogen mustard or* ***sarin*** *nerve gas. Although the Pentagon and Department of Defense had steadfastly insisted that there is no evidence that U.S. soldiers were exposed to nerve gas during the Gulf War, there was the admission (end of September 1996) that more than 20,000 troops "might have been exposed" to low levels of toxic gas wafting over unprotected U.S. soldiers. Czech soldiers--whose sole responsibility was chemical detection--have repeatedly said they warned U.S. military commanders that sensitive detection equipment had identified Iraqi chemical weapons on the battlefield. The Pentagon has now conceded two specific events, when a U.S. unit blew up ammunition at the Kamisiyah weapons depot (Bunker 73) in southern Iraq on 4 March 1991 and then members of the 37th Engineers destroyed an unknown number of crates containing chemical rockets in a pit several miles south of Bunker 73 on March 10th. Can you imagine, being asked to serve as a scientist on a Gulf War Syndrome panel, where much of the information is regarded by the military as "classified" and therefore inaccessible to you--although you've been asked to provide your scientific opinion on the subject?*

*Although it had been known for decades that significant amounts of nerve agents (sufficient to cause near-immediate harm) are dangerous, "studies are now underway" to determine whether exposure to very low levels (just a few molecules for a few days) of such poisons can cause the chronic symptoms being seen 5 years later in these soldiers. The U.S. Government still maintains that it cannot explain "why some soldiers in a unit have become ill, and others have not, if they were all presumably exposed to the same low levels." Back in issue #1 we proposed a possible link between the Gulf War Syndrome and the human paraoxonase (****PON****) gene polymorphism (individuals having "high," "intermediate," or "low" enzyme activity for breaking down organophosphates). In issue #6 we described the work of M. Abou-Donia (Duke University) in which he suggested that the combination of dermal exposures to permethrin and N,N-diethyl-m-toluamide (DEET), plus high doses of oral pyridostigmine, might have led to a delayed toxic effect known as "organophosphate-induced delayed neurotoxicity" (OPIDN). In issue #8 we discussed C. Furlong's work from the University of Washington (Seattle), in which he shows direct evidence for the metabolism of* ***sarin*** *by human paraoxonase. The possibility--that* ***genetic differences*** *in the U.S. troops might account for the observation that some soldiers have become ill while others have not, given the same very low level of nerve agents--remains valid.*

The latest fascinating development (end of November) is that family members and other persons caring for Gulf War Syndrome patients have been reported as developing the same disease! This suggests strongly that a contageous (or infectious) might be involved. ***Mycoplasma*** *has now been cultured from the blood of almost half of Gulf War Syndrome patients tested, and this organism is known to be responsible for many of the above-mentioned symptoms seen in this syndrome. It is easily possible that Iraq included a mixture of chemical and microbial agents in their chemical rockets. Stay tuned as the mystery continues to unfold!*

COMMENT **In issue #2 we described the possible genetic differences in human toxicity and cancer caused by dioxin. But how prevalent is dioxin in the environment?**

Now a report has appeared [C. Clunies-Ross*et al.*, *Nature* 381: 379 (1996)], showing a significant increase in dioxin emissions when diesel fuels are made more "environmentally friendly." Diesel engine particulates (especially soot) can be controlled by inserting a ceramic "regenerative" trap, or filter, into the exhaust pipe. The filter is cleaned (or regenerated) when the carbonaceous deposits ignite and burn away. This is promoted by catalytically burning the deposits, the combustion of which is enhanced by adding an organic metal compound (such as one containing copper) to the fuel. These authors show, however, that particulate generation can be ameliorated by adding the copper compound to the diesel fuel--but at the expense of increased dioxin emissions (at least 6-fold increases at low load).

COMMENT **In previous issues we have discussed that both *BRCA1* and *BRCA2* genes together are responsible for probably the majority of early-onset hereditary breast and ovarian cancer. Moreover, *BRCA1* and *BRCA2* are two of a minimum of four or more genes that provide an increased risk of breast cancer. The function(s) of the BRCA1 and BRCA2 proteins still remain to be elucidated.**

Prostate-specific antigen (PSA) is a serine protease of the kallikrein gene family that is found in the female breast and in milk of lactating women. Women with PSA in their breast tumors live longer and relapse less frequently than women without PSA in their breast tumors [H. Yu *et al.*, *Cancer Res* 55: 2104-10 (1995)]. These results suggest that PSA and BRCA1--both regulated by steroid hormones--might interact as an enzyme-substrate pair for the release of peptides that are protective against the process of breast cancer [E.P. Diamandis, *Nature Genet* 13: 268 (1996)].

Back in issue #7 we mentioned the possibility that BRCA1 and BRCA2 might be members of the "granin" family (acid proteins that bind calcium and are involved in neuroendocrine and endocrine growth suppression). The human vs mouse BRCA1 granin consensus regions exhibit only 6 of 10 amino acids that are identical, however, while experimentally-proven granins are 100% conserved between species. This and other evidence [Nature Genet 13: 268-72 (1996)] has caused one laboratory (Baylor College of Medicine, Houston) to question seriously the granin hypothesis, whereas two other laboratories (Vanderbilt University, Nashville TN; University of Washington, Seattle) continue to support this likely function for BRCA1. The phenotype of the *Brca1(-/-)* knockout mouse is an embryonic lethal with neural tube defects, consistent with the BRCA1 granin function of growth suppression in neuroendocrine cells [L.C. Gowen *et al.*, *Nature Genet* 12: 191-94 (1996)].

The finding of a conserved domain shared by BRCA1, 53BP1 (a p53-binding protein), and RAD9 (a yeast cell cycle control protein)--suggests the possibility that BRCA1 might function in the cell's nucleus at one or more cell cycle checkpoints [E.V. Koonin *et al.*, *Nature Genet* 13: 266-67 (1996)]. The subcellular location of BRCA1 has been disputed in recent months, but this appears to be due to a problem with anti-BRCA1 antibody specificity and antibody-tagging experiments. Whereas one antibody is specific for BRCA1, another antibody recognizes the epidermal growth factor receptor (EGFR) as well as BRCA1 [*Nature Genet* 13: 264-65 (1996)]. An important breakthrough in understanding the true function(s) of BRCA1 and BRCA2 is expected at any moment.

COMMENT

In issue #7 we described the *Nature Genet* 12: 78-81 (1996) report that the "7-repeat" allele of the D4 dopamine receptor (*D4DR*) gene was associated with a "novelty-seeking personality"--as determined by answers given on the Tridimensional Personality Questionnaire (TPQ). However, studying 193 psychiatrically screened normal controls and 138 alcoholic offenders and assessed with the TPQ, A.K. Malhotra and coworkers [*Molec Psychiat* 1:388-91 (1996)] have found no such correlation--suggesting that this *D4DR* polymorphism as a candidate for genetic differences in personality variability may require re-evaluation.

Interestingly, researchers at the University of Toronto and the University of California at Irvine have reported that children having the attention-deficit hyperactivity disorder (ADHD) are more likely to have the "7-repeat" allele than healthy controls [G.J. LaHoste *et al.*, *Molec Psychiat* 1: 128-131 (1996)].

HAPPY BIRTHDAY TO YOU!!

The Human Genome Project (HPG) celebrated its ***6th anniversary*** on October 1996 as a federally funded effort in the United States. Many scientists thought that this effort was too "clerical," so routine, that they would never find a sufficient number of labs, postdoctoral fellows and graduate students interested in doing such "DNA sequencing" work. To everyone's surprise, however, the HGP has not only succeeding in satisfying all the skeptics but has gone far beyond all original expectations. Sequencing the human genome has already spawned the sequencing of other genomes (*e.g.* the baker's yeast *Saccharomyces cerevisiae* [***Trends Genet* 12:** 263-70 (1995)]; the eubacteria *Haemophilus influenzae* [***Science* 269:** 496-512 (1995)] and *Mycoplasma genitalium* [***J Bacteriol 177***: 3199-3204 (1996)]; and the archaebacterium *Methanococcus jannaschii* [***Science* 273:** 1058-72(1996)] have already been completed; and sequencing of the mouse genome [***Nature* 380:** 149-52 (1996)] is ahead of schedule).

The new technologies, available resources, and applications have increasingly become available to many diverse scientific fields--including cancer research, drug discovery, medical genetics, and environmental genetics. Many of these advances and promises are described in several recent reviews [***Genome Res* 6:** 771-72 and 773-80 (1996); ***Nature* 383:** 739-40 (1996); ***Am J Hum Genet* 59:** 764-71 (1996)]. Our Center for Environmental Genetics **(CEG)**, for example, began integrating closely with the HGP in early 1995, when we began using mouse and human DNA markers for quantitative trait loci (QTL) analysis of genes that affect environmental toxicity and cancer.

CEG Members in the News

Sohaib Khan was presented the STAR AWARD for his research in breast cancer by the Ohio Cancer Research Associates at a reception in the Westin Hotel, September 1996 (Cincinnati OH).

George Leikauf presented an invited lecture entitled ***"Air pollution and asthma"*** at the Meharry Medical College, Nashville, TN, October 1996. While he was there, Dr. Leikauf spoke with Dr. Vincent Nathan, Environmental Health Scientist, Department of Family and Preventive Medicine, regarding the design of a study to identify risk factors that are associated with increasing incidence of asthma among the African-American community. Dr. Leikauf also interacted with Dr. Daryl Hood who is investigating the effects of oxidant air pollutants on the structural biology of lung proteins.

Grace Lemasters is co-Principal Investigator of a grant entitled: "A study of changes in liquid dietary habits and the association with hormone levels of early pregnancy," which was funded by the National Coffee Association. She also presented a lecture, August 1996, to the HQ Air Force Medical Operations Environmental and Occupational Health Division, Andrews AFB (Maryland).

Dan Nebert has been invited by the Centers for Disease Control and Prevention (CDC) Task Force on Genetics in Public Health to participate in a small meeting (in Atlanta, Georgia) this winter on "***Translating advances in genetics into public health action.***"

Nancy Steinberg-Warren presented a workshop entitled ***"Human genetics: changing medicine, changing lives"*** to teachers at the Children's Hospital, July 1996 (Akron, OH). She also presented a workshop entitled ***"Inherited metabolic diseases: putting together the pieces of the puzzle"*** to dietitians and graduate students at the Children's Hospital Medical Center, September 1996 (Cincinnati, OH).

Glenn Talaska presented an invited lecture entitled ***"Chronic exposures, chronic effects: necessity for new approaches to BEI (biological exposure indices) development"*** November 1996 at the Asian Industrial Hygiene Conference, Institute for Occupational Health, Yonsei University School of Medicine (Seoul, Korea). He presented a seminar on ***"Surrogate and target tissues analysis of carcinogen-DNA adducts"*** at the National Center for Toxicological Research, October 1996 (Jefferson, AR).

JIGSAW PUZZLE GENE

Some children (and adults) enjoy and are greatly challenged by complicated jigsaw puzzles, whereas others are not. Is it genetic? Of course!

Kids with Williams syndrome are mentally retarded and cannot do spatial tasks such as jigsaw puzzles. They also exhibit other curious signs such as elfin facies, shortness of stature, fine bones and narrowed aorta. How can all these signs and symptoms be related?

In the 12 July 1996 issue of ***Cell***, the defective gene was shown to be ***LIM-kinase1***. Mice with this mutated kinase gene have specific problems with spatial learning. On human chromosome 7, the gene for elastin (important in making blood vessels, skin and lung tissue resilient) sits right next door to the gene for LIM-kinase1. It now appears that patients with Williams syndrome have defects in, or total deletion of, the ***elastin*** gene--in addition to defects in the ***LIM-kinase1*** gene. The extent of the elfin facies, shortness of stature, fine bones and narrowed aorta depends upon the severity of the ***elastin*** gene defect. Additional studies on families of Williams syndrome are being carried out to see if other nearby genes on chromosome 7 are also defective or missing.

CEG-SPONSORED SPEAKERS

Andrew J Henderson, Ph.D.
Postdoctoral Fellow, Department of Microbiology, College of Physicians and Surgeons,
Columbia University, NY, NY
OCTOBER 25, 1996 ***"C/EBP transcription factors are required for HIV-1 proviral induction and replication."***

Sri Prakash Srivastava, Ph.D.
Assistant Research Scientist, Department of Biological Chemistry, University of Michigan Medical School, Ann Arbor, MI
NOVEMBER 22, 1996 ***"Stress-induced signaling leading to apoptosis: role of an interferon-inducible, double-stranded RNA-dependent kinase (PKR)."***

Paul Rothman, M.D.
Director, Laboratory of Allergy and Inflammatory Lung Diseases, College of Physicians and Surgeons, Columbia University, NY, NY
DECEMBER 4, 1996 ***"Cytokine signaling during lymphocyte development."***

Ranjan Deka, Ph.D.
Department of Human Genetics, Graduate School of Public Health, University of Pittsburgh, PA
DECEMBER 16, 1996 ***"The unstable genome: dynamic mutations and evaluation of repeats with special reference to myotonic dystrophy.***

SCIENCE LITE

NEW SCIENTIFIC THEORIES STILL IN NEED OF PROVING THAT THEY MIGHT WORK

The following responses were received in a contest sponsored by ***OMNI*** magazine**:**

Grand Prize Winner

When a cat is dropped, it always lands on its feet. When toast is dropped, it always lands with the buttered side facing down. I propose ***to strap buttered toast to the back of a cat;*** the two will hover, spinning inches above the ground. With a giant buttered toast/cat array, a high-speed monorail could easily link New York with Chicago.

Runners-up

- If an infinite number of ***rednecks***, riding in an infinite number of ***pick-up trucks***, would fire an infinite number of ***shotgun rounds*** at an infinite number of ***highway signs***--they will eventually produce all of the world's great literary works in Braille.
- ***Why Yawning Is Contagious*:** You yawn in order to equalize the pressure on both sides of your eardrums. This pressure change outside your eardrums unbalances other people's eardrum pressures, so they must yawn in order to even things out.
- The earth may spin faster on its axis due to all the ***deforestation*** going on. Just as a figure skater's rate of spin increases when the arms are brought in close to the body, the cutting of tall trees may cause our planet to spin dangerously fast.

Honorable Mentions

- Birds take off at ***sunrise***. On the opposite side of the world, they are all landing at ***sunset***. This causes the earth to spin on its axis.
- The reason why ***hot-rod owners*** raise the backs of their cars is that it's easier to go faster when you're always going downhill.
- The quantity of consonants in the English language is constant. If omitted in one place, they turn up in another. For example, when a Bostonian "pahks" his "cah," the lost r's migrate southwest, causing a Texan to "warsh" his car and invest in "erl wells."

----Extracted from the Internet, with modifications.....

CLINTON DEPLOYS VOWELS TO BOSNIA

Cities of ***Sjlbvdnzv***, ***Grzny*** to Be First Recipients

Before an emergency joint session of Congress yesterday, President Clinton announced U.S. plans to deploy at least 75,000,000 vowels to the war-torn region of ***Bosnia***. This deployment, the largest of its kind in American history, will provide the region with the critically needed letters "A, E, I, O and U," and it is hoped to render countless Bosnian names more pronounceable.

"For 6 years, we have stood by--while names like '***Ygrjvslhv***' and '***Tzlynhr***' and '***Glrm***' have been horribly butchered by hundreds of newscasters around the world," Clinton said. "Today, the United States must finally stand up and say 'Enough!' It is time the people of Bosnia finally had some vowels in their incomprehensible words. The U.S. is therefore proud to lead the crusade in this noble endeavour."

This deployment, dubbed "Operation Vowel Storm" by the State Department, is set for early next week, with the Adriatic port cities of ***Sjlbvdnzv*** and ***Grzny*** slated to be the first recipients. Two C-130 transport planes, each carrying more than 500 24-count boxes of "E's," will fly from Andrews Air Force Base across the Atlantic and airdrop the letters over these two cities.

Citizens of ***Sjlbvdnzv*** and ***Grzny*** are eagerly awaiting the arrival of the vowels. "My God, I do not think we can last another day," ***Trszg Grzdnjkln***, 44, said. "I have six children and none of them has a name that is understandable to me or to anyone else. Mr. Clinton, please send my poor, wretched family just one 'E.' Please!"

Said ***Sjlbvdnzv*** resident ***Grg Hmphrs***, 67: "With just a few key letters, I could be George Humphries. This is my dream."

The airdrop represents the largest deployment of any letter to a foreign country since 1984. During the summer of that year, the U.S. shipped 92,000 consonants to ***Ethiopia***--providing for the first time cities like ***Ouaouoaua***, ***Eaoiiuae***, and ***Aao*** with vital, life-giving supplies of L's, S's and T's.

----Extracted from the Internet, with modifications.....

Observations by a Biologist

Autumnal colors and genetic predisposition?

As I sit here at my desk, staring out the window before me, I am noticing that the leaves of the maple trees in the front yard have changed from green to red, to gold, to brown and then have fallen off. Or have I, really? No! The largest tree in the middle goes from green to brilliant reddish-gold (absolutely breath-taking against the blue sky and bright sunshine), and then the leaves fall off. These leaves have almost all disappeared before the tree on the right turns from green to a reddish tinge; and these leaves fall much later--without going through any yellow or brown colors. The tree on the left is even more extraordinary (and the most difficult for us leaf-rakers), because it retains its green leaves well into mid-December and the leaves then fall--basically still green or with only a slightly yellowish-green color.

The same thing happened in autumn of 1995. The same thing happened in autumn of 1994, and in every previous year that I've lived here.

What is going on? Could it be that each tree is genetically programmed, relative to each surrounding tree, such that the leaves go through the same sequence of color changes and departure from the tree? Environmental factors (such as amount of sunshine, warm weather of an "Indian Summer," heavy rain, early frosts) undoubtedly swing the program from a few days earlier one year to a few days later the next year. But, here is yet another example of an interaction between genes and the environment.

WHO SHOULD REGULATE GENETIC TESTING?

THE U.S. FOOD AND DRUG ADMINISTRATION (FDA) IS PROPOSED

As discussed in the last issue of ***Interface***, at least two cloning companies have already begun to sell patented test kits for detecting the most common mutations in the ***BRCA1*** and ***BRCA2*** genes--known to be responsible for probably the majority of early-onset hereditary human breast cancer. This action is contrary to the recommendations by the American Society of Human Genetics, which feels that more data are needed before widespread commercial testing can be requested of the physician by the patient. ***Myriad Genetics*** (Salt Lake City, Utah) has already begun charging $2,400 for initial testing (full-sequence analysis of the ***BRCA1*** and ***BRCA2*** genes) and $395 for tests of each additional family member.

There are three major concerns about such commercialization of genetic testing. **[a]** Some tests might have a positive result, but this does not imply a high probability that the individual will develop the disease in question. **[b]** Some tests might have a negative result, but this does not imply a high probability that the individual will remain free from the disease. **[c]** Some tests are being developed for detecting mutations that predispose an individual to severe diseases (*e.g.* Alzheimer's disease, Huntington's disease) for which there is no known or accepted treatment. It is therefore likely that a federal agency will have to police such genetic testing.

A **Task Force on Genetic Testing**, sponsored jointly by the National Institutes of Health (NIH) and Department of Energy (DOE), has proposed that the **FDA** be responsible for federal regulation of such genetic testing. The FDA, on the other hand, is very reluctant to take on this role, because this agency does not have this kind of expertise at present. The final recommendations of the 15-member Task Force will be published in final form next March.

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